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Updated 2025 ACG Clinical Guideline for the Management of Crohn's Disease

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IBD

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STRUCTURED ABSTRACT

Question: What are the major updates in the 2025 American College of Gastroenterology clinical guideline for the management of Crohn's disease (CD) compared with the 2018 guideline? How do these new guidelines incorporate recent therapeutic advances and evolving evidence into clinical practice?

Design: Evidence-based clinical practice guideline using the GRADE framework, incorporating systematic literature review and consensus expert opinion.

Setting: Multicenter, multidisciplinary guideline panel convened by the American College of Gastroenterology.

Patients: Adult patients with suspected, newly diagnosed, or established Crohn's disease, including luminal, fistulizing, and stricturing phenotypes.

Exposure or Interventions: Recommendations encompass diagnostic strategies, dietary and lifestyle interventions, corticosteroids, immunomodulators, biologics, and small molecule therapies, with special attention to new agents approved since the 2018 guidelines.

Outcomes: Induction and maintenance of clinical, endoscopic, and radiographic remission; prevention of complications; reduction in corticosteroid dependence; and patient-centered outcomes.

Data Analysis: Evidence was graded as high, moderate, low, or very low using the GRADE approach, with formulation of recommendations as strong or conditional.

Funding: American College of Gastroenterology.

Results: The 2025 updated guideline incorporates significant changes from 2018, reflecting both refinement in diagnostic approaches as well as therapeutic advances.

Diagnosis: The guidelines now provide a practical fecal calprotectin cut-off of >50-100 mg/g to distinguish inflammatory from non-inflammatory disease. It also formally endorses intestinal ultrasound (IUS) as a non-invasive, radiation-free adjunct for both diagnostic and monitoring, alongside other imaging techniques like CT or MR enterography.

Treatment. Most importantly, while mucosal healing on endoscopy remains the goal of therapy, the panel suggests against requiring patients to fail conventional therapies such as thiopurines or methotrexate before starting advanced therapies in moderate-to-severe CD, as new evidence emerged showing early intervention with advanced therapy is superior to accelerated step-up therapy.[1]

Mild-to-moderate CD. Mesalamine is now strongly discouraged for both induction and maintenance of luminal CD due to limited efficacy. Sulfasalazine should only be considered for patients with mild colonic CD. Budesonide at 9 mg daily remains recommended for induction in mild-to-moderate ileocecal CD but is recommended against for maintenance.

The role of dietary therapy is now recognized only in mild-to-moderate disease,

citing specific data from the DINE-CD trial, which supports Mediterranean or specific carbohydrate diets in select low-risk patients with mild disease, provided close monitoring is ensured.[2]

Moderate-to-severe CD. Systemic corticosteroids remain induction-only agents with a strong recommendation to limit use to fewer than 3 months, and to initiate a structured taper with rapid transition to steroid-sparing regimens.

Since 2018, the therapeutic landscape has expanded considerably, and the new guidelines incorporates new IL-23 inhibitors like risankizumab, guselkumab, and mirikuzumab, as well as JAK inhibitor upadacitinib alongside established agents such as anti-TNF therapies, vedolizumab, and ustekinumab for induction and maintenance. In particular, risankizumab is preferred over ustekinumab in patients previously exposed to anti-TNF agents. New subcutaneous infliximab and vedolizumab formulations are added as new maintenance options. No specific guidance for treatment selection is provided based on the location of the disease.

Fistulizing CD. Management of fistulizing disease has also broadened. Infliximab remains first-line therapy, but adalimumab, vedolizumab, ustekinumab, and upadacitinib are now considered reasonable options for induction.

Postoperative CD. Guidelines newly recommend endoscopic monitoring at 6-12 months after surgery. It continues to support continued observation in low-risk patients, but now adds vedolizumab, in addition to infliximab, to post-operative prevention regimens in high-risk patients.

COMMENTARY

Why Is This Important?

Since the 2018 guideline, multiple new biologic and small molecule agents have been approved for Crohn's disease, and data have emerged supporting earlier initiation of advanced therapies to improve long-term outcomes. The 2025 update reflects this shift toward early treat-to-target strategies, the de-implementation of ineffective agents, and individualized therapy selection based on disease phenotype, prior exposures, and patient preferences.

Key Study Findings

The update provides several practice-changing recommendations.

