Mastering Perianal Fistulas in Crohn's Disease: Approach to Evaluation and Management

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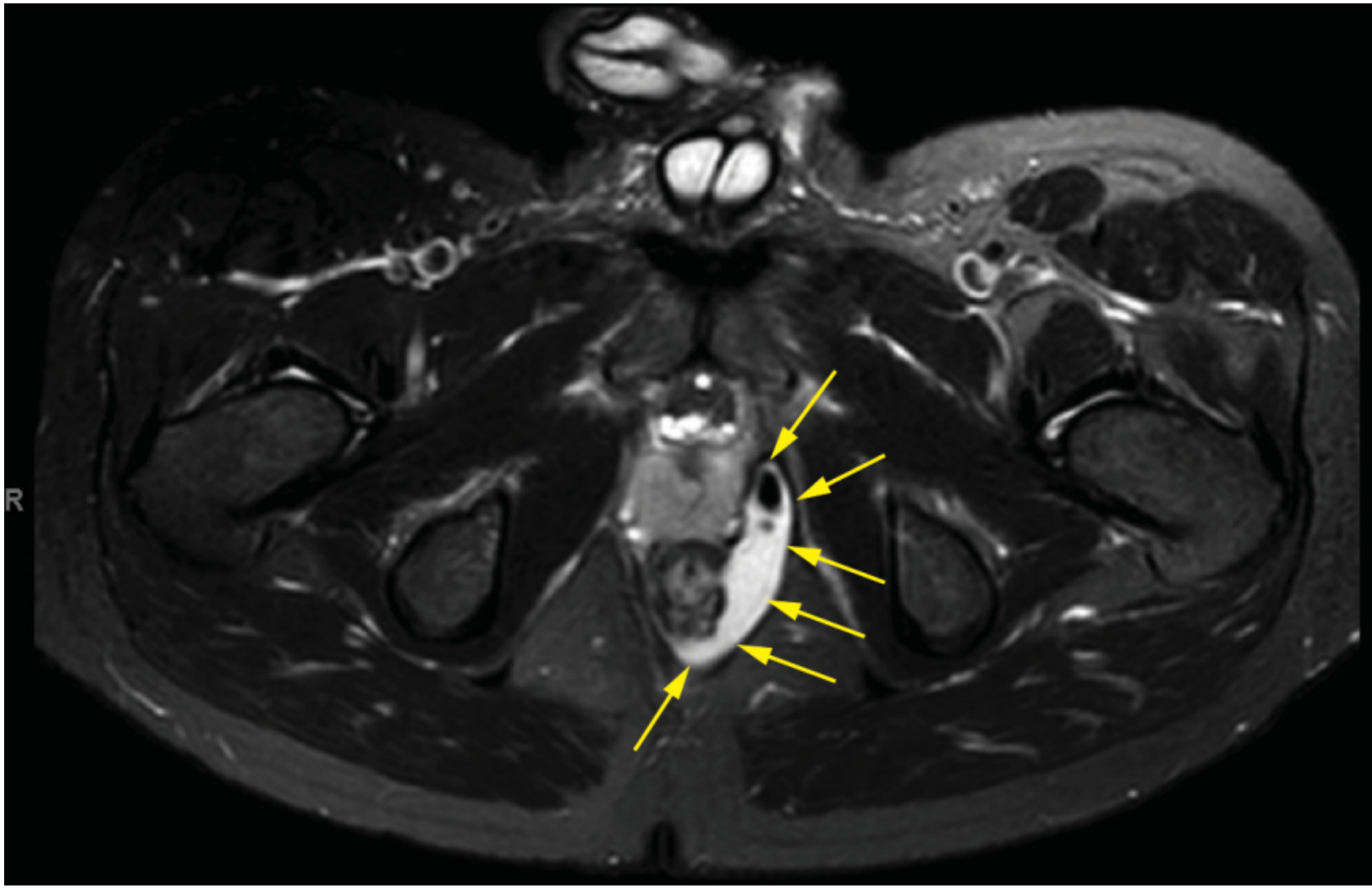
26 yo Man With New Perianal Fistula and Abscess

- 1-year hx of ileocolonic CD receiving mesalamine
- Presents with perianal pain, swelling x 3 days. Upon further questioning he notes leakage of fluid in between bowel movement
- Perianal exam—left sided erythema and induration. Purulent fluid expressed with gentle compression. DRE not tolerated

26 yo Man With New Perianal Fistula and Abscess

- Pelvic MRI shows peri-rectal abscess with fistula to skin
- EUA with drainage and seton placement

