Canadian Clinical Practice Guidelines: Management of Luminal Crohn's Disease

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CanMEDS Roles Covered

X	**Medical Expert** (as *Medical Experts*, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. *Medical Expert* is the central physician Role in the CanMEDS Framework and defines the physician's clinical scope of practice.)
	Communicator (as *Communicators*, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
	Collaborator (as *Collaborators*, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
	Leader (as *Leaders*, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
	Health Advocate (as *Health Advocates*, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
X	**Scholar** (as *Scholars*, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
	Professional (as *Professionals,* physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

Conflict of Interest Disclosure

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(Over the past 24 months)
Name: **Waqqas Afif**

Commercial or Non-Profit Interest	Relationship
Organization	Committee Member, Chair
Janssen/Abbvie/Takeda/Arena Pharmaceuticals	Advisory board/consultant/investigator
Pfizer/Merck/Ferring/Novartis/Amgen/ Innomar	Advisory board
Prometheus/Theradiag/Eli-Lilly/Roche/Dynacare	Investigator

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CLINICAL PRACTICE GUIDELINES

Canadian Association of Gastroenterology Clinical Practice Guideline for the Management of Luminal Crohn's Disease

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CAG Luminal CD CPG

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- Review guidelines
  - GRADE approach → 40 statements
  - Face-to-face meeting in September 2016 (20 voting participants)
  - Separate guidelines on fistulizing CD
  - Most recommendations are conditional, and based on low or very low evidence
- Compare/contrast to recent ECCO (2019)/ACG (2018) Guidelines
- Future directions

Patient Perspectives

- Although treatment recommendations help provide guidance to the clinician, treatment decisions should be made in collaboration with the individual patient.

- Patient Related Outcomes (PROs) as clinical trial endpoints for CD
  - Improving QOL and completely resolving symptoms

- Less than 15% of patients indicated having a completely normal colonoscopy as a preferred treatment objective.

Casellas F, Herrera-de Guise C, Robles V, et al. Patient preferences for inflammatory bowel disease treatment objectives. Dig Liver Dis 2017;49:152–156.

Statement 1

- We recommend determination of disease severity be based on a combination of symptoms, objective measures of inflammation, and factors that predict an increased risk of complications.
  - GRADE: Strong recommendation. Good practice statement, quality of evidence not assessed. Vote: strongly agree, 55%; agree, 40%; uncertain, 5%.

Table 1. Factors Associated With High Risk of Relapse, Surgery, or Complicated Luminal CD

Clinical factors	Younger age
	Smoking
	Longer disease duration
	Early use of corticosteroids
	Presence of fistulizing perianal CD
	Previous intestinal resection
Disease factors	Disease location (rectal, upper GI, jejunal)
	Disease extent
Laboratory factors	Low hemoglobin
	Low albumin
	High C-reactive protein (CRP)
	High fecal calprotectin levels
Endoscopic factors	Presence of deep ulceration

What NOT to use !

- In patients with CD of any severity, we recommend/suggest **against** the use of the following to induce OR maintain complete/symptomatic remission:
  - Systemically absorbed antibiotics
  - Probiotics (recommend)
  - Omega-3 fatty acids (recommend)
  - Marijuana
  - Naltrexone
  - Enteral nutrition or dietary modification

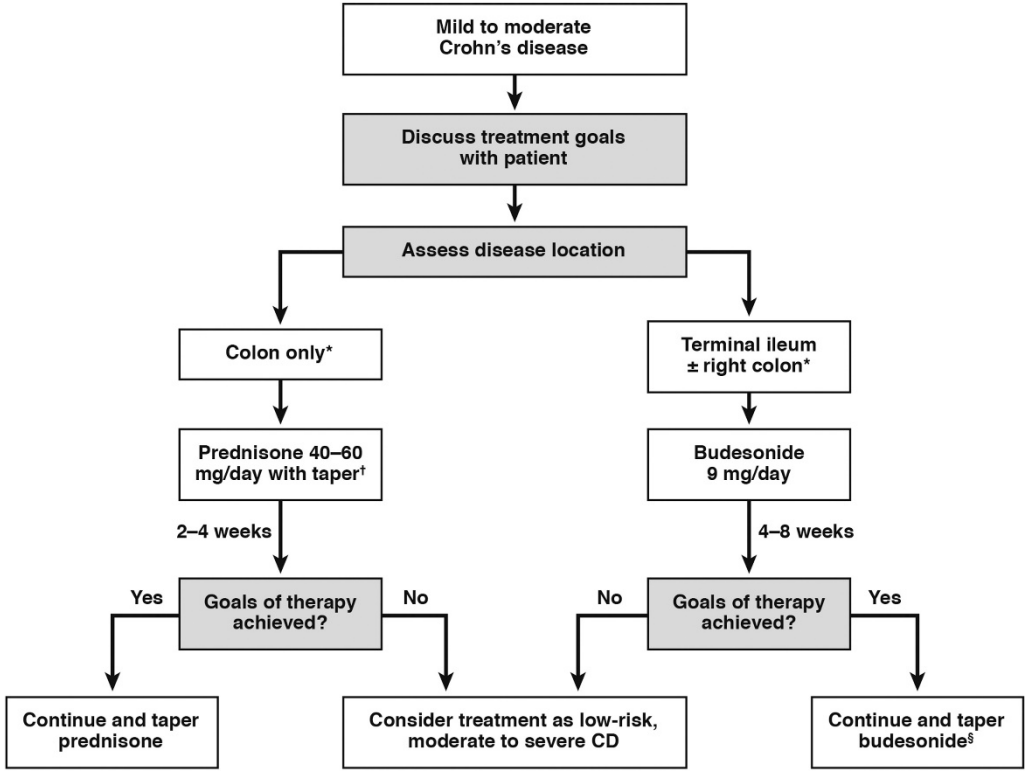
What NOT to use !

