



Updated treatment targets in inflammatory bowel disease (STRIDE-III): an initiative of the International Organization for the Study of IBD

Dan Turner*, Amanda Ricciuto*, Shira Yuval Bar-Asher, Sudheer K Vuyyuru, Virginia Solitano, Nadine Bock, Maria Manuela Estevinho, Yuhong Yuan, Marietta Iacucci, Florian Rieder, Rupert W Leong, Walter Reinisch, Edward V Loftus Jr, Laurent Peyrin-Biroulet, Silvio Danese, Remo Panaccione, Takayuki Yamamoto, Stefan Schreiber, Marla Dubinsky, Vineet Ahuja, Charles N Bernstein, David T Rubin, Gerassimos J Mantzaris, Fernando Magro, Iris Dotan, Vipul Jairath, Axel Dignass*

Since Selecting Therapeutic Targets in Inflammatory Bowel Disease-II (STRIDE-II), new evidence has become available across inflammatory and patient-centred outcomes. We aimed to update the STRIDE recommendations for Crohn's disease and ulcerative colitis. We searched MEDLINE, Embase, and Cochrane CENTRAL for studies published after the STRIDE-II search period. Findings were integrated with surveys of International Organization for the Study of IBD (IOIBD) members and paediatric gastroenterologists from the Porto group of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition. Statements were subsequently voted on using a modified Delphi approach; consensus was defined as $\geq 75\%$ of participants rating a statement 7–10 on a 10-point scale. Of 13 071 records identified in the systematic review, 1018 were included. Surveys were completed by 60 of 79 IOIBD gastroenterologists and 23 of 30 paediatric gastroenterologists in the Porto group. STRIDE-III defines three conceptually distinct categories of treatment targets. Actionable targets include clinical response and remission, which reflect patient priorities, and objective inflammatory targets (C-reactive protein normalisation, faecal calprotectin within target range, and endoscopic remission), supported by interventional evidence demonstrating benefits of target-guided treatment modification. Adjunctive targets (ie, urgency, histological remission in ulcerative colitis, transmural remission in Crohn's disease, and growth) are supported by studies showing association with favourable outcomes and guide treatment optimisation and tighter monitoring but do not necessarily require a change in therapeutic class. Patient-centred targets (ie, disability, fatigue, and quality of life) directly reflect patients' well-being and are impaired in a substantial proportion of patients with inflammatory bowel disease; impairment should prompt assessment of inflammation and alternative causes and management through shared decision-making. Targets are further classified as immediate, short-term, intermediate, and long-term. STRIDE-III also defines treatment-specific times to target achievement, new faecal calprotectin thresholds, and adaptations for resource-limited settings. STRIDE-III distinguishes targets that should prompt treatment change from those that primarily guide optimisation and monitoring, while establishing a separate patient-centred pathway based on shared decision-making. This framework supports consistent, evidence-based treat-to-target care.

Introduction

The Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) initiative embodies the treat-to-target approach, which has transformed inflammatory bowel disease (IBD) management by shifting therapeutic decision-making beyond symptom control towards objective assessment and suppression of intestinal inflammation and patient-centred outcomes.^{1,2} This strategy aims to alter the natural history of IBD through sustained control of inflammation while preserving patients' well-being.

The initial STRIDE publication established clinical remission and endoscopic healing as the key therapeutic targets while recognising biomarkers as important tools for disease monitoring.¹ STRIDE-II expanded the framework by incorporating time-dependent treatment targets, biomarkers, patient-reported outcomes (PROs), and treatment timelines, acknowledging that optimal disease control requires sequential assessment across multiple inflammatory domains.²

Since publication of STRIDE-II in 2021, the evidence base has expanded substantially. Randomised controlled

trials, prospective cohorts, real-world studies, and target-guided treatment strategies have refined thresholds for clinical, biochemical, endoscopic, histologic, and transmural remission, improved understanding of multidimensional disease assessment, and provided treatment-specific insights for the timing of target achievement. Simultaneously, advances in intestinal ultrasound (IUS), cross-sectional imaging, histopathology, biomarkers, and validated new PROs have broadened opportunities for objective disease monitoring while increasing complexity.

Increasing evidence suggests that achieving deeper levels of remission, including histological remission, transmural remission, disease clearance, and composite endpoints, is associated with improved long-term outcomes. However, observational associations cannot differentiate whether suboptimal target attainment justifies treatment escalation, or if not reaching the target simply serves as a prognostic marker for inherently treatment-refractory disease. Demonstrating that a target is actionable requires treat-to-target intervention trials showing that target-guided treatment change improves

Lancet Gastroenterol Hepatol
2026

Published Online
October 19, 2026
[https://doi.org/10.1016/S2468-1253\(26\)00292-X](https://doi.org/10.1016/S2468-1253(26)00292-X)

*Contributed equally as senior authors

The Juliet Keidan Institute of Pediatric Gastroenterology, Hepatology and Nutrition, The Eisenberg R&D Authority, Shaare Zedek Medical Center, Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel (Prof D Turner MD, S Yuval Bar-Asher MD); Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Department of Pediatrics, University of Toronto, Toronto, ON, Canada (A Ricciuto MD); Division of Gastroenterology, Department of Medicine, Western University, London, ON, Canada (S K Vuyyuru MD, Y Yuan PhD, Prof V Jairath MD); Division of Gastroenterology and Gastrointestinal Endoscopy, IRCCS Ospedale San Raffaele, Università Vita-Salute San Raffaele, Milan, Italy (V Solitano MD, Prof S Danese MD); Department of Medicine I, Agaplesion Markus Hospital, Goethe University Frankfurt, Frankfurt, Germany (N Bock MD, Prof A Dignass MD); Department of Gastroenterology, Unidade Local de Saúde Gaia Espinho, Vila Nova de Gaia, Portugal (M M Estevinho MD); Department of Biomedicine, Unit of Pharmacology and Therapeutics, Faculty of Medicine, University of Porto, Porto, Portugal (M M Estevinho); Department of Medicine and Health, University College Cork, Cork, Ireland (Prof M Iacucci MD);

Department of Gastroenterology, Hepatology and Nutrition, Digestive Diseases Institute, Cleveland Clinic, Cleveland, OH, USA (Prof F Rieder MD); Department of Gastroenterology, Concord Repatriation General Hospital, and Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia (Prof R W Leong MD); Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria (Prof W Reinisch MD); Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine and Science, Rochester, MN, USA (Prof E V Loftus Jr MD); Northwestern Medicine, Digestive Health Institute, Chicago, IL, USA (Prof L Peyrin-Biroulet MD); Division of Gastroenterology and Hepatology, Department of Medicine, University of Calgary, Calgary, AB, Canada (Prof R Panaccione MD); IBD Center, Yokkaichi Hazu

subsequent disease outcomes with an acceptable number needed to treat.

Using systematic literature reviews and international expert surveys, STRIDE-III integrates evidence from studies in adult and paediatric Crohn's disease and ulcerative colitis to update treatment targets, define evidence-based threshold values, and provide guidance on multidimensional disease assessment and practical treatment timelines. Rather than increasing the number of therapeutic goals, STRIDE-III establishes a pragmatic clinical framework that differentiates actionable treatment targets that should drive therapeutic change, from those that should primarily guide optimisation of disease management.

Methods

A flow diagram outlining the STRIDE-III development process is shown in figure 1. A steering committee comprising six International Organization for the Study of Inflammatory Bowel Disease (IOIBD) members (DT, AD, VJ, ID, FM, and DTR) defined the scope and formulated the review questions. The systematic review covered publications from July 1, 2019, the end of the STRIDE-II review period, through April 18, 2025. Evidence included in the STRIDE-II review was also retained and considered when formulating the

STRIDE-III recommendations.² MEDLINE, Embase, and Cochrane CENTRAL were searched through Ovid using controlled terms (MeSH and Emtree) and free-text related to IBD, treatment targets, and relevant outcomes, as detailed in the systematic reviews in Crohn's disease³ and ulcerative colitis.⁴ In general, the search strategy was aligned with the one used for STRIDE-I and STRIDE-II. The review examined clinical, biochemical, endoscopic, histological, imaging, PRO, and composite targets in both ulcerative colitis and Crohn's disease, consistent with those selected in the previous STRIDE manuscripts. Two of seven reviewers screened all abstracts, and potentially eligible studies were retrieved in full text. Summary tables tabulated the targets used, cutoff values for response, remission, and prediction of subsequent outcomes, as well as the time elapsed to reach the targets in the different studies, accompanied by support text drafted by the working groups. Pertinent selective manuscripts published after the systematic review date were included as relevant.

In parallel, a structured REDCap survey was distributed to all IOIBD members and to members of the Paediatric IBD Porto Group of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN). Respondents were asked to identify the most appropriate treatment targets for assessing adult and paediatric ulcerative colitis and Crohn's disease in clinical practice and to specify the optimal cutoff for target achievement. Paediatric instruments and endpoints were evaluated exclusively by paediatric gastroenterologists. The survey was used to refine the candidate targets and to integrate expert clinical judgement with the findings of the systematic review. Respondents also estimated the typical number of weeks after treatment initiation required to expect clinical response, clinical remission, and biomarker remission. These estimates derived from clinical experience were used to contextualise the treatment-specific time-to-target data identified in the systematic review. Endoscopic, transmural, and histological targets were not included in the time-to-target assessment because their apparent timing is largely determined by protocol-specified assessment schedules rather than the true time of target achievement. Two face-to-face meetings were held to discuss the concepts: one at the initiation of the project (Auckland, New Zealand) and one after completion of the systematic reviews and before formulation of the statements (Porto, Portugal).

Based on the above, consensus statements were drafted by the steering committee and then distributed to all IOIBD members for online voting. Where several tools or thresholds were supported by the systematic review and the survey, the steering committee selected the option considered most consistent with the totality of evidence and most feasible for routine practice. Paediatric recommendations were informed by paediatric-specific evidence and responses from the Porto group. Consistent

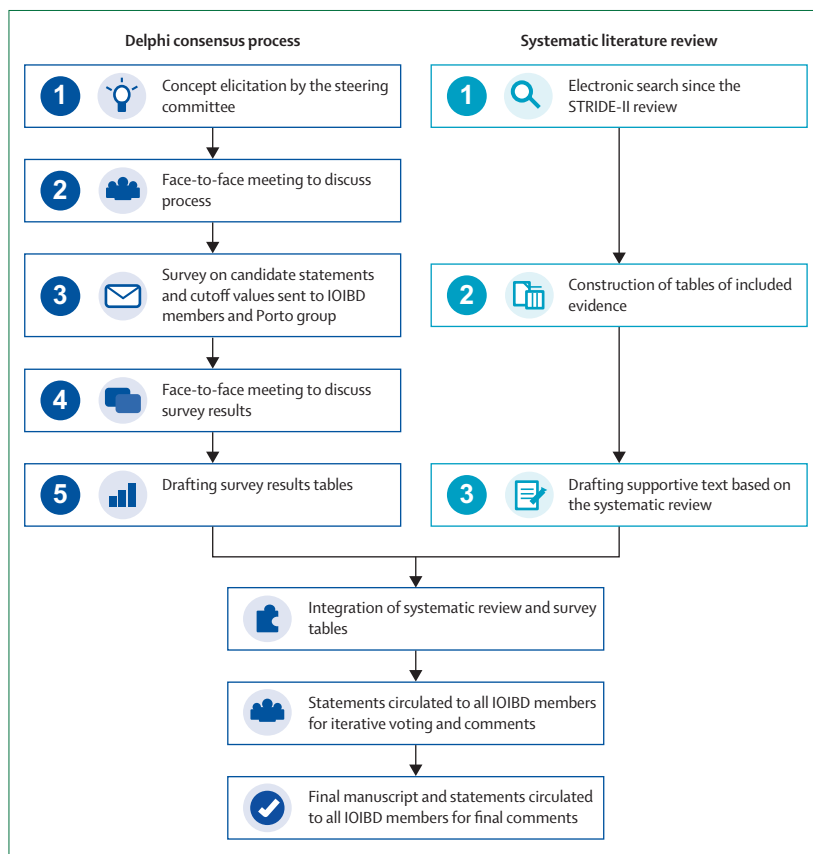


Figure 1: Methodological framework for developing STRIDE-III

	Definition	Explore adherence and alternative causes*	Optimise treatment and tighten monitoring†	Change treatment‡	Targets
Actionable targets	Targets supported by treat-to-target trials in either Crohn's disease or ulcerative colitis showing benefit from target-guided treatment modification	Yes	Yes	Yes, after adequate optimisation	Clinical response and remission, endoscopic remission, reduction of CRP and FC to target threshold
Adjunctive targets	Targets consistently associated with favourable outcomes, but without convincing treat-to-target evidence	Yes	Yes	Not only on the basis of this target being unmet	CRP and FC response, urgency, growth, histology in ulcerative colitis, transmural remission in Crohn's disease
Patient-centred targets	Outcomes directly reflecting patients' well-being, and clearly associated with IBD	Yes	Only if objective inflammation is present	Shared decision-making with the patient	Quality of life, disability, fatigue

CRP=C-reactive protein. FC=faecal calprotectin. IBD=inflammatory bowel disease. *Confirm adherence and reconsider differential diagnosis (eg, infection, medication adverse events, coeliac and other diseases and functional symptoms). †Improve the current strategy through adherence assessment, dose/interval adjustment, therapeutic drug monitoring where appropriate, and adjunctive nutritional or concomitant therapy; schedule tighter monitoring with early reassessments. For patient-centred targets, anti-inflammatory optimisation applies only when residual inflammation is present; otherwise address non-inflammatory contributors with targeted, often multidisciplinary care. ‡For actionable inflammatory targets, failure should generally prompt switch to, or add, a therapy with a different mechanism of action after adequate optimisation. An adjunctive target should not, by itself, trigger a treatment change. For patient-centred targets, decide together with the patient, considering inflammation, adverse effects, treatment burden, alternative causes, and the patient's priorities.

Table 1: Conceptual classification of STRIDE-III treatment targets

with the modified Delphi methodology in STRIDE and STRIDE-II, voting agreement was considered achieved if at least 75% of participants scored the statement as 7–10 on a 10-point rating scale (1: do not agree at all, 10: agree completely).

Definitions

STRIDE-III introduces three conceptually distinct categories of treatment targets (table 1, figure 2).

Actionable targets are supported by clinical trials showing improved long-term outcomes after target-guided treatment modification, with a clinically meaningful benefit and acceptable benefit-to-risk profile; failure to achieve them should generally prompt a change in therapy after adequate optimisation. In ulcerative colitis, given the limited trial evidence, the steering committee considered a target actionable also when supported by an appropriate treat-to-target trial in Crohn's disease, provided that its association with disease outcomes was supported by a substantial body of evidence in ulcerative colitis and endorsed through the IOIBD survey and formal voting. Additionally, symptom-based outcomes were designated actionable a priori in both diseases as patient priorities.

Adjunctive targets are supported by consistent observational studies demonstrating association with favourable outcomes but lack treat-to-target trials showing their benefit over the established actionable targets; if unmet they can guide treatment optimisation and tighter monitoring, but do not necessarily require switching to a different treatment class.

Patient-centred targets directly reflect patients' well-being and are impaired in a substantial proportion of patients with IBD; impairment should prompt assessment of inflammation and shared decision-making management guided by the severity of the condition, underlying aetiology, inflammatory activity, treatment

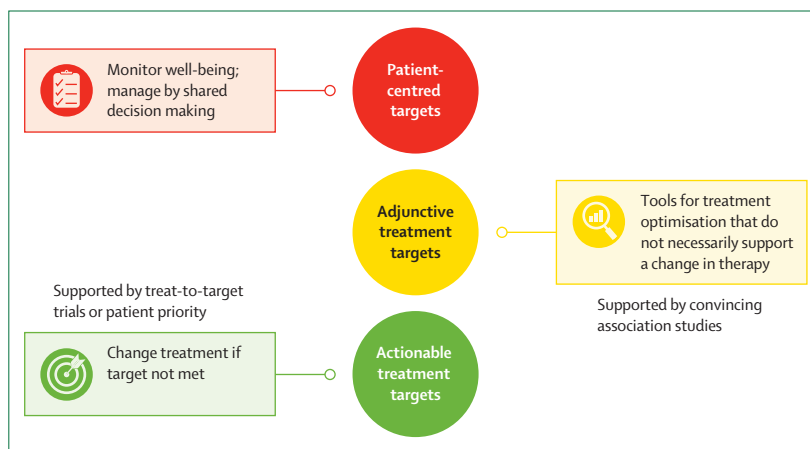


Figure 2: STRIDE-III treatment target concepts

burden, and patient preferences. This framework aligns the strength of clinical recommendations with the strength of available evidence while accommodating the increasing complexity of personalised medicine in IBD.