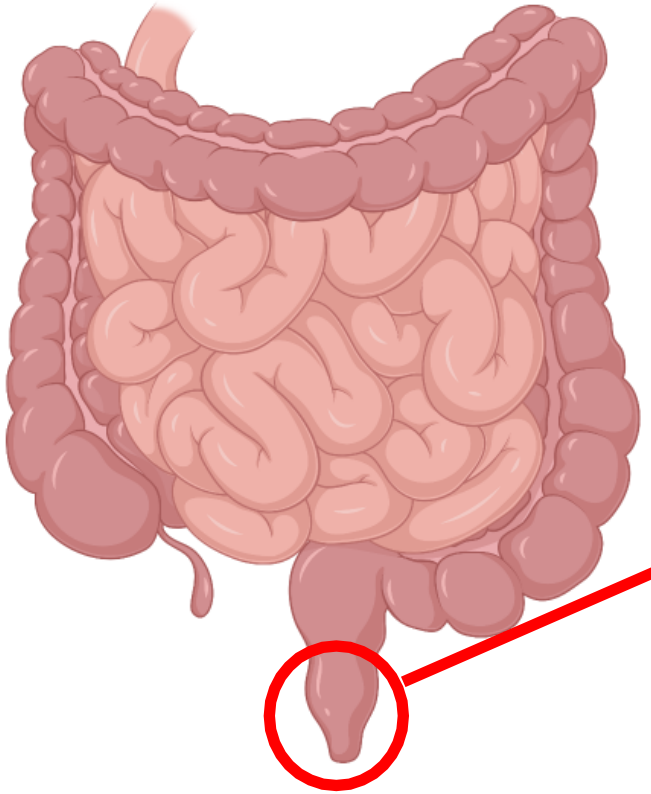


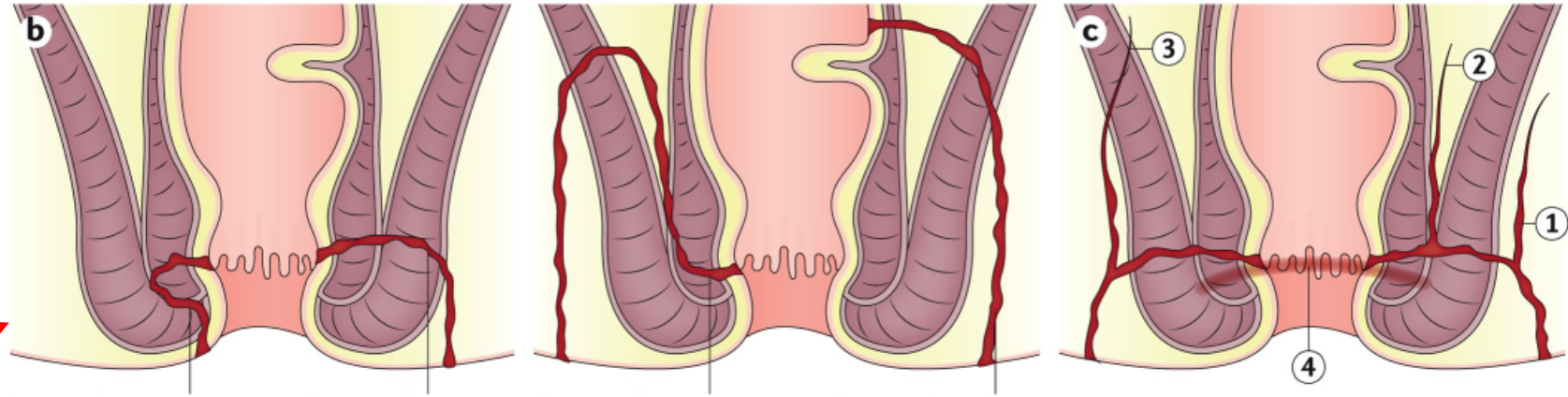
26 yo Man With New Perianal Fistula and Abscess

- Pelvic MRI shows peri-rectal abscess with fistula to skin
- EUA with drainage and seton pl

1. What medical therapy should he start?
2. How should we monitor response to therapy?
3. What should we do if he doesn't respond?