	Key Updates in 2025 Recommendations	What's New since 2018
Diagnostics	• Fecal calprotectin cut-off of 50–100 mg/g to differentiate inflammatory from noninflammatory colonic disease • Intestinal ultrasound offers a non-invasive, radiation free-method of assessing the bowel wall, mesentery, and adjacent structures and is an adjunct to the diagnosis and monitoring to therapy	• A fecal calprotectin threshold to differentiate noninflammatory disease. • IUS is formally endorsed to assess inflammation.
Mild-to-moderate CD	• Recommend against mesalamine for induction/maintenance • Recommend budesonide 9 mg daily for ileocecal induction but not for maintenance • For mild CD and low risk of progression, diet-based strategies along with careful monitoring for inadequate symptom relief, worsening inflammation, or disease progression may be considered	• A clear recommendation against the mesalamine for Crohn's disease • A clear recommendation against budesonide for maintenance • Recognition that diet-based strategies alone may be reasonable in select patients with mild disease and low risk of disease progression
Moderate-to-severe CD	• Suggest against requiring failure of conventional therapy before initiation of advanced therapy • Recommend oral corticosteroids for short-term induction of remission • Anti-TNFs remain foundational, but other recommended therapies include: Subcutaneous infliximab after IV induction; vedolizumab IV induction and SC for maintenance; ustekinumab for induction and maintenance; risankizumab; mirikizumab; guselkumab • Recommend the use of risankizumab over ustekinumab if there is prior exposure to anti-TNF therapy • Recommend upadacitinib use for induction and maintenance of remission for patients with moderate-to-severe CD who have prior exposure to anti-TNF	• A major shift away from step-up for moderate-severe Crohn's disease. • New suggestion of tapering rapidly to steroid-sparing agents and explicitly using a ≤3-month taper • Additional therapies are recognized including subcutaneous infliximab and vedolizumab for maintenance, and recognition of risankizumab, mirikizumab, and guselkumab as possible agents • New guidance on positioning risankizumab over ustekinumab in patients with prior anti-TNF exposure • Upadacitinib is also recommended for those with prior exposure to anti-TNF
Fistulizing CD	• Recommend infliximab use as induction therapy • Suggest the use of adalimumab, vedolizumab, ustekinumab, and upadacitinib for induction	• Expands prior recommendations with vedolizumab, ustekinumab, and upadacitinib as possible induction therapies

	Key Updates in 2025 Recommendations	What's New since 2018
Postoperative CD	• Recommend postoperative monitoring at 6–12 months over no monitoring • In patients with CD with low postoperative risk of recurrence, suggest continued observation as compared with immediate initiation of medical therapy for CD • In patients with high-risk CD, recommend anti-TNF therapy or vedolizumab to prevent postoperative endoscopic recurrence	• Formal recommendations on timing of post-operative monitoring • In addition to infliximab, vedolizumab is added as prophylaxis option in those with high risk of recurrence

Table 1. Key Updates in Recommendations.

First, it recommends against step-up approach, allowing clinicians to initiate advanced therapy for appropriate moderate-severe cases. Second, it strongly recommends against ineffective therapies like mesalamine, which remains common in community practice. Third, it strengths steroid stewardship by explicitly recommending less than 3 months of use. Fourth, it expands the treatment armamentarium including new IL-23 antagonists, JAK inhibitors, and subcutaneous formulations of infliximab and vedolizumab. Fifth, for perianal disease, the therapeutic options now extend beyond infliximab, as does for post-operative recurrence.

Caution

Despite these advances, many recommendations remain conditional and based on low-quality evidence, particularly concerning comparative positioning of agents and sequencing strategies after biologic failure. Evidence for dietary therapies also remain limited, and while they may benefit select motivated patients with low-risk disease, reliance on diet alone should not delay timely escalation in more severe phenotypes.

My Practice

In light of these updates, I will more readily consider initiating advanced therapies in treatment-naïve patients with moderate-to-severe CD, particularly those with high-risk features. Mesalamine will no longer be used in my practice for luminal disease. I will continue to be mindful of duration of corticosteroid use, and taper as soon as appropriate, with early transition to steroid-sparing maintenance therapies. With the expansion of IL-23 antagonists and upadacitinib as well as subcutaneous formulations of select advanced treatment, I will increasingly individualize treatment selection based on prior drug exposure, comorbidities, and patient preference for mode of administration.

For Future Research

Comparative effectiveness and head-to-head trials among newer biologics and small molecules are urgently needed, as are studies on sequencing strategies after treatment failure. Long-term safety data for JAK inhibitors in CD, and optimal dietary intervention protocols, are also priorities.

Conflict of Interest

None.

REFERENCES

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