Tools for measuring the targets were prioritised according to their feasibility for routine clinical practice rather than their suitability as endpoints in clinical trials. The latter was beyond the scope of STRIDE-III and is addressed elsewhere.⁵ Definitions of response emphasised improvement from baseline rather than the absolute thresholds commonly used in clinical trials, where patients are typically enrolled with moderate-to-severe disease activity and residual mild activity might therefore still represent a meaningful response. In a survey conducted as part of this initiative, IOIBD members preferred the term transmural remission over radiologic remission, because IUS is not considered a radiologic examination in some countries. Transmural

Medical Center, Yokkaichi, Japan (T Yamamoto MD); Department of Internal Medicine I and Institute of Clinical Molecular Biology, University Hospital Schleswig-Holstein and Kiel University, Kiel, Germany (Prof S Schreiber MD); Susan and Leonard Feinstein IBD Clinical Center, Icahn School of Medicine at Mount Sinai, New York, NY, USA (Prof M Dubinsky MD); Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, India (Prof V Ahuja MD); University of Manitoba IBD Clinical and Research Centre, Max Rady College of Medicine, University of

Manitoba, Winnipeg, MB, Canada (Prof C N Bernstein MD); Inflammatory Bowel Disease Center, University of Chicago Medicine, Chicago, IL, USA (Prof D T Rubin MD); Department of Gastroenterology, Medical Center of Athens, Athens, Greece (G J Mantzaris MD); Department of Gastroenterology, University Hospital of São João, Porto, Portugal (Prof F Magro MD); Division of Gastroenterology, Rabin Medical Center, Petah Tikva, and Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv, Israel (Prof I Dotan MD)

Correspondence to: Prof Axel Dignass, Department of Medicine I, Agaplesion Markus Hospital, Goethe University Frankfurt, Wilhelm-Epstein-Strasse 4, 60431 Frankfurt am Main, Germany axel.dignass@agaplesion.de

	Met	Partly met, limited, or conflicting	Not demonstrated		
	Causal evidence		Accuracy and prognostic evidence	Consensus	
	Treat-to-target trial Randomised escalation to the target in this disease		Observational Accuracy, association with outcomes, value beyond endoscopy	Certainty Treating to the target improves outcomes	STRIDE-III position Category and basis of the position
Crohn's disease					
Clinical response and remission	REACT: primary endpoint not met, secondary composite positive*	Poor proxy for inflammation; mostly at high risk of bias	Very low Trial very low Observational very low	Actionable Basis: consensus, patient priority	
Faecal calprotectin and CRP	CALM: primary endpoint met†	Accurate for inflammation; associated with later outcomes	Moderate Trial moderate Observational moderate	Actionable Basis: direct trial, observational data	
Endoscopic remission	CURE-CD: primary endpoint met, STARDUST null‡	Reference standard; strongest prognostic signal	Moderate Trial low Observational moderate	Actionable Basis: observational data, trial (lower certainty)	
Histological remission	No trial	Mixed findings; few studies beyond endoscopy	Very low No trial Observational very low	Not a target Basis: consensus, evidence mixed	
Transmural remission	No trial (VECTORS ongoing)	Accurate, consistently associated, also beyond endoscopy	Low No trial Observational low	Adjunctive Basis: observational, no trial	
Ulcerative colitis					
Clinical response and remission	VERDICT: inferior to endoscopic targets§	Moderate proxy for inflammation; consistently associated	Moderate Trial moderate Observational low	Actionable Basis: consensus, patient priority	
Faecal calprotectin and CRP	OPTIMISE, DEAR, Lasson: benefit not established¶	Accurate for inflammation; strong observational evidence	Moderate Trial very low Observational moderate	Actionable Basis: consensus, observational data, Crohn's disease extrapolation	
Endoscopic remission	VERDICT: superior to symptomatic remission (MES 0–1)§	Mostly associated with outcomes; association strongest at MES=0	Moderate Trial moderate Observational low	Actionable Basis: consensus, VERDICT, observational (though low)	
Histological remission	VERDICT: not superior to endoscopic remission (MES 0–1)§	Associated with outcomes; adds value mainly within MES ≤1	Moderate Trial moderate Observational low	Adjunctive Basis: observational, VERDICT, no gain beyond endoscopy	
Transmural remission	No trial	Accurate for inflammation; few prognostic studies	Very low No trial Observational very low	Not a target Basis: expert opinion, small evidence base	

Figure 3: Evidence base, certainty of evidence, and consensus position for each STRIDE-III treatment target in adults

Patient-centred targets, bowel urgency, growth, and composite targets were not graded and are not shown. CRP=C-reactive protein. MES=Mayo endoscopic subscore. *REACT did not meet its primary endpoint but reduced a prespecified secondary composite. †CALM escalated on faecal calprotectin or CRP with clinical criteria, so its evidence applies to the pair. ‡STARDUST assessed endoscopy once, at week 16, with escalation limited to more frequent ustekinumab dosing, so it was treated as an indirect test and CURE-CD set the interventional grade. §VERDICT compared symptomatic remission alone with symptomatic plus endoscopic remission (MES ≤1), with or without histological remission. ¶OPTIMISE and Lasso did not achieve their primary endpoints; DEAR achieved a primary endpoint that contained the target with no difference in relapse; all three were graded very low, so the ulcerative colitis biomarker grade rests on observational evidence.

response and remission refer herein to findings assessed by cross-sectional imaging, irrespective of endoscopic findings.

Treatment optimisation refers to measures intended to improve the effectiveness of the current therapeutic

strategy without replacing its principal mechanism (including confirmation of adherence, dose or interval adjustment, therapeutic drug monitoring [TDM] when relevant, and addition of nutritional or other concurrent therapy). Treatment change refers to replacing the

current therapeutic strategy or adding a therapy with a different mechanism of action when disease activity remains inadequately controlled despite appropriate optimisation.

Findings

The systematic reviews supporting the STRIDE-III statements are presented in the two companion manuscripts with detailed methods, results, and PRISMA flow diagrams.^{3,4} The reviews also graded, for each target, the certainty that treating to that target improves outcomes, using risk-of-bias assessments and a framework in which interventional and observational evidence were evaluated separately; these grades are presented alongside the voting results in figure 3. The reviews assessed the evidence supporting the inclusion of specific targets in IBD and summarised the instruments used to measure them, the most widely applied thresholds for response and remission, potential cutoffs of various targets for predicting future outcomes and the estimated time required to achieve

specific targets with different therapeutic interventions (appendix pp 1–5). Briefly, the database search identified 13 071 unique records. Of these, 10 811 were excluded during title and abstract screening; the remaining 2260 reports underwent full-text review, of which 1242 were excluded, resulting in 1018 studies included for the STRIDE-III synthesis. In total, 462 focused exclusively on Crohn's disease, 335 on ulcerative colitis, and 221 included mixed populations, yielding 683 Crohn's disease-relevant and 556 ulcerative colitis-relevant studies.

60 (76%) of 79 IOIBD gastroenterologists and 23 (77%) of 30 paediatric gastroenterologists from the Porto group completed the survey (figure 1; appendix pp 6–7). Overall, substantial agreement was observed across most clinical, endoscopic, and biomarker domains regarding the preferred assessment tools. For clarity, only tools and thresholds selected by at least 20% of respondents are tabulated in the appendix (pp 6–7). This threshold was used to limit presentation to the more commonly selected survey responses and did not represent a definition of

See Online for appendix

	Crohn's disease	Ulcerative colitis
Clinical disease activity	Adults: HBI (remission: <5; response: ≥Δ3, ≥Δ50%) Children: wPCDAI (remission: <12.5; response: ≥Δ17.5)	Adults: partial Mayo score (remission: ≤1 and rectal bleeding=0; response: ≥Δ30%, ≥Δ2 with either rectal bleeding decrease of ≥Δ1 or rectal bleeding score of ≤1) Children: PUCAI (remission: <10; response: ≥Δ20)
Patient-reported outcome remission	Adults: PRO2 (remission: abdominal pain ≤1 and stool frequency ≤3; alternatively, abdominal pain=0 and stool frequency=0; response: ≥Δ50%) Children: TUMMY-CD (in development)	Adults: PRO2 (remission: rectal bleeding=0 and stool frequency ≤1; response: ≥Δ50%); Urgency numeric rating scale (≤2) Children: TUMMY-UC (remission: <9; response: ≥Δ10)
Faecal calprotectin (μg/g)*	Acceptable range: <200 μg/g for low inflammation or <100 μg/g for transmural remission (mean value in the survey 196 [SD 49] μg/g and 100 [38] μg/g, respectively); 100–200 μg/g grey zone Response: ≥Δ50%	Acceptable range: <200 μg/g for low inflammation or <100 μg/g for histological remission (mean value in the survey 135 [44] μg/g and 100 [38] μg/g, respectively); 100–200 μg/g grey zone Response: ≥Δ50%
Composite of biologic remission	Adults: CRP within normal limits* and faecal calprotectin <200 μg/g Children: MINI index (<8)	CRP within normal limits* and faecal calprotectin <200 μg/g
Endoscopic remission	Ileocolonoscopy: SES-CD (remission: ≤2; response: ≥Δ50%) Capsule endoscopy: Lewis score (remission: <135; response: ≥Δ50%)	Ileocolonoscopy: Mayo endoscopic subscore (remission: 0; response: ≥Δ1 point)
Transmural healing	Adults: MRI—MaRIA (remission: <7; response: ≥Δ25%); sMaRIA (remission: <1; response: ≥Δ50%) IUS—remission: BWT ≤3 mm and Limberg or CDS 0; response: ≥Δ25% decrease in BWT and ≥Δ1 in Limberg or CDS score Children: MRI—PICMI (remission: ≤10; response: >Δ20) IUS—remission: BWT ≤2.5 mm in small bowel and <3 mm in colon and Limberg or CDS 0; response: as in adults	IUS—remission: BWT ≤3 mm and Limberg or CDS=0 in all segments; response: Δ≥25% in BWT and Limberg or CDS score Δ≥1
Histological activity	Absence of neutrophils in epithelium and lamina propria, erosions, or ulcers; NHI (remission: ≤1; response: ≥Δ1)	Absence of neutrophils in epithelium and lamina propria, erosions, or ulcers; NHI (remission: ≤1; response: ≥Δ1)
Quality of life	Adults: Short IBDQ (remission: ≥50; response: ≥Δ9 points) Children: IMPACT-III (remission: ≥143; response: none defined)	Adults: Short IBDQ (remission: ≥50; response: ≥Δ9 points) Children: IMPACT-III (remission: ≥143; response: none defined)
Fatigue	Adults: IBD-F (no fatigue: Section-1 <7.5) Children: PIFI or non-paediatric IBD-specific tools as some items are from IMPACT-III or PROMIS-pediatric	Adults: IBD-F (no fatigue: Section-1 <7.5) Children: PIFI or non-paediatric IBD-specific tools as some items are from IMPACT-III or PROMIS-pediatric
Disability	Adults: IBD-DI (no disability: 0–20) Children: PIDI or non-paediatric IBD-specific tools as some items are from IMPACT-III	Adults: IBD-DI (no disability: 0–20) Children: PIDI or non-paediatric IBD-specific tools as some items are from IMPACT-III

Recommended tools and cutoff values were determined based on a combination of evidence from the systematic review, survey responses from IOIBD members, and steering committee consensus, prioritising measures with the strongest support for clinical feasibility and consistency across settings. BWT=bowel wall thickness. CDS=colour Doppler signal. HBI=Harvey–Bradshaw Index. IBD-DI=IBD Disability Index. IBD-F=IBD Fatigue Index. IBDQ=Inflammatory Bowel Disease Questionnaire. IOIBD=International Organization for the Study of IBD. IUS=intestinal ultrasound. MaRIA=Magnetic Resonance Index of Activity. MINI=Mucosal Inflammation Non-Invasive. NHI=Nancy histological index. PICMI=Pediatric Inflammatory Crohn's Magnetic Resonance Enterography Index. PIDI=Pediatric IBD Disability Index. PIFI=Pediatric IBD Fatigue Index. PROMIS=Patient-Reported Outcomes Measurement Information System. PRO2=Patient-Reported Outcome 2. PUCAI=Pediatric Ulcerative Colitis Activity Index. SES-CD=Simplified Endoscopic Score for Crohn's Disease. sMaRIA=simplified Magnetic Resonance Index of Activity. wPCDAI=weighted Pediatric Crohn's Disease Activity Index. *Serial faecal calprotectin assessment is essential given its modest test-retest reliability and mildly elevated CRP less than twice the upper normal limit of the respective test system should be interpreted on an individual basis.

Table 2: STRIDE-III recommended measurement tools for assessing treatment targets in Crohn's disease and ulcerative colitis in clinical practice

consensus. The survey findings were broadly consistent with the assessment tools and cutoff values identified in the systematic review (appendix pp 1–5). Likewise, the survey-based estimates of the time required to achieve each target were also generally aligned with the ranges proposed by the steering committee based on the systematic review. Nevertheless, the considerable variability

among respondents indicates that these timelines should be regarded as pragmatic clinical guidance rather than fixed treatment targets (appendix pp 8–9).^{3,4}

Finally, the steering committee integrated these findings with the survey results to select the final STRIDE-III tools and thresholds that were subsequently included in the consensus statements (table 2), as well as the time required to achieve the targets (figure 4). These integrated findings informed the development of the consensus statements, which were subsequently voted on by 60 IOIBD members (table 3).

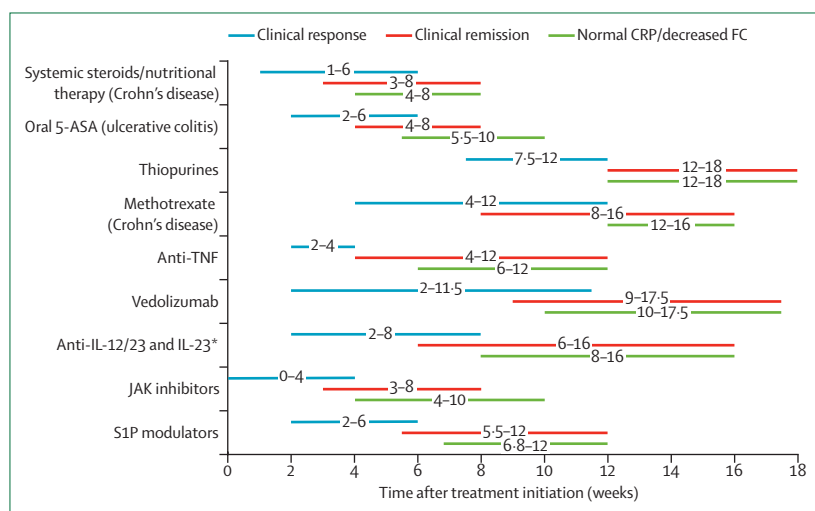


Figure 4: Estimated time to achieving targets for Crohn's disease and ulcerative colitis by treatment type
Estimated minimum and maximum times from the systematic review and survey, with further minor adaptation made by the steering committee. The figure should be interpreted as providing rough estimates only. Decreased FC to below a desired threshold outlined in the text and table 2. 5-ASA=5-aminosalicylic acid. CRP=C-reactive protein. FC=faecal calprotectin. *IL-23 might act somewhat faster than IL-12/23 regimens.

Clinical response and remission

Rapid relief of symptoms is the highest priority for both patients and clinicians, and therefore serves as an immediate actionable target, preceding the achievement of any other.

The Crohn's Disease Activity Index (CDAI) and the highly correlated Harvey–Bradshaw Index (HBI)⁶ remain the most widely used indices in clinical trials of adults with Crohn's disease. In paediatric Crohn's disease, the Pediatric CDAI (PCDAI) and the weighted PCDAI (wPCDAI) are the standard reference indices, with the wPCDAI demonstrating somewhat better performance while being easier to complete.^{7,8} However, clinical symptoms alone are insufficient as a standalone treatment target, as their correlation with objective markers of inflammation is modest.⁹ This reinforces the STRIDE-III emphasis on multimodal assessment to enhance the likelihood of sustained disease control.