Features of Perianal Crohn's Disease

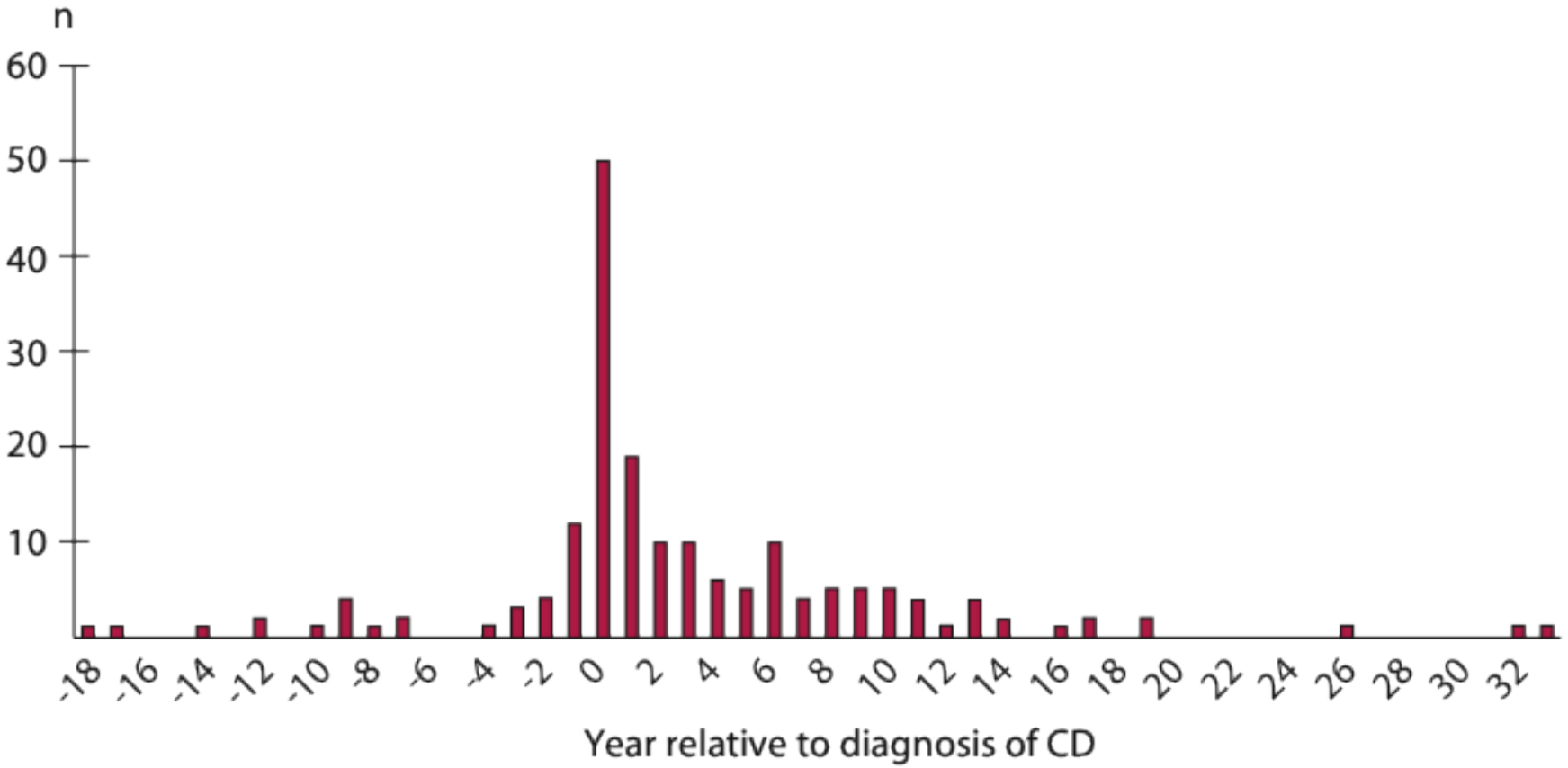




- Fistulas, abscesses, fissures, anal stenosis, skin tags (?)
- Common
  - 25% of all CD patients
- Consequences:
  - More frequent surgery
  - Worse quality of life
  - Limited therapeutic options

Panes and Rimola. Nat Rev Gastro 2017.

Timing of pCD Development



- Perianal lesions can develop before, at the same time, or after the diagnosis of luminal CD

- Perianal symptoms should be assessed at **every visit**.

Eglinton et al. Dis Colon Rectum. 2012.

Is it Crohn's?