- In patients with Crohn's disease of any severity, we suggest **against** the use of oral 5-ASA to induce OR maintain complete remission.
  - Evidence suggests a minimal benefit for sulfasalazine in a subgroup of patients with mild colonic CD (not used clinically and older study with poor methodology)

- In patients with mild to moderate Crohn's disease, we suggest **against** the use of oral budesonide/corticosteroids to maintain complete remission.

- In patients with Crohn's disease of any severity, we suggest **against** the use of thiopurine monotherapy to induce complete

Mild to Moderate CD Algorithm



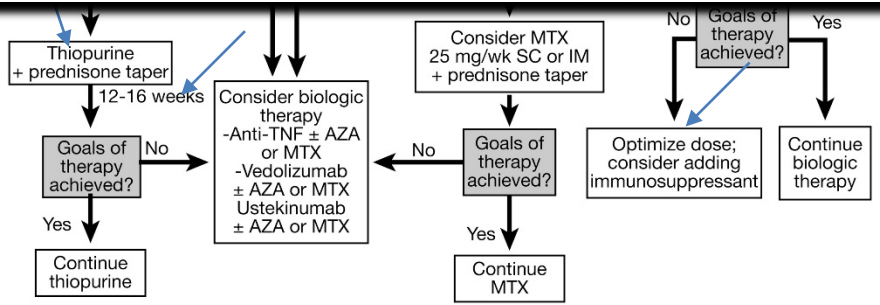
ACG Guidelines 2018

- ACG: For patients with low risk of progression, treatment of active symptoms with anti- diarrheals, other non-specific medications, and dietary manipulation, along with careful observation for inadequate symptom relief, worsening inflammation, or disease progression, is acceptable (strong recommendation, very low level of evidence).

Moderate to Severe CD Algorithm

- In patients with active Crohn's disease, when starting anti-TNF therapy:

"Thiopurines should be restricted to select low-risk patients who are steroid dependent or as part of combination therapy with biologics. It was acknowledged that sometimes physician choice is limited because payers may require the use of immunosuppressants before prescribing biologic therapy. This represents a knowledge translation gap between the medical literature and these payers whose decisions are often driven by cost containment."



- We suggest that dose optimization for patients with Crohn's disease who lose response to anti-TNF therapy (10-20%/year) be informed by TDM
  - No recommendation for VDZ/UST

ECCO Guidelines 2019

- **ECCO**: Agreement on a recommendation for the use of MTX for inducing clinical remission in patients with CD could not be reached.

- **ECCO**: We suggest **against** the combination of adalimumab and thiopurines over adalimumab alone to achieve clinical remission and response

- **ECCO**: In patients with Crohn's disease who have achieved long-term remission with the combination of infliximab/adalimumab and immunosuppressants, we suggest monotherapy with infliximab/adalimumab

Future Directions

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- Antibiotics and Altering the Microbiome
  - Non-absorbable antibiotics and FMT
- Sequencing or Combining Biologic Therapies
  - All biologics can be used as first-line agents (head to head studies are coming)
    - Special situations: fistulizing CD, pregnancy, older age or malignancy
  - Need more data on sequencing
  - Case reports with biologic combinations
- Treat-to-Target Approach
  - Endoscopic healing (REACT-2) and histologic healing
- Therapeutic drug monitoring
  - Need more studies for proactive TDM

My Conclusions (in my IBD clinic)

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- No role for 5-ASA's in CD
- No role for thiopurines for induction & almost no role in maintenance (monotherapy)
- For luminal CD (no special circumstances) all biologics are effective, but newer biologics have improved benefit/risk profiles (infectious risks)
- CALM-like approach to treatment within the 1st year of treatment
- For anti-TNF reactive TDM **YES** and proactive TDM **LIKELY** (PAILOT

Thank-you !

Questions ?

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