	Voting results	
	Strength of recommendation†	% votes 7–10
Immediate treatment targets (<1–2 months, depending on the type of intervention)		
Clinical response is an immediate actionable target. Consider changing treatment if this target has not been achieved despite optimised dosing*	8.8	93%
Clinical response in Crohn's disease should be measured by PRO2 (≥Δ50%), HBI (≥Δ50%) or, in children, wPCDAI (≥Δ17.5)	8.4	87%
Clinical response in ulcerative colitis should be measured by PRO2 (≥Δ50% and either rectal bleeding decrease by ≥1 or rectal bleeding score ≤1), PMS (≥Δ30%), and, in children, PUCAI (≥Δ20) or TUMMY-UC (≥Δ10)	8.8	90%
Short-term treatment targets (2–3 months, depending on the type of intervention)		
Clinical remission is a short-term actionable target. Consider changing treatment if this target has not been achieved despite optimised dosing*	8.6	85%
Clinical remission in Crohn's disease should be measured by PRO2 (abdominal pain ≤1 and stool frequency ≤3), HBI (<5), and, in children, wPCDAI (<12.5)	8.6	87%
Clinical remission in ulcerative colitis should be measured by PRO2 (rectal bleeding=0 and stool frequency ≤1), PMS (≤1 and rectal bleeding=0) or, in children, PUCAI (<10) or TUMMY-UC (<9)	9.0	92%
Resolution of urgency (defined as a 10-point NRS ≤2 in both Crohn's disease and ulcerative colitis) is an adjunctive short-term target. Consider optimising current treatment if this has not been achieved*	8.2	85%
Intermediate-term treatment targets (4–6 months)		
Normalisation of CRP and reduction of faecal calprotectin‡ to a reasonable threshold are intermediate actionable targets in ulcerative colitis and Crohn's disease. Consider changing treatment if these targets have not been achieved despite optimised dosing.* In children, the MINI index that combines these measures may be used	8.8	93%
In Crohn's disease, faecal calprotectin <200 µg/g reflects acceptable range and <100 µg/g transmural remission; in children, also MINI<8	8.5	90%
In ulcerative colitis, faecal calprotectin <200 µg/g reflects acceptable range and <100 µg/g histological remission‡	8.2	87%
These faecal calprotectin values should be verified by repeated testing	7.9	77%
In children, restoration of normal growth velocity is an adjunctive intermediate-term target. Consider optimising current treatment if this target has not been achieved*	9.3	100%

(Table 3 continues on next page)

	Voting results	
	Strength of recommendation†	% votes 7–10
(Continued from previous page)		
Long-term treatment targets (7–12 months)		
Clinical remission is insufficient to be used as a long-term treatment target	9-1	93%
Endoscopic remission is a long-term actionable target. Consider changing treatment if this target has not been achieved despite optimised dosing*§	9-1	92%
Endoscopic remission can be assessed by sigmoidoscopy in ulcerative colitis and ileocolonoscopy or capsule endoscopy¶ in Crohn's disease	9-0	95%
Endoscopic remission in Crohn's disease should be measured by SES-CD ≤2 for ileocolonoscopy with complete remission optimally measured by SES-CD ≤1, or by Lewis score <135 for capsule endoscopy	8-8	92%
Endoscopic remission in ulcerative colitis should be measured by MES=0 points while MES ≤1 may serve as acceptable interim target when supported by clinical and biochemical remission	9-3	97%
Histological remission is an adjunctive target in ulcerative colitis. Consider optimising current treatment if this has not been achieved*	8-3	88%
Assess histological remission in ulcerative colitis by the absence of erosions, ulcers, and neutrophils in the epithelium and lamina propria; this can be operationalised by standardised scores such as NHI ≤1, which is most feasible for clinical practice	9-0	93%
Histological remission is not a target in Crohn's disease	8-7	87%
Transmural remission is an adjunctive target in Crohn's disease (MR enterography, CT enterography, IUS). Consider optimising current treatment if this has not been achieved*	8-8	95%
Using MR enterography: assess remission by sMaRIA (remission: <1; response: ≥Δ50%); in children, assess with PICMI (remission: ≤10; response: >Δ20)	8-7	92%
Using IUS: assess transmural remission by BWT ≤3 mm and Limberg score or CDS=0, and response by BWT ≥Δ25% and Limberg ≥Δ1; in children, assess remission by BWT ≤2.5 mm in the small bowel and <3 mm in the colon and Limberg 0; response: as in adults	8-9	92%
Absence of disability and fatigue, as well as normalised health-related quality of life are long-term patient-centred targets. Consider changing treatment if this target has not been achieved and inflammation has not been fully controlled despite optimised dosing	8-7	92%
Disability could be assessed by the IBD-DI in adults (no disability: 0–20)	8-9	95%
Fatigue could be assessed by the IBD-F in adults (no fatigue: Section-1 <7.5)	9-0	97%
Quality of life could be assessed by the Short IBDQ in adults (remission: ≥50; response: ≥Δ9 points) and the IMPACT-III in children (remission: ≥143; response: none defined)	9-1	98%
Persistent fatigue despite deep remission warrants evaluation for psychological factors, sleep quality, and nutritional deficiencies, with multidisciplinary team support	9-4	100%
BWT=bowel wall thickness. CRP=C-reactive protein. CDS=colour Doppler signal. HBI=Harvey-Bradshaw Index. IBD-DI=IBD-Disability Index. IBD-F=IBD Fatigue Index. IBDQ=Inflammatory Bowel Disease Questionnaire. IUS=intestinal ultrasound. MaRIA=Magnetic Resonance Index of Activity. MES=Mayo endoscopic score. MINI=Mucosal Inflammation Non-Invasive. NHI=Nancy histological index. NRS=numerical rating scale. PICMI=Pediatric Inflammatory Crohn's Magnetic Resonance Enterography Index. PIDI=Pediatric IBD Disability Index. PIFI=Pediatric IBD Fatigue Index. PMS=partial Mayo score. PROMIS=Patient-Reported Outcomes Measurement Information System. PRO2=Patient-Reported Outcome 2. PUCAI=Pediatric Ulcerative Colitis Activity Index. SES-CD=Simplified Endoscopic Score for Crohn's Disease. sMaRIA=simplified Magnetic Resonance Index of Activity. UCEIS=Ulcerative Colitis Endoscopic Index of Severity. wPCDAI=weighted Pediatric Crohn's Disease Activity Index. *For details see table 1; time-to-target achievement varies based on therapy and mechanism of action (figure 4). †Calculated as the mean score of all responders (on a scale of 1–10 where 10 denotes complete agreement and 1 complete disagreement). ‡Faecal calprotectin values should be interpreted longitudinally and verified by repeated testing given the modest test–retest reliability of faecal calprotectin. Interpretation should consider change from baseline, treatment-specific time to response, disease phenotype and location, concordance with other objective measures, and relevant confounders. Values of 100–200 µg/g may represent a grey zone requiring individualised interpretation. Mildly elevated CRP less than twice the upper normal limit should be interpreted on an individual basis. §In selected patients with limited residual activity and otherwise good disease control, continued therapy with close monitoring may be appropriate following shared decision-making. ¶Capsule endoscopy should be used according to disease location: pan-enteric capsule endoscopy for colonic and/or small bowel disease and small bowel capsule for disease limited to the small bowel.		

Table 3: Recommended treatment targets and adjunctive targets* in Crohn's disease and ulcerative colitis

The Patient-Reported Outcome 2 (PRO2) measurement, derived from the daily stool frequency and abdominal pain components of the CDAI, has emerged as a practical clinical tool for repeated assessment of symptoms in adults.¹⁰ The increasing recognition of the importance of bowel urgency as a PRO in Crohn's disease, measured by numeric rating scale (NRS; ranging from 0 to 10), made urgency a short-term adjunctive target in STRIDE-III. Patients with significant urgency have lower health-related quality of life and higher work impairment.¹¹

In ulcerative colitis, the short-term clinical targets are normalisation of stool frequency and rectal bleeding, with bowel urgency increasingly recognised as a clinically relevant outcome. In adults, the full, partial, and modified Mayo scores are the clinical indices most commonly used in clinical trials and strongly correlate with each other.¹² However, the most commonly adopted index in

clinical practice is the PRO2 that combines stool frequency with rectal bleeding.¹³ In children, the Pediatric Ulcerative Colitis Activity Index (PUCAI) is the standard reference tool in both clinical trials and in clinical practice as incorporated in clinical guidelines of both ambulatory¹⁴ and severe¹⁵ ulcerative colitis.

Compared with Crohn's disease, achievement of clinical remission is more strongly correlated with endoscopic activity in ulcerative colitis, and is associated with reduced risk of relapses, hospitalisation, and colectomy.¹⁶ In paediatric ulcerative colitis, the PUCAI strongly correlates with endoscopic disease activity, supporting its use as a reliable early and intermediate target. However, its performance is weaker in the presence of primary sclerosing cholangitis because symptoms in this clinical context correlate less closely with endoscopic activity.^{14,17–24} PUCAI-defined remission

was not inferior to sigmoidoscopy in predicting long-term sustained remission.^{25,26}

The most widely used PROs in adults with ulcerative colitis are the stool frequency and rectal bleeding subscores of the Mayo score (PRO2). Normalisation of these two items showed close agreement with endoscopic improvement and remission.²⁷ PRO2 can improve within days, and early improvement or resolution is associated with improved clinical and endoscopic outcomes at later timepoints.²⁸ PRO measures in paediatrics require a version for adolescents and a conceptually equivalent caregivers' version for children younger than 8 years. In ulcerative colitis, the TUMMY-UC includes rectal bleeding, stool frequency, abdominal pain, stool consistency, nocturnal stools, and weakness.^{29–31} The TUMMY-UC correlates well with multiple constructs of disease activity and quality of life, including endoscopic activity.²⁹

The most commonly used measure of bowel urgency, an increasingly recognised PRO in ulcerative colitis,³² is the NRS. No urgency is typically defined as NRS of 1 or less or, less stringently, as NRS of 2 or less.³³

Faecal calprotectin and C-reactive protein

In STRIDE-II, faecal calprotectin (FC) and C-reactive protein (CRP) were established as the key biomarker targets for treatment response and long-term disease control. Review of numerous adult and paediatric studies confirms that both markers remain reliable, reproducible, and clinically actionable for STRIDE-III.³⁴ FC is highly sensitive to mucosal inflammation but less so for proximal small bowel disease,³⁴ whereas CRP is more specific but less sensitive to mild activity, especially in ulcerative colitis. Used together, they are associated closely with clinical, endoscopic, and transmural targets and are central to modern treat-to-target care. While FC improvement can be anticipated shortly after initiation of successful therapies, further declines occur in a considerable proportion of patients within the subsequent 6 months,^{24,35} consistent across adult, paediatric, and elderly populations.^{36,37} Therefore, persistently elevated FC or CRP through 4–6 months indicates a need for treatment optimisation or, if borderline, endoscopic and/or cross-sectional assessment. Although most studies used the upper limit of normal as the CRP threshold, mildly elevated levels, recommended by the steering committee as less than twice the upper limit of normal, should be interpreted on an individual basis. CRP can be influenced by factors unrelated to intestinal inflammation, including intercurrent infection, obesity, and comorbidities; discordant or mildly elevated values should therefore be interpreted in the broader clinical context.

Similarly, false positive elevations in FC can occur in the setting of transient infection, certain medications such as non-steroidal anti-inflammatory drugs, diverticulitis, inflammatory pseudopolyps, colorectal cancer, and coeliac disease. FC measurements are also affected by

inter-assay variability, as results obtained using different commercial assays are not directly interchangeable. Because of these potential confounders,³⁸ clinical decisions should be based on serial measurements rather than on a single FC result. Furthermore, the selected FC threshold should not be interpreted as a discrete biological boundary but, rather, in the context of magnitude and direction of change from baseline, treatment-specific time to response, disease location and phenotype, concordance with other inflammatory measures, and relevant clinical or technical confounders. Nonetheless, persistent FC above 200 µg/g after sufficient treatment-specific time and adequate treatment optimisation indicates that the STRIDE-III biochemical target has not been achieved and should prompt reassessment of the treatment strategy. In children younger than 5 years, physiologically elevated FC concentrations can be normal, and age-specific nomograms have been proposed.³⁹

Across studies, FC was the most sensitive non-invasive biomarker in Crohn's disease. Reported cutoffs clustered at 100–130 µg/g for both endoscopic remission, defined as a Simple Endoscopic Score for Crohn's Disease (SES-CD) ≤2 (median approximately 130 µg/g across studies), and transmural remission (median approximately 100 µg/g across studies).³ In the survey performed for this manuscript, the mean FC values were 196 (SD 49) µg/g for an acceptable low-inflammation range and 100 (38) µg/g for transmural remission (appendix pp 6–7). For predicting outcomes, post-treatment FC of less than 250 µg/g was the most commonly studied prognostic threshold associated with more favourable disease outcomes; however, this cutoff was generally prespecified in study protocols rather than derived empirically from threshold-optimisation analyses.³

CRP normalisation within 8–14 weeks predicts favourable outcomes.^{40,41} Although normalisation of biomarkers should be pursued as an intermediate target, an early reduction of around 50% in FC⁴¹ and CRP^{42,43} has also been associated with improved disease outcomes. The CALM treat-to-target randomised controlled trial confirmed the role of CRP and FC as actionable targets in Crohn's disease over symptom-based management.^{44,45}

In ulcerative colitis, FC is strongly associated with endoscopic severity, although the association is somewhat weaker in proctitis.⁴ In the Lasso trial, FC-guided 5-aminosalicylic acid dose escalation did not reduce the overall 18-month relapse rate, but fewer relapses were seen in a post-hoc subgroup whose FC exceeded 300 µg/g.⁴⁶ In the randomised DEAR treat-to-target trial, mesalamine dose escalation in patients with clinically quiescent ulcerative colitis decreased FC to a low range compared with unchanged dosing, without a difference in relapse between arms.⁴⁷ In an exploratory analysis, FC of 200 µg/g or more at week 12 was associated with earlier clinical relapse. In the OPTIMISE

trial, FC-guided treatment escalation did not improve 12-month endoscopic remission over symptom-guided care, although imputed and pooled exploratory analyses numerically favoured the FC-guided arm.⁴⁸ FC under 250 µg/g 6 weeks after commencing treatment was associated with reduced risk of colectomy and hospitalisations, with even stronger effects at FC levels below 100 µg/g.^{49,50} In children, a decline in FC of at least 75% by week 12 was associated with a threefold increase in week-52 clinical remission.⁵¹

In the systematic review, median FC cutoffs clustered around 200 µg/g for Mayo endoscopic score (MES) ≤1 and around 80 µg/g for histological remission.⁴ In the STRIDE-III ulcerative colitis survey, the mean preferred FC threshold was 135 (SD 44) µg/g for an acceptable low-inflammation range and 100 (38) µg/g for histological remission (appendix pp 6–7), broadly consistent with the MES=0 threshold identified in the systematic review (median 135 µg/g, with the best-performing cutoffs near 100 µg/g).⁴ IOIBD members subsequently voted on 150 µg/g versus 200 µg/g as the preferred target threshold, with nearly identical mean scores on a 0–10 scale (8.2 vs 8.1, respectively). After reviewing the individual studies and expert opinion, the steering committee selected 200 µg/g as the target cutoff also for ulcerative colitis, while acknowledging that this represents a relatively conservative threshold.

CRP is less sensitive than FC in adults^{24,52} and children²⁴ with ulcerative colitis, even more so than seen in Crohn's disease.⁵³ Nonetheless, early normalisation of CRP, generally within 4–12 weeks depending on treatment class, together with improvements in FC and albumin, have been associated with clinically relevant outcomes.^{49,54}

Endoscopic remission and growth

Endoscopic remission is a central actionable target, being one of the strongest predictors of long-term outcomes.^{3,4}

In Crohn's disease, the evidence supporting endoscopic remission includes both interventional treat-to-target studies and prognostic association studies. The STARDUST trial did not demonstrate improved outcomes with ustekinumab dose intensification based on endoscopic assessment.⁵⁵ By contrast, the CURE-CD randomised treat-to-target trial showed that proactive treatment escalation guided by video-capsule endoscopy (VCE) findings was superior to standard care.⁵⁶ A post-hoc analysis of CALM provides prognostic evidence that patients who achieved combined endoscopic and clinical remission had a lower subsequent risk of major adverse outcomes.⁵⁷ These findings complement the large body of observational evidence linking endoscopic remission with a more favourable disease course.³ The negative STARDUST findings might reflect limitations of the specific escalation strategy evaluated rather than absence of value of endoscopic remission as a treatment target.⁵⁸

Substantial endoscopic improvement could represent an important early treatment target even when complete endoscopic remission has not yet been achieved, particularly when supported by concordant clinical and biochemical improvement. Persistent residual endoscopic inflammation after sufficient treatment-specific time and adequate treatment optimisation indicates that the long-term actionable target remains unmet and should prompt reassessment of the treatment strategy. However, in selected circumstances, when residual disease is limited, symptoms and biomarkers are well controlled, the patient has otherwise achieved sustained clinical remission, and the risks or disadvantages of switching an effective therapy are substantial, continuation of the current treatment with close monitoring might be appropriate following shared decision-making.

SES-CD remains the most widely adopted tool for assessing mucosal activity⁵⁹ and is highly correlated with the more complex Crohn's Disease Endoscopic Index of Severity (CDEIS).⁶⁰ Different thresholds for SES-CD are reported in the literature (table 2; appendix pp 1–7).^{60–64}

Newer indices such as the Simplified Endoscopic Mucosal Assessment for CD (SEMA-CD), the Modified Multiplier of SES-CD (MM-SES-CD), and EASE-CD correlate with SES-CD and demonstrate substantial predictive value for MM-SES-CD in particular, but further prospective validation is required.³

A Lewis VCE score of less than 135 indicates small bowel healing and predicts reduced relapse and hospitalisation.³ Integrating pan-enteric VCE in children, who have more extensive disease on average than adults, increased rates of mucosal healing.^{65,66} Indeed, early endoscopic remission represents a particularly meaningful target in paediatric Crohn's disease, as it predicts growth restoration.⁶⁷ The latter is a distinct therapeutic objective because impaired linear growth primarily reflects persistent inflammation, but could also represent malnutrition or steroid exposure, even when gastrointestinal symptoms improve. Accordingly, serial assessment of growth, pubertal development, and nutritional status should complement conventional targets in children.