- Most new-onset perianal fistulas are **NOT** Crohn's-related
- Consider EGD+Colonoscopy+MRE +/- VCE for evaluation

TABLE 4: Diagnostic Yield for CE and MRE: Patients With Lesions

SB lesions[a]	CE	MRE
Jejunum, no. (%)	15 (31.9%)	3 (6.4%)
Ileum, no. (%)	27 (57.4%)	10 (21.3%)
Terminal Ileum, no. (%)	33 (68.1%)	18 (38.3%)

Hanna et al. Lancet Gastro Hep 2025
Gonzalez-Suarez et al. IBD. 2018

Proposed Isolated pCD Diagnostic Criteria

Independently diagnostic criteria:

Histological diagnosis

- Epithelioid granulomata in fistula or surrounding perianal tissue
  - ↳ excluding cryptolytic and foreign-body type granuloma

or

Macroscopic (Crohn's perineum) diagnosis

- Anorectal stricturing or ≥1 inflammatory fissure(s) or ulcer(s) evident on examination
  - ↳ ie, significant perianal lesions in the absence of another cause (eg, medication, anastomosis)

If either are present, then consider an isolated perianal Crohn's disease diagnosis

Major criteria: (scores 3)

- **Advanced fistula complexity**
  >1 internal opening, >1 discrete fistula, or organ fistulation (without an alternative provoked or iatrogenic cause)
- **Family history of IBD**
  First or second degree relative
- **Confirmed diagnosis of classic EIM of IBD or orofacial granulomatosis**

Minor criteria: (scores 1)

- **Potential, current, or previous EIM of IBD**
  (diagnosis unconfirmed)
- **Suspected oral Crohn's disease**
- **Suspected genital Crohn's disease**
- **Coexistent hidradenitis suppurativa**
- **Minor associated perianal disease***
- **Recurrence following fistula repair or lay-open with curative intent**

If major and minor score ≥5, then consider isolated perianal Crohn's disease diagnosis

Hanna et al. Lancet Gastro Hep 2025

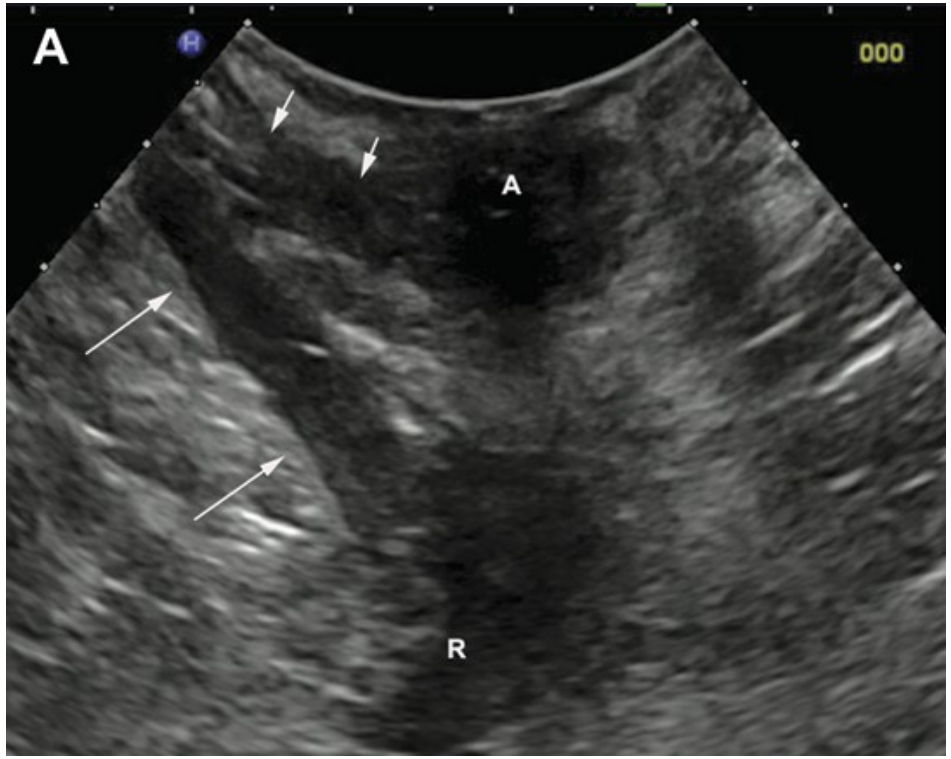
pCD Diagnosis—Comparison of EUS, EUA, and MRI

- All three methods showed excellent accuracy in assessing patients
  - EUS: 91% (95% CI 75% - 98%)
  - EUA: 91% (95% CI 75% - 98%)
  - MRI: 87% (95% CI 69% - 96%)
- Combining any 2 imaging modalities increased the accuracy to 100%