For ulcerative colitis, the MES and Ulcerative Colitis Endoscopic Index of Severity (UCEIS) are the most widely used tools for evaluating endoscopic inflammation.⁴ Used less often in clinical practice, other emerging indices offer refined prognostic stratification such as the Paddington International Virtual Chromoendoscopy Score (PiCaSSO score), the modified Mayo endoscopic score (MMES), and the Toronto IBD Global Endoscopic Reporting (TIGER) score (appendix pp 1–5).⁴

In clinical trials, endoscopic improvement is commonly defined as an MES of 1 or less⁴ but this threshold is particularly applicable to the research setting with typical baseline MES scores of 2–3. In clinical practice, however, where patients might also have mild disease at baseline, improvement is more

often assessed using the change in MES from baseline (table 2). Endoscopic remission, defined as MES=0, is the preferred long-term goal as it was consistently associated with sustained remission and lower risk of hospitalisations and colectomy,^{68–78} with most observational studies suggesting better outcomes than MES=1.^{4,74,77,79–81} Nonetheless, a short segment of mild residual inflammation (MES ≤1) might be acceptable following shared decision-making, particularly when supported by biomarker and histological quiescence.^{77,82,83}

The recent VERDICT trial showed that treating to endoscopic remission (MES ≤1) as a target was superior to symptom-based management.⁸⁴ Sigmoidoscopy shows high concordance with complete colonoscopy for assessing disease activity and can be used for routine monitoring in most patients, as shown in both adults and children.^{85–87}

Histological remission

Despite encouraging findings from some association studies, several uncertainties limit the generalisability of histology as a treatment target in Crohn's disease, including inconsistent measuring tools, conflicting prognostic associations, sampling variability, and the absence of treat-to-target trials demonstrating that treating to histological in addition to endoscopic remission benefits patients.⁸⁸ In some studies, histological remission was associated with improved outcomes compared with endoscopic remission alone,^{89–92} while others failed to show such association.^{93–95} Most studies have not used a specific histopathological score but defined remission using variable parameters, most notably absence of neutrophils in the epithelium or lamina propria.^{89,90,96–100} Among formal indices, the Robarts Histopathology Index (RHI), the Global Histologic Disease Activity Score (GHAS), and the Geboes score are most frequently studied, with the simpler Nancy histological index (NHI) used less often (table 2; appendix pp 1–7). Best accuracy has been shown if biopsies are taken from the ulcer edge; biopsies of areas without ulcers or from the centre of an ulcer have resulted in high variability.¹⁰¹

For ulcerative colitis, numerous studies published since STRIDE-II provide consistent definitions of histological remission as absence of neutrophils in the epithelium and lamina propria, with no erosions or ulcers, corresponding to NHI of 1 or less, a Geboes score of 2B.0 or less, and RHI of 3 or less with neutrophil subscores of 0 (appendix pp 1–5).⁴ Histological indices in ulcerative colitis are reproducible, with inter-rater intra-class correlation coefficients of 0.70–0.85.⁴ Available evidence, including in the VERDICT trial,⁸⁴ indicated that histological remission may be achieved in approximately 30–50% of patients,^{71,102,103} showing its feasibility with current treatments. The accumulating observational evidence shows that histological remission is associated with a significant reduction in relapse

risk^{70,75,102,104–106} and colectomy.^{78,107,108} Although the data broadly support the additional prognostic value of histological remission in patients with an MES of 1 or less,^{71,75,78,80,104,105,107,109–122} the benefit over MES=0, which is the endoscopic remission definition favoured by STRIDE-III (tables 1 and 2), is more conflicting, with some suggesting that residual neutrophilic infiltrate confers higher relapse risk^{80,115,119} while others found no such added prognostic value.^{4,110,113} The VERDICT trial provides the first randomised evidence on this question.⁸⁴ Treating to combined endoscopic and histological remission reduced ulcerative colitis-related complications compared with symptomatic remission alone, but not compared with endoscopic remission alone; histological remission was not tested on its own.⁸⁴ Taken together, histological remission is presented as an adjunctive target to consider in treatment optimisation with other disease variables, most notably complete endoscopic remission (MES=0; table 3).

Transmural remission

Magnetic resonance enterography (MRE) is generally preferred over CT enterography (CTE) because it avoids ionising radiation while providing comparable diagnostic accuracy. With the increasing availability of IUS as a non-invasive bedside modality, repeated assessments are now feasible, enabling close monitoring of transmural response to therapy. Given the moderate interobserver reliability of IUS,¹²³ assessment of transmural remission should emphasise bowel wall thickness, owing to its greater reproducibility (table 2). Because IUS is non-invasive and particularly suitable for repeated assessment, changes can provide a dynamic measure of early treatment response and residual inflammatory activity. Moreover, the accuracy of bowel wall thickness assessed with IUS alone for identifying endoscopic activity or remission is similar to the various composites scores in use and can be easily implemented in clinical routine use. This monitoring role also applies in ulcerative colitis, where transmural remission itself is not currently designated as either an actionable or adjunctive target.

In Crohn's disease, transmural remission (ie, no inflammation evident on imaging irrespective of the endoscopic findings) has been associated with improved disease course.³ Importantly, discordance between transmural and endoscopic activity is observed in 25–30% of both adult and paediatric patients, with persistent transmural inflammation despite endoscopic remission or endoscopic activity despite transmural remission.^{124–126} Numerous observational studies suggest that achieving transmural remission in addition to endoscopic remission is associated with superior disease outcomes compared with endoscopic remission alone.^{127–130} Hence, despite the lack of treat-to-target trials for transmural healing, cross-sectional imaging, including CTE, MRE, and IUS, are increasingly used to

monitor disease activity and treatment response and should be considered as adjunctive long-term targets in Crohn's disease (figure 5, table 3). The ongoing phase 4 VECTORS randomised controlled trial is evaluating whether targeting IUS response or transmural healing, in addition to clinical and biomarker remission, improves endoscopic outcomes compared with targeting clinical and biomarker remission alone.¹³¹ Although STRIDE-III focuses on controlling inflammation, imaging assessment of stricturing and penetrating complications could independently influence management.

In general, disease activity assessed by IUS scores correlates with endoscopy, small bowel capsule endoscopy, and other cross-sectional imaging modalities.³ Most IUS scores in Crohn's disease (appendix pp 1–5) include bowel wall thickness and the Limberg score or colour Doppler signal. Assessing these two variables might be more feasible in clinical practice while preserving sufficient accuracy.

For ulcerative colitis, colonic assessment on MRE and CTE is limited by suboptimal luminal distension with oral contrast administration. The emergence of IUS has facilitated our understanding that ulcerative colitis involves mural changes beyond the submucosa and that transmural remission is associated with improved outcomes (appendix pp 1–5).⁴ Transmural improvement can be detected in some patients as early as 2 weeks after initiating treatment.^{132–134} No treat-to-target trial has demonstrated an added benefit of targeting transmural remission. Unlike in Crohn's disease, the added value of transmural remission beyond endoscopic remission has rarely been examined in ulcerative colitis. Moreover, the evidence base for transmural remission in ulcerative

colitis, particularly for prognostic associations, is substantially smaller, with approximately threefold to fourfold fewer studies than in Crohn's disease. For these reasons, IUS in ulcerative colitis is currently not considered either an actionable or adjunctive treatment target. This is distinct from the role of IUS as a non-invasive monitoring tool; the systematic review supports its accuracy in detecting endoscopic disease activity and its ability to detect early treatment response.

Composite scores

Composite indices integrating clinical, biochemical, endoscopic, histological, or radiographic parameters have been increasingly reported;^{3,4} however, the available evidence remains heterogeneous, with lack of standardised definitions, and no composite index is currently considered either an actionable or adjunctive treatment target. Nonetheless, studies generally demonstrate the association between deeper remission and better long-term outcomes and support the multi-target scheme of STRIDE-III. For instance, combining FC and CRP might mitigate the limitations of either marker alone: FC has high sensitivity but lower specificity, whereas CRP has lower sensitivity but higher specificity.¹³⁵ Their combined use might be particularly valuable when FC concentrations fall within a diagnostically indeterminate range. Discordance among objective measures should be interpreted according to the role assigned to each measure within the STRIDE-III framework rather than requiring concordance across all domains. Failure to achieve an actionable target remains relevant even when an adjunctive measure indicates remission; for example, persistent endoscopic

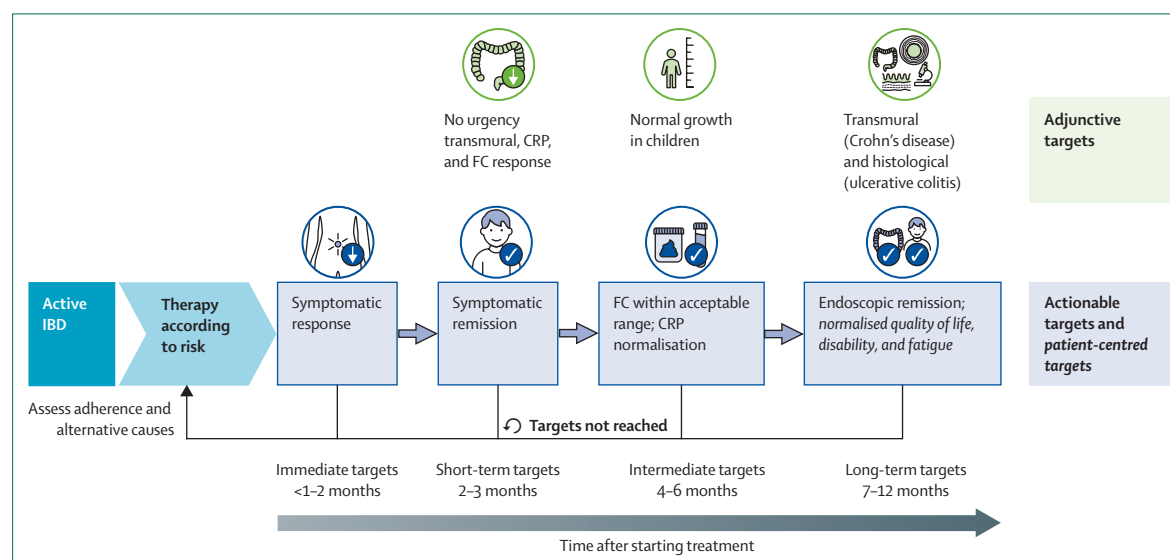


Figure 5: Treatment targets in Crohn's disease and ulcerative colitis

Given the modest test–retest reliability of FC, serial assessment is essential with values <200 µg/g considered reasonable range. Capsule endoscopy could be used to assess endoscopic remission according to disease location. Mildly elevated CRP (eg, less than twice the upper normal limit) should be interpreted on an individual basis. CRP=C-reactive protein. FC=faecal calprotectin.

inflammation should be addressed despite transmural remission.

For Crohn's disease, composite targets combining clinical remission with biochemical remission (FC <150–250 µg/g and CRP <5 mg/L) outperformed clinical-only approaches in some studies, although added value over FC alone was inconsistent.^{3,4} FC under 100 µg/g with CRP less than 5 mg/L correlated with combined endoscopic and transmural remission.^{126,136} Adding albumin to CRP and FC possibly further enhances identification of deep remission.¹²⁶

In children treated with infliximab, post-induction wPCDAI remission combined with FC less than 250 µg/g predicted 1-year endoscopic remission, whereas neither measure alone showed a significant association.¹³⁷ In adults, composite indices integrating clinical scores with CRP and FC outperformed clinical or biomarker endpoints alone in detecting mucosal inflammation,¹³⁶ reinforcing the cumulative targets concept of these three markers in STRIDE-III.

Acknowledging the utility of these three targets, the validated Mucosal Inflammation Non-Invasive (MINI) index incorporates stool frequency and character, FC, erythrocyte sedimentation rate (ESR), and CRP in a weighted index that accurately identifies endoscopic remission in children with Crohn's disease.^{37,138–144} In adults, the Disease Severity Index (DSI), which integrates endoscopic, imaging, biomarker, phenotypic, and PRO components, correlated with disease activity and quality of life.¹⁴⁵

In ulcerative colitis, further supporting the STRIDE-III concept, early objective monitoring of symptoms, CRP, and FC have been shown to facilitate earlier therapeutic optimisation and improved remission rates.¹⁴⁶ A model combining CRP less than 2.75 mg/L and FC less than 120 µg/g identified endoscopic improvement (MES ≤1) with high specificity, while lower thresholds were associated with histological remission.¹³⁵ Another composite model integrating FC, CRP, ESR, and haemoglobin achieved high diagnostic accuracy, although FC alone performed similarly.¹⁴⁷ In children, combining platelets, leukocytes, ESR, and FC improved identification of severe disease.¹⁴⁸ Albumin, rectal bleeding, and the CRP/albumin ratio contributed most to machine-learning prediction of endoscopic activity.¹⁴⁹

A composite defined by IUS activity (Milan Ultrasound Criteria >6.3) and/or FC of 100 µg/g or greater identified histological activity in adults with ulcerative colitis.¹⁵⁰ Early IUS and FC measurements were also associated with subsequent endoscopic remission in children.¹⁵¹ Similarly, combining clinical assessment with ESR and IUS improved prediction of endoscopic severity.¹⁵² Disease clearance, defined by steroid-free clinical, endoscopic, and histological remission, has been associated with improved disease outcomes.^{75,82,103–108,115,153} In the VERDICT trial, treating to this compound target reduced complications compared with symptomatic

remission alone, but not compared with endoscopic remission.⁸⁴

Patient-centred outcome measures

Long-term outcomes also encompass patient-centred targets that reflect sustained well-being. The inclusion of these targets in STRIDE-III is not merely symbolic. For example, through shared decision-making, treatment might be changed when a patient experiences substantial treatment-related adverse effects, even if the therapy has achieved deep remission. To support these discussions, patient-centred concepts must be measured and quantified periodically.

Quality of life

The most commonly used disease-specific health-related quality-of-life measure is the Inflammatory Bowel Disease Questionnaire (IBDQ) in adults and the IMPACT-III questionnaire in children.^{154,155} These indices are more suitable for research settings and are less commonly used in routine clinical practice. Nonetheless, monitoring quality of life is important for overall patient well-being, as it captures multiple dimensions of disease burden, including disease activity, fatigue, social functioning, and body image. Quality of life generally correlates with disease activity and could rapidly improve after treatment.^{156,157} However, quality of life also reflects burdens beyond disease activity, such as dietary restrictions and treatment-related adverse effects¹⁵⁸ and many patients continue to experience impaired quality of life despite disease remission.¹⁵⁹

Disability

Disability affects 30–50% of patients with IBD and reflects the combined effects of biological, psychological, and environmental factors on body functions and structures, activities, and participation.^{160,161} It may persist despite clinical remission, affecting 16–35% of patients.^{162,163} The IBD-specific Disability Index (IBD-DI) was developed from the International Classification of Functioning, Disability and Health core set,^{160,164} and later adapted into the IBD-Disk, a visual self-assessment tool of impaired daily functioning.¹⁶⁵ In children, age-appropriate patient-reported measures are required, including adolescent and caregiver versions; accordingly, the Pediatric IBD Disability Index (PIDI) is currently under development.¹⁶⁶

Fatigue

Fatigue is common but under-recognised in IBD, affecting 24–87% of children and adults.^{167,168} While substantially impairing quality of life and productivity,¹⁶⁹ it was not a formal STRIDE-II treatment target. Advanced therapies improve fatigue broadly in parallel with disease activity,^{157,170–172} but it often persists despite clinical or biochemical remission.¹⁷³ Validated measures include Functional Assessment of Chronic Illness

Therapy – Fatigue (FACIT-F), originally developed for cancer-related fatigue and later validated in IBD, fatigue items within the IBDQ, the Short IBDQ (SIBDQ), and IMPACT-III, and the IBD-specific fatigue numerical rating scale and IBD-Fatigue scale (appendix pp 1–7; table 2). In children, the Pediatric IBD Fatigue Index (PIFI), with conceptually equivalent patient-reported and caregiver-reported versions, is under development.¹⁷⁴ Since randomised trials support multidisciplinary lifestyle interventions,^{175,176} fatigue should be assessed routinely, and its persistence despite remission should prompt evaluation of contributing factors and targeted management.

Positioning treatment targets along the therapeutic timeline

The evidence supports a structured, response-based monitoring strategy (table 2, figure 5) with the expected time to reassessment and target attainment varying according to treatment and mechanism of action (figure 4). These treatment-specific timelines should be interpreted as expected reassessment windows rather than rigid treatment-failure thresholds. This section provides a summary of the aforementioned evidence, while positioning the targets on a treatment timeline. Longitudinal assessment is particularly important for measures that can be repeated readily, such as symptoms, CRP and FC, for which trajectory over time could provide additional information beyond a single measurement. Other modalities, such as endoscopy and cross-sectional imaging, are generally assessed at predefined or clinically indicated timepoints rather than serially at short intervals. IUS, however, can provide more frequent information on treatment response, although the frequency of assessment depends on clinical context and local availability. In general, persistent inability to achieve an actionable target beyond the expected treatment-specific timeframe despite adequate optimisation should prompt reassessment of the treatment strategy. The framework applies across age groups, including children and older adults.

Immediate and short-term stage (within 3 months of diagnosis or flare)

The immediate stage should focus on rapid symptom improvement within 1–2 months, and remission within 2–3 months (table 3, figures 4 and 5). Failure to achieve early clinical response warrants treatment reassessment and, after appropriate optimisation, consideration of treatment change. However, when persistent symptoms are not clearly attributable to active intestinal inflammation, or when symptoms are discordant with other measures of disease activity, objective assessment using biomarkers, IUS, endoscopy, or other appropriate modalities could help distinguish ongoing inflammatory activity from alternative causes before changing therapy.

In parallel, early biochemical improvement is expected, including a reduction in FC or CRP of at least 50% from baseline. Failure to achieve clinical and biochemical improvement by this stage should prompt revision of the management plan, as well as reassessment of adherence, dosing, and diagnosis. A substantial early improvement from baseline might represent a meaningful treatment response even when the absolute target has not yet been reached. However, persistent residual inflammatory activity beyond the expected reassessment window, particularly when values plateau despite adequate treatment optimisation, indicates that the target remains unmet and should prompt reassessment of the treatment strategy. Although not designated as treatment targets, other clinically relevant measures should also be assessed from this stage onward, such as nutritional status, serum albumin, and haemoglobin.

Intermediate stage (4–6 months)

During this stage, targets shift toward objective biochemical remission. Persistent FC values over 200 µg/g on repeated testing after sufficient treatment-specific time and appropriate optimisation suggest significant inflammation and are associated with a higher risk of an adverse disease course in both Crohn's disease and ulcerative colitis. FC values below 100 µg/g strongly support deep inflammatory control. CRP is less sensitive than FC and values less than 5 mg/L represent the target threshold. Intermediate FC values of 100–200 µg/g and mildly elevated CRP values up to twice the upper normal limit should be interpreted within the broader clinical context, including symptoms, disease location and phenotype, concurrent biomarkers, and longitudinal trends; further evaluation with endoscopy or cross-sectional imaging might be warranted.

Endoscopic evaluation should generally be deferred to the long-term stage but could be considered earlier when treatment response or the clinical picture remains unclear, such as in cases of discordance between symptoms and biochemical markers. Early endoscopic evaluation is particularly common in ulcerative colitis, in which endoscopic remission typically occurs earlier than in Crohn's disease and assessment is more readily performed, with flexible sigmoidoscopy being sufficient in most cases. If performed during this stage, endoscopic response (eg, >50% reduction in SES-CD or a 1-point decrease in MES) predicts favourable 1-year outcomes. Failure to demonstrate meaningful endoscopic response should prompt reassessment of the treatment strategy. In patients with substantial endoscopic improvement but residual activity, the decision to further optimise or change therapy should consider treatment-specific timing, the extent and location of residual disease, concordant clinical and biochemical findings, treatment burden, available alternatives, and patient preferences.

Repeated sonographic evaluation is recommended already during the intermediate stage. Transmural

improvement supports a deeper level of disease control and might guide treatment optimisation and timing of endoscopic assessment, particularly in Crohn's disease, but also in ulcerative colitis.

Long-term stage (7–12 months)

Treating to endoscopic remission, defined as SES-CD of 2 or less in Crohn's disease, with deeper remission ideally reflected by SES-CD of 1 or less or a Lewis score less than 135 on capsule endoscopy, and as MES=0 in ulcerative colitis, is associated with more durable remission (table 3). The timing of endoscopic evaluation might be guided by FC, CRP, and IUS findings. For example, endoscopy could be deferred in patients with mild-to-moderate disease who achieve rapid normalisation of FC and IUS. Histological assessment should be considered at this stage, particularly in ulcerative colitis, where histological remission, defined by the absence of neutrophils and erosions, has emerged as an adjunctive target. However, treatment should not generally be changed solely because of persistent histological activity in patients who have achieved complete clinical and endoscopic remission, because the added prognostic value of histological remission in this setting is inconsistent and switching therapy might jeopardise otherwise sustained steroid-free clinical and endoscopic remission. Thus, transmural remission in Crohn's disease and histological remission in ulcerative colitis are not actionable targets that support a treatment change if not achieved but they are important adjunctive targets that should inform a broader assessment and could lead to optimisation of the current regimen, such as dose adjustment, TDM, or addition of nutritional therapy, as well as intensified monitoring, including shorter visit intervals and earlier endoscopic reassessment (table 1).

Quality of life, disability, and fatigue should be assessed repeatedly, with improvement expected during the intermediate stage and resolution during the long-term

stage. These patient-centred outcomes often improve with effective control of inflammation, anaemia, and nutritional deficiencies. Persistent fatigue could also reflect psychosocial factors, sleep disturbance, treatment-related adverse effects, or functional symptoms. Such findings should be managed through a holistic, multidisciplinary approach while thoroughly addressing any inflammatory activity. Persistent urgency despite endoscopic and biomarker remission might indicate functional disturbance or impaired rectal compliance and warrants pelvic floor evaluation.

In addition, symptoms, FC, and CRP should be assessed every 3–4 months during the long-term stage, with monitoring intervals subsequently extended to up to 6–12 months according to the depth of remission achieved.

Adaptations for resource-limited settings

An IOIBD survey across 85 countries demonstrated substantial variation in access to specialised IBD expertise, biomarkers, advanced endoscopy, cross-sectional imaging and ultrasound, TDM, and advanced therapies.^{177,178} Similar findings were reported by the BRICS IBD consortium, indicating that although treat-to-target is widely accepted conceptually, its implementation remains inconsistent in many low-resource settings.¹⁷⁹ As the global burden of IBD increases, these disparities represent an important challenge for the widespread implementation of evidence-based treat-to-target care.

Implementation of treat-to-target in low-resource countries should focus on maximising the use of available objective measures and treatment modalities rather than lowering therapeutic goals (table 4). Wherever possible, widely accessible objective measures such as CRP and FC should be incorporated into routine monitoring.¹⁷⁹ Because clinical remission correlates more closely with mucosal inflammation in ulcerative colitis, the combination of PRO2 with low FC and normal CRP might be sufficient in most patients. In Crohn's disease,

	STRIDE-III approach	Pragmatic approach in resource-limited settings
Treatment targets	Apply actionable and adjunctive STRIDE-III targets	Maintain identical targets; adapt the methods used to assess target achievement when necessary
Monitoring frequency	Regular longitudinal monitoring according to disease activity	Maintain regular follow-up with the most accessible objective tools rather than relying on symptoms alone
Clinical monitoring	Use validated symptom-based assessment and simple PROs at every visit	Use validated symptom-based assessment and simple PROs at every visit
Biomarkers	Serial FC and CRP measurements	Prioritise CRP and FC whenever available; serial CRP alone is preferable to symptom-based monitoring if FC is unavailable
Endoscopic assessment	Scheduled high resolution endoscopic evaluation to confirm mucosal healing	Perform endoscopy whenever feasible; use flexible sigmoidoscopy or even rigid proctoscopy in ulcerative colitis when appropriate
Transmural assessment	MRI and/or IUS according to disease phenotype	Use of IUS where expertise exists while MRI and/or CT enterography reserved for selected indications
Future priorities	Precision medicine integrating multiple disease domains	Improve access to biomarkers, IUS, specialist training, and advanced therapies while evaluating pragmatic treat-to-target algorithms in prospective studies

CRP=C-reactive protein. FC=faecal calprotectin. IUS=intestinal ultrasound. PRO=patient-reported outcome.

Table 4: Pragmatic implementation of STRIDE-III in resource-limited settings

IUS might be an attractive modality because it is non-invasive, repeatable, relatively inexpensive, and becoming increasingly available worldwide; however, global training and affordable equipment might be needed. Where advanced imaging or endoscopic assessment is not readily accessible, serial or combined assessments using clinical symptoms, biomarkers, and IUS, could provide a practical alternative for longitudinal monitoring until definitive endoscopic assessment becomes feasible. Future prospective studies evaluating pragmatic algorithms adapted to resource-limited health-care systems are needed to determine the most effective and cost-efficient implementation strategies.

Discussion

STRIDE-III integrates evidence that has accumulated since STRIDE-II into a more practical and explicit evidence-based framework. Clinical remission, biomarker normalisation, and endoscopic remission remain the principal goals. The major conceptual advance is the distinction among actionable targets, which support target-guided treatment change when the current therapy has been adequately optimised, adjunctive targets, which support treatment optimisation and tighter monitoring but do not necessarily warrant a change in therapeutic class, and patient-centred targets, which should be addressed through shared decision-making following careful aetiological evaluation and, when appropriate, multidisciplinary care.

Requiring prospective interventional evidence, including consideration of the number needed to treat to achieve one additional favourable outcome, before designating an endpoint as a treatment target helps balance therapeutic ambition against adverse effects, treatment burden, and cost. This is particularly important because associations between deeper remission and favourable outcomes do not necessarily establish that further treatment escalation to achieve that endpoint will improve outcomes. Conversely, there is a risk that some patients could cycle through all available therapies without achieving the increasingly stringent targets, or that a newly selected therapy might provide poorer overall disease control than the preceding one. Future strategies incorporating addition rather than replacement of therapies could mitigate this concern, but the evidence is currently insufficient to recommend such an approach routinely.

STRIDE-III should, therefore, be interpreted as a pragmatic framework of treatment principles rather than a rigid algorithm in which crossing a single numerical threshold automatically determines treatment change. Adjunctive targets, such as histological remission in ulcerative colitis and transmural remission in Crohn's disease, should not independently trigger treatment switching. Even when an actionable target remains unmet, decisions regarding treatment change should consider whether sufficient treatment-specific time has

elapsed, the magnitude of response, the location, severity and extent of residual inflammation, other objective targets, previous treatment response, available therapeutic alternatives, and patient preferences. In selected patients with limited residual activity and otherwise good disease control, continued therapy with close monitoring might be appropriate following shared decision-making. Conversely, persistent inflammatory activity above an actionable target after an adequate treatment interval and appropriate optimisation should prompt reconsideration of the treatment strategy. Optimisation of the current treatment should precede a change in therapeutic class where appropriate. Optimisation might include confirmation of adherence, dose or interval adjustment, TDM when relevant, and addition of nutritional or other concomitant therapy. TDM should be regarded as a tool to guide treatment optimisation, rather than as an independent treatment target by itself.

STRIDE-III introduces several additional updates. Bowel urgency is added as an early PRO, while fatigue is added to disability and quality of life as patient-centred treatment targets. The acceptable FC target threshold is refined to less than 200 µg/g, recognising that values less than 100 µg/g are associated with deeper disease control. Histological remission in ulcerative colitis and transmural remission in Crohn's disease are upgraded to adjunctive long-term targets. Timelines are updated for contemporary advanced and nutritional therapies.

This update also emphasises serial, multidimensional assessment rather than reliance on a single measure. Combining symptoms, CRP, FC, endoscopy, cross-sectional imaging, histology, growth, and patient-centred outcomes provides a more complete picture of inflammatory control and prognosis. A further addition is the adaptation for resource-limited settings in which the ambition of achieving objective treatment targets should not be reduced. Instead, monitoring strategies should be adapted to the objective measures available locally while maintaining the principles of treat-to-target care.

Several limitations of STRIDE-III should be acknowledged. First, although the recommendations were informed by systematic reviews, expert surveys, and formal consensus voting, the strength and nature of the supporting evidence differ across treatment targets. Interventional treat-to-target evidence remains limited. Therefore, some recommendations necessarily integrate indirect evidence across Crohn's disease and ulcerative colitis as well as age groups when direct evidence is unavailable. This applies mostly to the ulcerative colitis biomarker targets (figure 3). Moreover, proposed thresholds and treatment-specific timelines should be interpreted as pragmatic clinical guidance rather than absolute biological cutoffs. Finally, STRIDE-III applies to medically managed luminal IBD and should not be extrapolated directly to perianal disease, pouchitis, extraintestinal manifestations, or postoperative management.

As the evidence base evolves, future iterations of STRIDE could incorporate more complex longitudinal and multi-domain approaches that move beyond categorical target attainment. Emerging artificial intelligence (AI) tools might enable the integration of these multimodal patient-specific data to improve individualised risk prediction and treatment selection. Emerging multi-omics-based biomarkers could facilitate the assessment of molecular remission as a treatment target.¹⁸⁰ Priorities include predicting disease course and response, defining biological endotypes, and validating AI-supported decision tools. STRIDE-III should therefore be viewed as an adaptable framework rather than a final definition of care. By distinguishing actionable targets from prognostic and complementary measures, STRIDE-III allows new evidence to be incorporated while preserving the flexibility required for individualised decisions.

Contributors

DT and AD conceived the project, co-chaired the initiative, supervised the work, interpreted the evidence, and drafted the manuscript. DT, AD, VJ, ID, FM, and DTR served on the steering committee, defined the scope and review questions, developed the surveys and consensus statements, interpreted the findings, and guided the voting process. AR, SYB-A, SKV, VS, NB, MME, and YY conducted the systematic literature reviews, extracted and synthesised the evidence, and contributed to drafting the manuscript. MI, FR, RWL, WR, EVL Jr, LP-B, SD, RP, TY, SS, MD, VA, GJM, and CNB participated in the systematic review, and contributed to interpretation of the evidence, development of the consensus recommendations, and critical revision of the manuscript. All authors approved the final manuscript, accept responsibility for its content, and approved its submission. DT and AD had full access to the evidence summaries and take responsibility for the integrity of the work and the decision to submit. Members of IOIBD and Porto group who participated in the survey or statement voting can be found in the appendix (pp 10–12).

Declaration of interests

DT has received consulting fees, research grants, royalties, or honoraria from Janssen, Pfizer, Shaare Zedek Medical Center, Hospital for Sick Children, Ferring, AbbVie, Takeda, Lilly, SorrisoPharma, Boehringer Ingelheim, Galapagos, Bristol Myers Squibb (BMS), Alfasigma, Merck, and Genentech. SKV reports consulting fees from Alimentiv and speaker fees from Takeda. VS reports consulting fees from Johnson & Johnson (J&J) and Celltrion; speaker's fees from Pfizer, Takeda, Giuliani, Tillotts, Alfasigma; and travel grants from Lilly and AbbVie. MME reports speaker fees from Celltrion, Dr Falk, J&J, and Lilly. MI has received consulting fees, research grants, or honoraria from J&J, Takeda, Lilly, Olympus, Pentax, and Helmsley Charitable Trust. FR has served as a consultant to or on an advisory board for AbbVie, Abivax, Adiso, Adnovate, Agomab, Alimentiv, Allakos, Allergan, Anaptys, Arena, AstraZeneca, Bausch & Lomb, Boehringer-Ingelheim, Cabaletta, Cage, Cellarity, Celgene/BMS, Celltrion, CDISC, Celsius, Chemomab, Cowen, 89Bio, Empress, Enveda, Equillium, Eugit, Falk, Ferring, Flow Therapeutics, Forth Therapeutics, Frequency Therapeutics, Galapagos, Galmed, Genentech, Gilead, Gossamer, Granite, GSK, Guidepoint, Helios, Helmsley, Horizon Therapeutics, Image Analysis Limited, Imidomics, Index Pharma, Janssen, JT Pharma, Koutif, Landos, Lassen, Lilly, Medbiopharma, Merck, Mestag, Metacrine, Mirador, Mirum, Mobius, Mopac, Morpich, Myka Labs, Nxera, Ono, Organovo, Origo, Palisade, Pfizer, Pharvaris, Plant, Prometheus Biosciences, Radyus, Receptos, RedX, Roche, Rubix, Samsung, Sanofi, Sironax, SRT, Surmodics, Surrozen, Takeda, Techlab, Tentatrix, Teva, Thabor, Theravance, Thetis, Tillots, Transcenta, Tr1x Bio, UCB, Ventus, Versant, Viatrix, Virgo, Xencor, and Ysios. RWL has served on advisory boards for AbbVie, Aspen, BMS, Celgene, Celltrion, Chiesi, Ferring, Glutagen, Hospira, Janssen, Lilly, MSD, Novartis, Pfizer, Prometheus Biosciences, Takeda, and SPYRE; and received research grants from Joanna Tiddy University of Sydney, McCusker Charitable Foundation, Celltrion, Shire, Janssen, Takeda, Gastroenterological Society

of Australia, National Health and Medical Research Council, Gutsy Group, Pfizer, Medical Research Future Fund, and MSD. WR has served as a speaker for AbbVie, Alfasigma, Celltrion, Ferring, JNJ, Galapagos Medice, Lilly, MSD, Roche, Pfizer, Sobi, and Takeda; as a consultant for AbbVie, Alfasigma, Agomab, Alvotect, Anaptys Bio, Amgen, AOP Orphan, Boehringer Ingelheim, BMS, Calyx, Celltrion, Lilly, Galapagos, Gilead, Index Pharma, JNJ, Medahead, Microbiotica, MSD, OSE-Immunotherapeutics SA, Pfizer, Redex, Sanofi, Teva, Takeda, and Xencor; as an advisory board member for AbbVie, Agomab, Amgen, Boehringer Ingelheim, BMS, Celltrion, Galapagos, Janssen, Pfizer, Sanofi, and Teva; and has received research funding from AbbVie, Janssen, Sandoz, Sanofi, Takeda, and Xencor. EVL Jr has consulted for AbbVie, Abivax, Astellas, Biocon, Celltrion, Lilly, Gilead, Iota Bioscience, Iterative Health, J&J, Kymera, Merck, Ono Pharma, RegCell, Takeda, TRIX Bio, and Xencor; received research support from AbbVie, Gilead, J&J, Merck, and TRIX Bio; served on data monitoring committees for Lilly, Genentech, Morpich, Shattuck Labs, and Spyre; and owns shares in Exact Sciences and Moderna. LP-B reports consulting for AbbVie, Abivax, Adacyte, Alfasigma, Alimentiv, Amgen, Apini, Applied Molecular Transport, Arena, Banook, BMS, Celltrion, Cytokine Pharma, Enthera, Ferring, Fresenius Kabi, Galapagos, Genentech, Gilead, GlaxoSmithKline (GSK), IAG Image Analysis, Index Pharmaceuticals, Inotrem, Iterative Health, J&J, LifeMine, Lilly, Medac, Mopac, Morpich, MSD, Nordic Pharma, Novartis, Oncodesign, Precision Medicine, ONO Pharma, OSE Immunotherapeutics, Par Immune, Pfizer, Prometheus, Roche, Roivant, Samsung, Sandoz, Sanofi, Sorriso, Spyre, Takeda, Teva, ThirtyFiveBio, Tillotts, Vectivbio, Vedanta, and Ventyx; and received lecture fees from AbbVie, Alfasigma, Amgen, Arena, Biogen, Celltrion, Ferring, Galapagos, Genentech, Gilead, Iterative Health, J&J, Lilly, Medac, MSD, Nordic Pharma, Pfizer, Sandoz, Takeda, and Tillotts. SD has received honoraria as a speaker, consultant, and/or advisory board member from AbbVie, Allergan, Amgen, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Lilly, Enthera, Ferring, Gilead, Hospira, Inotrem, Janssen, J&J, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, TiGenix, UCB, and Vifor. RP reports consulting and/or speaker fees from Abbott, AbbVie, Abivax, Alimentiv, Alentis Therapeutics, Amgen, AnaptysBio, Apogee Therapeutics, AstraZeneca, Biogen, Boehringer Ingelheim, BMS, Caldera, Candid Therapeutics, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Lilly, Enthera, Ferring, Galapagos, Inviva, Fresenius Kabi, Genentech, Gilead Sciences, GSK, JAMP Bio, Janssen, Merck, Mirador, Net Biotix, Novartis, Oppilan Pharma, Odyssey Therapeutics, Organon, Oruka Therapeutics, Palisade, Pandion Pharma, Pendopharm, Pfizer, Progenity, Prometheus Biosciences, Protagonist Therapeutics, Repertoire Immune Medicines, Roche, Sandoz, Sanofi, Satisfai Health, Shire, Sorriso, Simcare Therapeutics, Shattuck Labs, Sublimity Therapeutics, Spyre Therapeutics, Takeda Pharmaceuticals, Teva, Tillotts, Theravance, Trellus, Union Biopharma, Viatrix, Ventyx, and UCB. TY declares fees for lectures and speakers bureaus from AbbVie, EA Pharma, JIMRO, Kissei Pharmaceutical, Gilead Sciences, Kyorin Pharmaceutical, Celltrion Healthcare Japan, Takeda, Mitsubishi Tanabe, Nippon Kayaku, Pfizer Japan, BMS, Mochida Pharmaceutical, and Janssen. SS has received personal fees from AbbVie, Amgen, Arena, Biogen, BMS, Celgene, Celltrion, Falk, Ferring, Fresenius Kabi, Galapagos, Gilead, IMAB, Janssen, Lilly, MSD, Mylan, Novartis, Pfizer, Protagonist, Prevention Bio, Roche, Sandoz/Hexal, Shire, Takeda, and Ventyx. SS is a co-inventor of intellectual property owned by CONARIS (the company holds patents for the IL-6 trans-signalling inhibitor olamkcept, of which development is at a pre-commercial stage; no payments have been or are yet received by SS). MD has acted as a consultant and received advisory fees from Abivax, AbbVie, AstraZeneca, Boehringer Ingelheim, BMS, Celltrion, Lilly and Company, Genentech, Janssen, J&J, Merck, Novartis, Pfizer, Prometheus Laboratories, Sanofi, Spyre Therapeutics, Takeda, Target RWE, and Tentatrix. CNB is supported by the Bingham Chair in Gastroenterology, and has served on advisory boards for AbbVie Canada, Amgen Canada, BMS Canada, Celltrion, Lilly Canada, Ferring Canada, Fresenius-Kabi Canada, Janssen Canada, Pendopharm Canada, Sandoz Canada, Takeda Canada, and Pfizer Canada; received educational grants from AbbVie Canada, Boston Scientific, BMS Canada, Lilly, Ferring Canada, Pfizer Canada, Takeda Canada, Janssen Canada, Organon Canada, Lilly

Canada, and Amgen Canada; has acted on speaker's panels for AbbVie Canada, Fresenius-Kabi Canada, Janssen Canada, Pfizer Canada, and Takeda Canada; and received research funding from AbbVie Canada, Amgen Canada, Sandoz Canada, Takeda Canada, and Pfizer Canada. DTR has received grant support from Takeda, Pfizer, and Gastrointestinal Research Foundation; has served as a consultant for AbbVie, Abivax, Altrubio, Athos Therapeutics, BMS, Celltrion, Clostrabio, Connect BioPharma, Lilly, Genentech (Roche), Gilead, Iterative Health, J&J, Merck, Mirador, Odyssey Therapeutics, Pfizer, Sanofi, Spyre, Takeda Pharmaceuticals, Throne, Vedanta Biosciences, and Ventyx; has received honoraria for lectures from AbbVie, J&J, Pfizer and Takeda; has received payment for expert testimony from Goldman Ismail, has participated in a data safety monitoring board (DSMB) for TRX; and holds stock options from Iterative Health. GJM reports consulting fees from AbbVie, Takeda, and Sandoz; speaker's fees from Pfizer, Takeda, AbbVie, J&J, Ferring, Sandoz, Inovis, Cube, BMS, High5MD, and Vianex; travel grants from Ferring, AbbVie, J&J, Cube, Sandoz, and Vianex; and fees for participation in DSMBs or advisory boards from Takeda, AbbVie, J&J, BMS, Sandoz, and Vianex. FM has received lecture fees from AbbVie, Abivax, Adaclyte, Alfasigma, Amgen, BMS, Celltrion, Ferring, Falk, Fresenius Kabi, Galapagos, Gilead, GSK, Janssen, Lilly, Laboratorios Vitoria, MSD, OM Pharma, Pfizer, Roche, Sandoz, Sanofi, Takeda, Teva, and Tillotts. ID reports fees for consultation, advisory boards, honoraria for speaking and teaching, royalties, or grant support from AbbVie, American Gastroenterology Association, AstraZeneca, Athos, Agomab, BMS, Lilly, Falk Pharma, Ferring, Friedevents AG, Gilead, Galapagos, IBDnet, Institut des MICI, Roche, Janssen, Materia Prima, Mirador, MSD, Nestle, Pfizer, Prometheus Biosciences, Sandoz, Sangamo, Spyre Therapeutics, and Takeda; she is shareholder, co-founder, and medical director of Harp Diagnostics (a medical diagnostics company developing a rapid remote and point-of-care monitoring platform for inflammatory bowel disease and other gastrointestinal conditions, which had no involvement with any aspect of this paper). VJ has received consulting fees from AbbVie, Abivax, Alimentiv, Amgen, Anaptys Bio, Asahi Kasei, Asieris, AstraZeneca, Attovia, Blackbird Labs, BMS, Boehringer Ingelheim, BiomeBank, Cabaletta, Caldera, Calluna, Campfield, Catalytic Health, Celltrion, Ensho, Enthera, Enveda, Equilibrium, Exeliome Biosciences, Ferring, Fresenius Kabi, Gilead, Granite Bio, GSK, Hengrui, Janssen, Lilly, Merck, Mobius, MRM Health, Nxera, Orbimed, Organon, OSE Immunotherapeutics, Palisade Bio, Pendopharm, Pioneering Medicine, Pfizer, Pharmanest, Pipr Therapeutics, Prometheus, Protillion, Roche/Genentech, Sanofi, SCOPE, Shattuck Labs, Sinomab, Sorriso, Spyre, Synedgen, Takeda, Teva, ThirtyFiveBio, Tillotts, Throne Scientific, TriX, UCB, Union Therapeutics, Ventus, Ventyx, Vividion, Xencor, and Zealand Pharma; payment for lectures from AbbVie, Ferring, Janssen, Pfizer, Takeda, and Lilly; and has participated in DSMBs for AbbVie, Takeda, Janssen, BMS, Fresenius Kabi, Gilead, Roche, Lilly, Boehringer Ingelheim, BiomeBank, Caldera, Celltrion, Pfizer, and Abivax. AD reports fees for participation in clinical trials, review activities such as DSMBs, statistical analysis, and endpoint committees from Abivax, AbbVie, Falk, J&J, Pfizer, and Takeda; consultancy fees from AbbVie, Alfasigma, Amgen, J&J, Lilly, MSD, Pfizer, Pharmacosmos, Roche, Sandoz, Stada, and Takeda; payment from lectures including service on speakers bureaus from AbbVie, Alfasigma, CED Service GmbH, Celltrion, Falk, Fresenius Kabi, Ferring, Gilead, Hexal, High5MD, J&J, Materia Prima, MedToday, MSD, Pfizer, Sandoz, Streamed-Up, Takeda, and Vifor Pharma; and payment for manuscript preparation from AbbVie, Falk, J&J, Takeda, Thieme, and UniMed Verlag. AR, SYB-A, NB, YY, and VA declare no competing interests.

Acknowledgments

This work was supported by the International Organization for the Study of Inflammatory Bowel Disease. The authors used ChatGPT and Claude to assist with language editing, grammar, and readability as well as to summarise the responses to the surveys and to improve the presentation of the figures. The authors reviewed and edited all AI-assisted output and take full responsibility for the content of the manuscript.

References

- Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): determining therapeutic goals for treat-to-target. *Am J Gastroenterol* 2015; **110**: 1324–38.
- Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: an update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): determining therapeutic goals for treat-to-target strategies in IBD. *Gastroenterology* 2021; **160**: 1570–83.
- Ricciuto A, Yuval Bar-Asher S, Solitano V, et al. Evidence for treatment targets in Crohn's disease: a systematic review and evidence map informing STRIDE-III. *Lancet Gastroenterol Hepatol* (in press).
- Ricciuto A, Yuan Y, Bock N, et al. Evidence for treatment targets in ulcerative colitis: a systematic review and evidence map informing STRIDE-III. *Lancet Gastroenterol Hepatol* (in press).
- Ma C, Hanzel J, Panaccione R, et al. CORE-IBD: a multidisciplinary international consensus initiative to develop a core outcome set for randomized controlled trials in inflammatory bowel disease. *Gastroenterology* 2022; **163**: 950–64.
- Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. *Lancet* 1980; **1**: 514.
- Turner D, Levine A, Walters TD, et al. Which PCDAI version best reflects intestinal inflammation in pediatric Crohn disease? *J Pediatr Gastroenterol Nutr* 2017; **64**: 254–60.
- Turner D, Griffiths AM, Walters TD, et al. Mathematical weighting of the pediatric Crohn's disease activity index (PCDAI) and comparison with its other short versions. *Inflamm Bowel Dis* 2012; **18**: 55–62.
- Lewis JD, Rutgeerts P, Feagan BG, et al. Correlation of stool frequency and abdominal pain measures with Simple Endoscopic Score for Crohn's Disease. *Inflamm Bowel Dis* 2020; **26**: 304–13.
- Khanna R, Zou G, D'Haens G, et al. A retrospective analysis: the development of patient reported outcome measures for the assessment of Crohn's disease activity. *Aliment Pharmacol Ther* 2015; **41**: 77–86.
- Ha C, Naegeli AN, Lukanova R, et al. Rectal urgency among patients with ulcerative colitis or Crohn's disease: analyses from a global survey. *Crohn's Colitis* 2023; **5**: otad052.
- Naegeli AN, Hunter T, Dong Y, et al. Full, partial, and modified permutations of the Mayo score: characterizing clinical and patient-reported outcomes in ulcerative colitis patients. *Crohn's Colitis* 2021; **3**: otab007.
- Jairath V, Khanna R, Zou GY, et al. Development of interim patient-reported outcome measures for the assessment of ulcerative colitis disease activity in clinical trials. *Aliment Pharmacol Ther* 2015; **42**: 1200–10.
- Wine E, Aloï M, Van Biervliet S, et al. Management of paediatric ulcerative colitis, part 1: ambulatory care—an updated evidence-based consensus guideline from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition and the European Crohn's and Colitis Organisation. *J Pediatr Gastroenterol Nutr* 2025; **81**: 765–815.
- Assa A, Aloï M, Van Biervliet S, et al. Management of paediatric ulcerative colitis, part 2: acute severe colitis—an updated evidence-based consensus guideline from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition and the European Crohn's and Colitis Organisation. *J Pediatr Gastroenterol Nutr* 2025; **81**: 816–51.
- Arias MT, Vande Casteele N, Vermeire S, et al. A panel to predict long-term outcome of infliximab therapy for patients with ulcerative colitis. *Clin Gastroenterol Hepatol* 2015; **13**: 531–38.
- Atia O, Klomberg RCW, de Ridder L, et al. Validation of predictive models for disease outcomes in paediatric ulcerative colitis: a multicentre prospective inception cohort. *Aliment Pharmacol Ther* 2023; **58**: 182–90.
- Gray FL, Turner CG, Zurakowski D, et al. Predictive value of the Pediatric Ulcerative Colitis Activity Index in the surgical management of ulcerative colitis. *J Pediatr Surg* 2013; **48**: 1540–45.
- Lee JJ, Colman RJ, Mitchell PD, Atmadja ML, Bousvaros A, Lightdale JR. Agreement between patient- and physician-completed Pediatric Ulcerative Colitis Activity Index scores. *J Pediatr Gastroenterol Nutr* 2011; **52**: 708–13.
- Turner D, Seow CH, Greenberg GR, Griffiths AM, Silverberg MS, Steinhart AH. A systematic prospective comparison of noninvasive disease activity indices in ulcerative colitis. *Clin Gastroenterol Hepatol* 2009; **7**: 1081–88.

- 21 Turner D, Hyams J, Markowitz J, et al. Appraisal of the pediatric ulcerative colitis activity index (PUCAI). *Inflamm Bowel Dis* 2009; 15: 1218–23.
- 22 Turner D, Otley AR, Mack D, et al. Development, validation, and evaluation of a pediatric ulcerative colitis activity index: a prospective multicenter study. *Gastroenterology* 2007; 133: 423–32.
- 23 Ricciuto A, Carman N, Benchimol EI, et al. Prospective evaluation of endoscopic and histologic indices in pediatric ulcerative colitis using centralized review. *Am J Gastroenterol* 2021; 116: 2052–59.
- 24 Shimizu H, Ebana R, Kudo T, et al. Both fecal calprotectin and fecal immunochemical tests are useful in children with inflammatory bowel disease. *J Gastroenterol* 2022; 57: 344–56.
- 25 Turner D, Griffiths AM, Veerman G, et al. Endoscopic and clinical variables that predict sustained remission in children with ulcerative colitis treated with infliximab. *Clin Gastroenterol Hepatol* 2013; 11: 1460–65.
- 26 Schechter A, Griffiths C, Gana JC, et al. Early endoscopic, laboratory and clinical predictors of poor disease course in paediatric ulcerative colitis. *Gut* 2015; 64: 580–88.
- 27 Golovics PA, Goncz L, Reinglas J, et al. Patient-reported outcome and clinical scores are equally accurate in predicting mucosal healing in ulcerative colitis: a prospective study. *Dig Dis Sci* 2022; 67: 3089–95.
- 28 Loftus EV Jr, Colombel JF, Takeuchi K, et al. Upadacitinib therapy reduces ulcerative colitis symptoms as early as day 1 of induction treatment. *Clin Gastroenterol Hepatol* 2023; 21: 2347–58.
- 29 Marcovitch L, Focht G, Carmon N, et al. Development and validation of the TUMMY-UC: a patient-reported outcome for pediatric ulcerative colitis. *Gastroenterology* 2023; 164: 610–18.
- 30 Marcovitch L, Focht G, Horesh A, et al. Agreement on symptoms between children with ulcerative colitis and their caregivers: towards developing the TUMMY-UC. *J Pediatr Gastroenterol Nutr* 2021; 73: e35–38.
- 31 Marcovitch L, Nissan A, Mack D, et al. Item generation and reduction toward developing a patient-reported outcome for pediatric ulcerative colitis (TUMMY-UC). *J Pediatr Gastroenterol Nutr* 2017; 64: 373–77.
- 32 Sninsky JA, Barnes EL, Zhang X, Long MD. Urgency and its association with quality of life and clinical outcomes in patients with ulcerative colitis. *Am J Gastroenterol* 2022; 117: 769–76.
- 33 Dubinsky MC, Shan M, Delbecq L, et al. Psychometric evaluation of the urgency NRS as a new patient-reported outcome measure for patients with ulcerative colitis. *J Patient Rep Outcomes* 2022; 6: 114.
- 34 Kopylov U, Yung DE, Engel T, et al. Fecal calprotectin for the prediction of small-bowel Crohn's disease by capsule endoscopy: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol* 2016; 28: 1137–44.
- 35 Dubinsky MC, Magro F, Steinwurz F, et al. Association of C-reactive protein and partial Mayo score with response to tofacitinib induction therapy: results from the ulcerative colitis clinical program. *Inflamm Bowel Dis* 2023; 29: 51–61.
- 36 Suárez Ferrer C, Mesonero Gismero F, Caballol B, et al. Efficacy and safety of biological treatment for inflammatory bowel disease in elderly patients: results from a GETECCU cohort. *Gastroenterol Hepatol* 2024; 47: 502197.
- 37 Atia O, Shavit-Brunschwig Z, Mould DR, et al. Outcomes, dosing, and predictors of vedolizumab treatment in children with inflammatory bowel disease (VEDOKIDS): a prospective, multicentre cohort study. *Lancet Gastroenterol Hepatol* 2023; 8: 31–42.
- 38 Lasso A, Stotzer PO, Öhman L, Isaksson S, Sapnara M, Strid H. The intra-individual variability of faecal calprotectin: a prospective study in patients with active ulcerative colitis. *J Crohns Colitis* 2015; 9: 26–32.
- 39 Zeng J, Yu W, Gao X, Yu Y, Zhou Y, Pan X. Establishing reference values for age-related fecal calprotectin in healthy children aged 0–4 years: a systematic review and meta-analysis. *PeerJ* 2025; 13: e19572.
- 40 Shiga H, Abe I, Onodera M, et al. Serum C-reactive protein and albumin are useful biomarkers for tight control management of Crohn's disease in Japan. *Sci Rep* 2020; 10: 511.
- 41 Sollelis E, Quinard RM, Bouguen G, et al. Combined evaluation of biomarkers as predictor of maintained remission in Crohn's disease. *World J Gastroenterol* 2019; 25: 2354–64.
- 42 Song JH, Hong SN, Lee JE, et al. C-Reactive protein reduction rate following initiation of anti-tumor necrosis factor α induction therapy predicts secondary loss of response in patients with Crohn's disease. *Scand J Gastroenterol* 2019; 54: 876–85.
- 43 Cornillie F, Hanauer SB, Diamond RH, et al. Postinduction serum infliximab trough level and decrease of C-reactive protein level are associated with durable sustained response to infliximab: a retrospective analysis of the ACCENT I trial. *Gut* 2014; 63: 1721–27.
- 44 Reinisch W, Panaccione R, Bossuyt P, et al. Biomarker correlation with endoscopic outcomes in patients with Crohn's disease: data from CALM. *J Crohn Colitis* 2018; 12 (suppl 1): S011 (OP5).
- 45 Colombel JF, Panaccione R, Bossuyt P, et al. Effect of tight control management on Crohn's disease (CALM): a multicentre, randomised, controlled phase 3 trial. *Lancet* 2017; 390: 2779–89.
- 46 Lasso A, Öhman L, Stotzer PO, et al. Pharmacological intervention based on fecal calprotectin levels in patients with ulcerative colitis at high risk of a relapse: a prospective, randomized, controlled study. *United European Gastroenterol J* 2015; 3: 72–79.
- 47 Osterman MT, Abernethy FN, Cross R, et al. Mesalamine dose escalation reduces fecal calprotectin in patients with quiescent ulcerative colitis. *Clin Gastroenterol Hepatol* 2014; 12: 1887–93.
- 48 Danese S, Fiorino G, Vicaute E, et al. Clinical trial: a pragmatic randomised controlled study to assess the effectiveness of two patient management strategies in mild to moderate ulcerative colitis-the OPTIMISE study. *J Clin Med* 2024; 13: 5147.
- 49 Dulai PS, Feagan BG, Sands BE, Chen J, Lasch K, Lirio RA. Prognostic value of fecal calprotectin to inform treat-to-target monitoring in ulcerative colitis. *Clin Gastroenterol Hepatol* 2023; 21: 456–66.
- 50 Helwig U, Krause TH, Maaser C, et al. Early Monitoring of Response (MORE) to golimumab therapy: results of a multicentre, prospective observational trial. *Dig Dis* 2023; 41: 239–49.
- 51 Krishnakumar C, Ananthakrishnan AN, Boyle BM, et al. Early change in fecal calprotectin predicts one-year outcome in children newly diagnosed with ulcerative colitis. *J Pediatr Gastroenterol Nutr* 2022; 74: 72–78.
- 52 Cui J, Li X, Zhang Z, Gao H, Li J. Common laboratory blood test immune panel markers are useful for grading ulcerative colitis endoscopic severity. *BMC Gastroenterol* 2022; 22: 540.
- 53 Vermeire S, Van Assche G, Rutgeerts P. Laboratory markers in IBD: useful, magic, or unnecessary toys? *Gut* 2006; 55: 426–31.
- 54 D'Haens G, Higgins PDR, Peyrin-Biroulet L, et al. Extended induction and prognostic indicators of response in patients treated with mirikizumab with moderately to severely active ulcerative colitis in the LUCENT trials. *Inflamm Bowel Dis* 2024; 30: 2335–46.
- 55 Danese S, Vermeire S, D'Haens G, et al. Treat to target versus standard of care for patients with Crohn's disease treated with ustekinumab (STARDUST): an open-label, multicentre, randomised phase 3b trial. *Lancet Gastroenterol Hepatol* 2022; 7: 294–306.
- 56 Ben-Horin S, Lahat A, Ungar B, et al. Capsule endoscopy-guided proactive treat-to-target versus continued standard care in patients with quiescent Crohn's disease: a randomized controlled trial. *Gastroenterology* 2025; 169: 85–93.
- 57 Ungaro RC, Yzet C, Bossuyt P, et al. Deep remission at 1 year prevents progression of early Crohn's disease. *Gastroenterology* 2020; 159: 139–47.
- 58 Bossuyt P, Rahier JF, Baert F, et al. The effect of dose intensification after secondary loss of response to ustekinumab in Crohn's disease: results of the RESCUE study. *Gastroenterology* 2026; 171: 99–109.
- 59 Gaidos JKJ, Al Bawady B, Farraye FA, Regueiro M. Use of standardized inflammatory bowel disease endoscopy scores in clinical practice. *Crohn's Colitis* 360 2023; 5: otad037.
- 60 Rivière P, D'Haens G, Peyrin-Biroulet L, et al. Location but not severity of endoscopic lesions influences endoscopic remission rates in Crohn's disease: a post hoc analysis of TAILORIX. *Am J Gastroenterol* 2021; 116: 134–41.
- 61 Danese S, Panaccione R, Feagan BG, et al. Efficacy and safety of 48 weeks of guselkumab for patients with Crohn's disease: maintenance results from the phase 2, randomised, double-blind GALAXI-1 trial. *Lancet Gastroenterol Hepatol* 2024; 9: 133–46.
- 62 Tang W, Hu W, Shi P, et al. The SES-CD could be a predictor of short- and long-term mucosal healing after exclusive enteral nutrition in pediatric Crohn's disease patients. *Front Pediatr* 2022; 10: 874425.
- 63 Lee SD, Singla A, Harper J, et al. Tofacitinib appears well tolerated and effective for the treatment of patients with refractory Crohn's disease. *Dig Dis Sci* 2022; 67: 4043–48.

- 64 Wu Y, Zhang L, Cao J, et al. Efficacy of infliximab treatment on the mucosal healing of different intestinal segments in patients with ileocolonic Crohn's disease. *Therap Adv Gastroenterol* 2020; **13**: 1756284820976923.
- 65 Oliva S, Aloï M, Viola F, et al. A treat to target strategy using panenteric capsule endoscopy in pediatric patients with Crohn's disease. *Clin Gastroenterol Hepatol* 2019; **17**: 2060–67.
- 66 D'Arcangelo G, Russo G, Aloï M, et al. A treat-to-target strategy guided by pan-enteric evaluation in children with Crohn's disease improves outcomes at 2 years. *Inflamm Bowel Dis* 2024; **30**: 1303–08.
- 67 Ricciuto A, Fish JR, Tomalty DE, et al. Diagnostic delay in Canadian children with inflammatory bowel disease is more common in Crohn's disease and associated with decreased height. *Arch Dis Child* 2018; **103**: 319–26.
- 68 Bossuyt P, Baert F, D'Heygere F, et al. Early mucosal healing predicts favorable outcomes in patients with moderate to severe ulcerative colitis treated with golimumab: data from the real-life BE-SMART cohort. *Inflamm Bowel Dis* 2019; **25**: 156–62.
- 69 Ito A, Murasugi S, Omori T, Nakamura S, Tokushige K. Relationship between mucosal healing by tacrolimus and relapse of refractory ulcerative colitis: a retrospective study. *BMC Gastroenterol* 2020; **20**: 203.
- 70 Rath T, Atreya R, Bodenschatz J, et al. Healing of the epithelial barrier in the ileum is superior to endoscopic and histologic remission for predicting major adverse outcomes in ulcerative colitis. *Front Med (Lausanne)* 2023; **10**: 1221449.
- 71 Magro F, Pai RK, Kobayashi T, et al. Resolving histological inflammation in ulcerative colitis with mirikizumab in the LUCENT induction and maintenance trial programmes. *J Crohns Colitis* 2023; **17**: 1457–70.
- 72 Di Ruscio M, Variola A, Vernia F, et al. Role of Ulcerative Colitis Endoscopic Index of Severity (UCEIS) versus Mayo endoscopic subscore (MES) in predicting patients' response to biological therapy and the need for colectomy. *Digestion* 2021; **102**: 534–45.
- 73 Zhang XF, Li P, Ding XL, et al. Comparing the clinical application values of the Degree of Ulcerative Colitis Burden of Luminal Inflammation (DUBLIN) score and Ulcerative Colitis Endoscopic Index of Severity (UCEIS) in patients with ulcerative colitis. *Gastroenterol Rep (Oxf)* 2021; **9**: 533–42.
- 74 Liang RF, Lin H, Chau CY, Lim WC. Histologic healing and clinical outcomes in ulcerative colitis. *Intest Res* 2025; **23**: 182–92.
- 75 Pai RK, Hartman DJ, Rivers CR, et al. Complete resolution of mucosal neutrophils associates with improved long-term clinical outcomes of patients with ulcerative colitis. *Clin Gastroenterol Hepatol* 2020; **18**: 2510–17.
- 76 Liu L, Ouyang H, Su J, et al. Increased modified DUBLIN scores are associated with serious ulcerative colitis and treatment failure. *Therap Adv Gastroenterol* 2022; **15**: 17562848221142671.
- 77 Shimodaira Y, Watanabe K, Fukuda S, et al. Limited endoscopic mucosal inflammation on equivalent to Mayo endoscopic subscore of 0 unaffected clinical relapse of ulcerative colitis. *Scand J Gastroenterol* 2022; **57**: 165–68.
- 78 Osterman MT, Scott FI, Fogt FF, et al. Endoscopic and histological assessment, correlation, and relapse in clinically quiescent ulcerative colitis (MARQUEE). *Inflamm Bowel Dis* 2021; **27**: 207–14.
- 79 Viscido A, Valvano M, Stefanelli G, et al. Systematic review and meta-analysis: the advantage of endoscopic Mayo score 0 over 1 in patients with ulcerative colitis. *BMC Gastroenterol* 2022; **22**: 92.
- 80 George LA, Feldman HT, Alizadeh M, et al. Histologic inflammation can predict future clinical relapse in ulcerative colitis patients in endoscopic remission. *Crohns Colitis* 2023; **5**: otad059.
- 81 Fukuda T, Naganuma M, Sugimoto S, et al. Efficacy of therapeutic intervention for patients with an ulcerative colitis Mayo endoscopic score of 1. *Inflamm Bowel Dis* 2019; **25**: 782–88.
- 82 Ruan GC, Jin X, Zhou WX, et al. External validation of the Paddington International Virtual Electronic ChromoendoScopy ScOre as a good endoscopic score to define mucosal healing and predict long-term clinical outcomes in ulcerative colitis. *J Dig Dis* 2022; **23**: 446–54.
- 83 Cannatelli R, Bazarova A, Furfaro F, et al. Reproducibility of the electronic chromoendoscopy PICaSSO score (Paddington International Virtual ChromoendoScopy ScOre) in ulcerative colitis using multiple endoscopic platforms: a prospective multicenter international study (with video). *Gastrointest Endosc* 2022; **96**: 73–83.
- 84 Jairath V, Colombel J-F, D'Haens GR, et al. Defining the optimal treatment target in moderate-to-severely active ulcerative colitis (VERDICT): a phase 4, randomised controlled trial. *Lancet* (in press).
- 85 Park SB, Kim SJ, Lee J, et al. Efficacy of sigmoidoscopy for evaluating disease activity in patients with ulcerative colitis. *BMC Gastroenterol* 2022; **22**: 83.
- 86 Patel ST, Jena A, Chandnani S, et al. Adequacy of sigmoidoscopy as compared to colonoscopy for assessment of disease activity in patients of ulcerative colitis: a prospective study. *Intest Res* 2024; **22**: 310–18.
- 87 Yuval Bar-Asher S, Orlanski-Meyer E, Shamasnah I, Yogev D, Turner D. Sigmoidoscopy is sufficient to assess endoscopic response to therapy in pediatric ulcerative colitis: A cohort study. *J Pediatr Gastroenterol Nutr* 2026; **82**: 98–102.
- 88 Shehab M, Al Akram S, Hassan A, Alrashed F, Jairath V, Bessissow T. Histological disease activity as predictor of clinical relapse, hospitalization, and surgery in inflammatory bowel disease: systematic review and meta-analysis. *Inflamm Bowel Dis* 2024; **30**: 563–72.
- 89 Christensen B, Erlich J, Gibson PR, Turner JR, Hart J, Rubin DT. Histologic healing is more strongly associated with clinical outcomes in ileal Crohn's disease than endoscopic healing. *Clin Gastroenterol Hepatol* 2020; **18**: 2518–25.
- 90 Yoon H, Jang S, Dulai PS, et al. Histologic remission is associated with lower risk of treatment failure in patients with Crohn disease in endoscopic remission. *Inflamm Bowel Dis* 2021; **27**: 1277–84.
- 91 Ahmad H, Click B, Morris HL, et al. Factors predicting loss of remission in Crohn's disease patients in endoscopic remission in the real world: results from TARGET-IBD. *J Clin Gastroenterol* 2025; **59**: 245–50.
- 92 Marion L, Amélie B, Zoubir D, et al. Histological indices and risk of recurrence in Crohn's disease: a retrospective study of a cohort of patients in endoscopic remission. *Inflamm Bowel Dis* 2022; **28**: 1395–404.
- 93 Hu AB, Tan W, Deshpande V, Ananthakrishnan AN. Ileal or colonic histologic activity is not associated with clinical relapse in patients with Crohn's disease in endoscopic remission. *Clin Gastroenterol Hepatol* 2021; **19**: 1226–33.
- 94 Reenaers C, Enea D, Nachury M, et al. Impact of histological remission for predicting clinical relapse in Crohn's disease: a post hoc analysis of the prospective STORI cohort. *J Crohns Colitis* 2025; **19**: jjae167.
- 95 Zhang T, Zhang QD, Jin T, et al. Is histological healing more clinically valuable than endoscopic healing in Crohn's disease? *Eur J Gastroenterol Hepatol* 2023; **35**: 1143–48.
- 96 Magro F, Protic M, De Hertogh G, et al. Effects of mirikizumab on histologic resolution of Crohn's disease in a randomized controlled phase 2 trial. *Clin Gastroenterol Hepatol* 2024; **22**: 1878–88.
- 97 Pabla BS, Alex Wiles C, Slaughter JC, et al. Safety and efficacy of vedolizumab versus tumor necrosis factor α antagonists in an elderly IBD population: a single institution retrospective experience. *Dig Dis Sci* 2022; **67**: 3129–37.
- 98 Danese S, Sandborn WJ, Colombel J-F, et al. Endoscopic, radiologic, and histologic healing with vedolizumab in patients with active Crohn's disease. *Gastroenterology* 2019; **157**: 1007–18.
- 99 Baldwin K, Goldfarb A, Brimacombe M, Hopkins D, Hyams JS. Methotrexate for primary maintenance therapy in mild-to-moderate Crohn disease in children. *J Pediatr Gastroenterol Nutr* 2022; **75**: 320–24.
- 100 Scarallo L, Alvisi P, Bolasco G, et al. Mucosal and histologic healing in children with inflammatory bowel disease treated with antitumor necrosis factor- α . *J Pediatr Gastroenterol Nutr* 2021; **72**: 728–35.
- 101 Lee SD, Mau B, Avalos CJ, Clark-Snustad KD, Kamp KJ, Gui X. Discordance between endoscopic and histopathologic assessment in ileal Crohn's disease. *World J Gastrointest Endosc* 2025; **17**: 101284.
- 102 He T, Zong L, Pan P, Sun S, Qu H. Predicting histological healing and recurrence in ulcerative colitis by assessing mucosal vascular pattern under narrow-band imaging endoscopy. *Front Med (Lausanne)* 2022; **9**: 869981.

- 103 Park J, Kang SJ, Yoon H, et al. Histologic evaluation using the Roberts Histopathology Index in patients with ulcerative colitis in deep remission and the association of histologic remission with risk of relapse. *Inflamm Bowel Dis* 2022; **28**: 1709–16.
- 104 Christensen B, Hanauer SB, Gibson PR, Turner JR, Hart J, Rubin DT. Segmental histological normalisation occurs in ulcerative colitis but does not improve clinical outcomes. *J Crohns Colitis* 2020; **14**: 1345–53.
- 105 Silva JC, Fernandes C, Rodrigues J, et al. Endoscopic and histologic activity assessment considering disease extent and prediction of treatment failure in ulcerative colitis. *Scand J Gastroenterol* 2020; **55**: 1157–62.
- 106 D'Amico F, Guillo L, Baumann C, Danese S, Peyrin-Biroulet L. Histological disease activity measured by the Nancy index is associated with long-term outcomes in patients with ulcerative colitis. *J Crohns Colitis* 2021; **15**: 1631–40.
- 107 Seong G, Song JH, Kim JE, et al. Histologic activity and steroid use history are risk factors of clinical relapse in ulcerative colitis with Mayo endoscopic subscore of 0 or 1. *Inflamm Bowel Dis* 2023; **29**: 238–44.
- 108 Parigi TL, Cannatelli R, Nardone OM, et al. Neutrophil-only histological assessment of ulcerative colitis correlates with endoscopic activity and predicts long-term outcomes in a multicentre study. *J Crohns Colitis* 2023; **17**: 1931–38.
- 109 Kaneshiro M, Takenaka K, Suzuki K, et al. Pancolonic endoscopic and histologic evaluation for relapse prediction in patients with ulcerative colitis in clinical remission. *Aliment Pharmacol Ther* 2021; **53**: 900–07.
- 110 Narula N, Aruljothy A, Alshahrani AA, et al. Histologic remission does not offer additional benefit for ulcerative colitis patients in endoscopic remission. *Aliment Pharmacol Ther* 2020; **52**: 1676–82.
- 111 Tse CS, Nguyen HP, Singh S, et al. Correlations between gastrointestinal symptoms and endoscopic-histologic disease activity in adults with ulcerative colitis. *Dig Dis Sci* 2023; **68**: 3254–58.
- 112 Kim JE, Kim M, Kim MJ, et al. Histologic improvement predicts endoscopic remission in patients with ulcerative colitis. *Sci Rep* 2024; **14**: 19926.
- 113 Jangi S, Yoon H, Dulai PS, et al. Predictors and outcomes of histological remission in ulcerative colitis treated to endoscopic healing. *Aliment Pharmacol Ther* 2020; **52**: 1008–16.
- 114 Zhang K, Xie J, Zhao J, Jia M. Predictive value of PHRI for recurrence within one year after UC treatment: a retrospective study. *Br J Hosp Med (Lond)* 2024; **85**: 1–11.
- 115 El-Zimaity H, Shaffer SR, Riddell RH, Pai RK, Bernstein CN. Beyond neutrophils for predicting relapse and remission in ulcerative colitis. *J Crohns Colitis* 2023; **17**: 767–76.
- 116 González-Partida I, Martínez-Lozano H, González-Lois C, et al. Histological inflammatory activity can predict endoscopic relapse in patients with ulcerative colitis who have achieved mucosal healing. *Eur J Gastroenterol Hepatol* 2021; **33** (suppl 1): e796–802.
- 117 Nardone OM, Bazarova A, Bhandari P, et al. PICaSSO virtual electronic chromoendoscopy accurately reflects combined endoscopic and histological assessment for prediction of clinical outcomes in ulcerative colitis. *United European Gastroenterol J* 2022; **10**: 147–59.
- 118 Zeina T, Gandhi S, Mittal A, et al. Predictors and etiologies of clinical relapse among patients with ulcerative colitis in deep remission. *J Clin Gastroenterol* 2024; **58**: 195–99.
- 119 Cushing KC, Tan W, Alpers DH, Deshpande V, Ananthakrishnan AN. Complete histologic normalisation is associated with reduced risk of relapse among patients with ulcerative colitis in complete endoscopic remission. *Aliment Pharmacol Ther* 2020; **51**: 347–55.
- 120 Shin SY, Kim HS, Kim K, et al. Histologic features and predicting prognosis in ulcerative colitis patients with mild endoscopic activity. *Korean J Intern Med* 2024; **39**: 68–76.
- 121 Li K, Strauss R, Marano C, et al. A simplified definition of histologic improvement in ulcerative colitis and its association with disease outcomes up to 30 weeks from initiation of therapy: post hoc analysis of three clinical trials. *J Crohns Colitis* 2019; **13**: 1025–35.
- 122 Rath T, Atreya R, Bodenschatz J, et al. Intestinal barrier healing is superior to endoscopic and histologic remission for predicting major adverse outcomes in inflammatory bowel disease: the prospective ERICA trial. *Gastroenterology* 2023; **164**: 241–55.
- 123 Goodsall TM, An YK, Andrews JM, et al. Reliability of intestinal ultrasound for evaluating Crohn's disease activity using point-of-care and central reading. *Clin Gastroenterol Hepatol* 2025; **23**: 1600–11.
- 124 Weinstein-Nakar I, Focht G, Church P, et al. Associations among mucosal and transmural healing and fecal level of calprotectin in children with Crohn's disease. *Clin Gastroenterol Hepatol* 2018; **16**: 1089–97.
- 125 Lafeuille P, Hordonneau C, Vignette J, et al. Transmural healing and MRI healing are associated with lower risk of bowel damage progression than endoscopic mucosal healing in Crohn's disease. *Aliment Pharmacol Ther* 2021; **53**: 577–86.
- 126 Noh SM, Oh EH, Park SH, et al. Association of faecal calprotectin level and combined endoscopic and radiological healing in patients with Crohn's disease receiving anti-tumour necrosis factor therapy. *J Crohns Colitis* 2020; **14**: 1231–40.
- 127 Oh K, Oh EH, Noh SM, et al. Combined endoscopic and radiologic healing is associated with a better prognosis than endoscopic healing only in patients with Crohn's disease receiving anti-TNF therapy. *Clin Transl Gastroenterol* 2022; **13**: e00442.
- 128 Lu Y, Xiong S, Zhang M, et al. Long-term outcomes and associated factors of Crohn's disease patients achieving transmural healing based on magnetic resonance enterography: a Chinese retrospective cohort study. *Ther Adv Chronic Dis* 2024; **15**: 20406223241259654.
- 129 Fernandes SR, Bernardo S, Saraiva S, et al. The degree of bowel remission predicts phenotype progression in Crohn's disease. *United European Gastroenterol J* 2024; **12**: 891–900.
- 130 Takenaka K, Kawamoto A, Kitazume Y, et al. Transmural remission characterized by high biologic concentrations demonstrates better prognosis in Crohn's Disease. *J Crohns Colitis* 2023; **17**: 855–62.
- 131 Jairath V, Vuyyuru SK, Zou G, et al. Evaluating treatment to a target of transmural healing in patients with moderately to severely active Crohn's disease: rationale, design and protocol for the randomised controlled VECTORS trial. *BMJ Open Gastroenterol* 2026; **13**: e002088.
- 132 de Voogd FA, Bots SJ, van Wassenae EA, et al. Early intestinal ultrasound predicts clinical and endoscopic treatment response and demonstrates drug-specific kinetics in moderate-to-severe ulcerative colitis. *Inflamm Bowel Dis* 2024; **30**: 1992–2003.
- 133 Sagami S, Kobayashi T, Aihara K, et al. Early improvement in bowel wall thickness on transperineal ultrasonography predicts treatment success in active ulcerative colitis. *Aliment Pharmacol Ther* 2022; **55**: 1320–29.
- 134 Ellrichmann M, Schulte B, Conrad CC, et al. Contrast-enhanced endoscopic ultrasound detects early therapy response following anti-TNF therapy in patients with ulcerative colitis. *J Crohns Colitis* 2024; **18**: 1012–24.
- 135 Bakkaloglu OK, Sen G, Kepil N, et al. Comparative value of CRP and FCP for endoscopic and histologic remissions in ulcerative colitis. *Diagnostics (Basel)* 2024; **14**: 2283.
- 136 Castiglione F, Imperatore N, Testa A, et al. Exploring the concept of deep remission in Crohn's disease: correlation between transmural healing and biomarkers. *Therap Adv Gastroenterol* 2022; **15**: 1756284822110643.
- 137 D'Arcangelo G, Oliva S, Dilillo A, et al. Predictors of long-term clinical and endoscopic remission in children with Crohn disease treated with infliximab. *J Pediatr Gastroenterol Nutr* 2019; **68**: 841–46.
- 138 Cozijnsen MA, Ben Shoham A, Kang B, et al. Development and validation of the mucosal inflammation noninvasive index for pediatric Crohn's disease. *Clin Gastroenterol Hepatol* 2020; **18**: 133–40.
- 139 D'Arcangelo G, Imondi C, Terrin G, Catassi G, Aloï M. Is fecal calprotectin a useful marker for small bowel Crohn disease? *J Pediatr Gastroenterol Nutr* 2021; **73**: 242–46.
- 140 Gonzalez-Perez J, Pujol Muncunill G, Vila Miravet V, Martin de Carpi J. Validation of a new score for paediatric Crohn's disease on a paediatric tertiary hospital: the MINI-Index (Mucosal Inflammation Non-Invasive Index). *J Pediatr Gastroenterol Nutr* 2019; **69** (suppl 1): O-010.
- 141 Hurych J, Mascellani Bergo A, Lerchova T, et al. Faecal bacteriome and metabolome profiles associated with decreased mucosal inflammatory activity upon anti-TNF therapy in paediatric Crohn's disease. *J Crohns Colitis* 2024; **18**: 106–20.
- 142 Rodriguez Azor B, Martin-Masot R, Dayaldasani Khialani A, et al. Proactive monitoring of anti-TNF agents improves follow-up of paediatric patients with Crohn disease. *An Pediatr (Engl Ed)* 2023; **98**: 165–74.
- 143 Bronsky J, Copova I, Dostalíkova J, et al. Validation of the MINI (Mucosal Inflammation Non-Invasive Index) in paediatric Crohn's disease: a prospective national registry study. *JPGN Rep* 2026; **7**: S194.

- 144 Herman RB, Pieczkowski S, Dumnicka P, Wyzgowska A, Fyderek K. Clinical usefulness of the Mucosal Inflammation Noninvasive Index in newly diagnosed paediatric Crohn's disease patients. *Prz Gastroenterol* 2022; 17: 213–18.
- 145 Swaminathan A, Fulforth JM, Frampton CM, et al. The disease severity index for inflammatory bowel disease is a valid instrument that predicts complicated disease. *Inflamm Bowel Dis* 2024; 30: 2064–75.
- 146 Al Khoury A, Xiao Y, Golovics PA, et al. Assessing adherence to objective disease monitoring and outcomes with adalimumab in a real-world IBD cohort. *Dig Liver Dis* 2021; 53: 980–86.
- 147 Dranga M, Mihai C, Drug V, Dumitrescu G, Prelipcean CC. A rapid test for assessing disease activity in ulcerative colitis. *Turk J Gastroenterol* 2016; 27: 149–55.
- 148 Mack DR, Saul B, Boyle B, et al. Analysis of using the total white blood cell count to define severe new-onset ulcerative colitis in children. *J Pediatr Gastroenterol Nutr* 2020; 71: 354–60.
- 149 Li X, Yan L, Wang X, et al. Predictive models for endoscopic disease activity in patients with ulcerative colitis: practical machine learning-based modeling and interpretation. *Front Med* 2022; 9: 1043412.
- 150 Goodsall TM, Day AS, Andrews JM, Ruszkiewicz A, Ma C, Bryant RV. Composite assessment using intestinal ultrasound and calprotectin is accurate in predicting histological activity in ulcerative colitis: a cohort study. *Inflamm Bowel Dis* 2024; 30: 190–95.
- 151 Dolinger MT, Aronsky I, Spencer EA, Pittman N, Dubinsky MC. Early intestinal ultrasound response to biologic and small molecule therapy is accurate to predict treat-to-target endoscopic outcomes in children with ulcerative colitis: results from the prospective super sonic-UC study. *J Crohns Colitis* 2025; 19: jja075.
- 152 Zhang M, Zhang H, Zhu Q, et al. Bowel ultrasound enhances predictive value based on clinical indicators: a scoring system for moderate-to-severe endoscopic activities in patients with ulcerative colitis. *Therap Adv Gastroenterol* 2021; 14: 17562848211030050.
- 153 Arkteg CB, Wergeland Sørbye S, Buhl Riis L, Dalen SM, Florholmen J, Goll R. Real-life evaluation of histologic scores for ulcerative colitis in remission. *PLoS One* 2021; 16: e0248224.
- 154 Cushman GK, Stolz MG, Shih S, et al. Parent IMPACT-III: development and validation of an inflammatory bowel disease-specific health-related quality-of-life measure. *J Pediatr Gastroenterol Nutr* 2020; 70: 205–10.
- 155 Otley A, Smith C, Nicholas D, et al. The IMPACT questionnaire: a valid measure of health-related quality of life in pediatric inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 2002; 35: 557–63.
- 156 Danese S, Vermeire S, Zhou W, et al. Upadacitinib as induction and maintenance therapy for moderately to severely active ulcerative colitis: results from three phase 3, multicentre, double-blind, randomised trials. *Lancet* 2022; 399: 2113–28.
- 157 Ghosh S, Feagan BG, Parra RS, et al. Impact of upadacitinib induction and maintenance therapy on health-related quality of life, fatigue, and work productivity in patients with moderately-to-severely active Crohn's disease. *J Crohns Colitis* 2024; 18: 1804–18.
- 158 Attauabi M, Madsen GR, Bendtsen F, Seidelin JB, Burisch J. Multidimensional patient-reported outcomes and quality of life at diagnosis of IBD: a population-based inception cohort study. *Clin Gastroenterol Hepatol* 2025; 23: 1418–27.
- 159 Lin L, Wang T, Lu Y, et al. Mucosal healing and quality of life in therapeutic goals of ulcerative colitis: occurrence and related factors of functional bowel disorder-like symptoms. *Therap Adv Gastroenterol* 2022; 15: 1756284821092597.
- 160 Peyrin-Biroulet L, Cieza A, Sandborn WJ, et al. Disability in inflammatory bowel diseases: developing ICF core sets for patients with inflammatory bowel diseases based on the International Classification of Functioning, Disability, and Health. *Inflamm Bowel Dis* 2010; 16: 15–22.
- 161 Gower-Rousseau C, Sarter H, Savoye G, et al. Validation of the Inflammatory Bowel Disease Disability Index in a population-based cohort. *Gut* 2017; 66: 588–96.
- 162 Tannoury J, Nachury M, Martins C, et al. Determinants of IBD-related disability: a cross-sectional survey from the GETAID. *Aliment Pharmacol Ther* 2021; 53: 1098–107.
- 163 Williet N, Sarter H, Gower-Rousseau C, et al. Patient-reported outcomes in a French nationwide survey of inflammatory bowel disease patients. *J Crohns Colitis* 2017; 11: 165–74.
- 164 Peyrin-Biroulet L, Cieza A, Sandborn WJ, et al. Development of the first disability index for inflammatory bowel disease based on the international classification of functioning, disability and health. *Gut* 2012; 61: 241–47.
- 165 Meeralam Y, Al-Zanbagi AB, Al Saedi M, et al. IBD-Disk as a tool estimating the prevalence of inflammatory bowel disease-related disability and associated influencing factors in Saudi Arabia: a cross-sectional study. *Saudi J Gastroenterol* 2023; 29: 309–15.
- 166 Rappaport R, Hannaux O, Focht G, et al. Disability in pediatric inflammatory bowel diseases: a systematic review and a single center experience. *J Pediatr Gastroenterol Nutr* 2026; jpn3.70596.
- 167 D'Silva A, Fox DE, Nasser Y, et al. Prevalence and risk factors for fatigue in adults with inflammatory bowel disease: a systematic review with meta-analysis. *Clin Gastroenterol Hepatol* 2022; 20: 995–1009.
- 168 Turner ST, Focht G, Orlanski-Meyer E, et al. Fatigue in pediatric inflammatory bowel diseases: a systematic review and a single center experience. *J Pediatr Gastroenterol Nutr* 2024; 78: 241–51.
- 169 Feagins LA, Moore P, Crabtree MM, et al. Impact of fatigue on work productivity, activity impairment, and healthcare resource utilization in inflammatory bowel disease. *Crohns Colitis* 360 2024; 7: otae073.
- 170 Danese S, Tran J, D'Haens G, et al. Upadacitinib induction and maintenance therapy improves abdominal pain, bowel urgency, and fatigue in patients with ulcerative colitis: a post hoc analysis of phase 3 data. *Inflamm Bowel Dis* 2023; 29: 1723–29.
- 171 Louis E, Schreiber S, Panaccione R, et al. Risankizumab for ulcerative colitis: two randomized clinical trials. *JAMA* 2024; 332: 881–97.
- 172 Panaccione R, Feagan BG, Afzali A, et al. Efficacy and safety of intravenous induction and subcutaneous maintenance therapy with guselkumab for patients with Crohn's disease (GALAXI-2 and GALAXI-3): 48-week results from two phase 3, randomised, placebo and active comparator-controlled, double-blind, triple-dummy trials. *Lancet* 2025; 406: 358–75.
- 173 Borren NZ, Tan W, Colizzo FP, et al. Longitudinal trajectory of fatigue with initiation of biologic therapy in inflammatory bowel diseases: a prospective cohort study. *J Crohns Colitis* 2020; 14: 309–15.
- 174 Focht G, Marcovitch L, Kenigsberg S, et al. Item generation and reduction toward developing the pediatric IBD Fatigue Index (PIFI): concept elicitation interviews. *JPGN Rep* 2025; 6 (suppl 1): S213–S4 (G-OP070).
- 175 van Erp LW, Roosenboom B, Komdeur P, et al. Improvement of fatigue and quality of life in patients with quiescent inflammatory bowel disease following a personalized exercise program. *Dig Dis Sci* 2021; 66: 597–604.
- 176 Scheffers LE, Vos IK, Utens EMWJ, et al. Physical training and healthy diet improved bowel symptoms, quality of life, and fatigue in children with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 2023; 77: 214–21.
- 177 Bernstein CN, Kaplan GG, Nugent Z, et al. Inflammatory bowel disease phenotypes in diverse populations: a global comparative analysis. *J Crohns Colitis* 2026; 20: jja051.
- 178 Bernstein CN, Geary R, Nugent Z, et al. Global discrepancies in inflammatory bowel disease care reflect health care expenditure per capita. *Gastroenterology* 2026; 170: 203–06.
- 179 You Z, Shen J, Ahuja V, et al. Gastroenterologists' attitudes and challenges toward treat-to-target strategies in inflammatory bowel disease: a multinational survey. *Therap Adv Gastroenterol* 2025; 18: 17562848251383792.
- 180 Honap S, Dignass A, Jairath V, Danese S, Magro F, Peyrin-Biroulet L. Defining molecular remission in inflammatory bowel disease: lessons from oncology. *Lancet Gastroenterol Hepatol* 2026; 11: 944–46.

Copyright © 2026 Elsevier Ltd. All rights reserved, including those for text and data mining, AI training, and similar technologies.