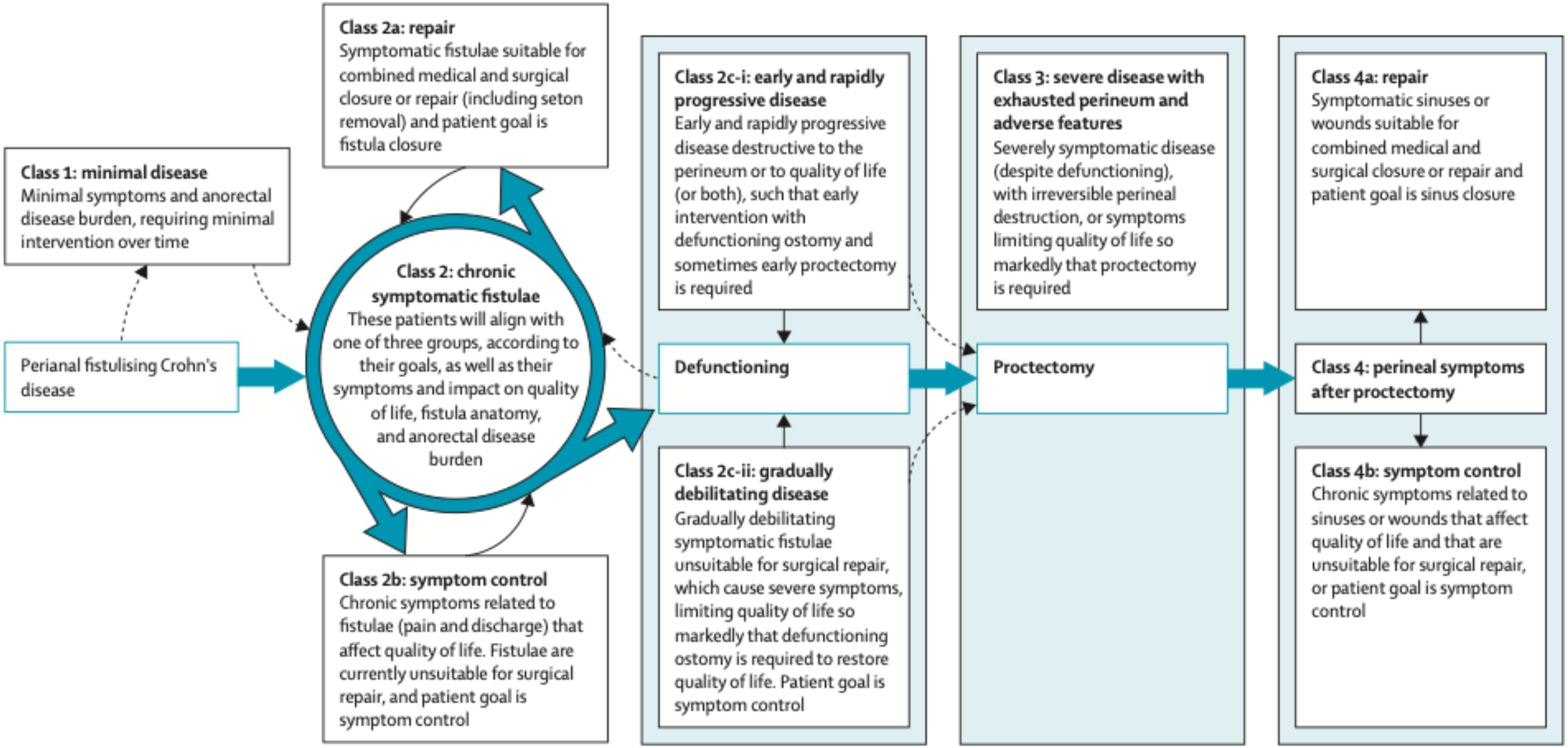
Schwartz DA, et al. *Gastroenterology*. 2001;121(5):1064-1072.

pCD Diagnosis—Role of Transperineal Ultrasound

- 59 patients with suspected pCD underwent MRI and TPUS
- TPUS detected:
  - 51/54 fistula tracts (94% sensitive)
  - 9/10 anovaginal fistula (90% sensitive)
  - 91% correctly classified by Park's Classification
  - 11/23 abscesses (48% sensitive)



Maconi et al IBD 2013
Maconi et al Ultraschall Med 2017
Greer et al AJR 2022



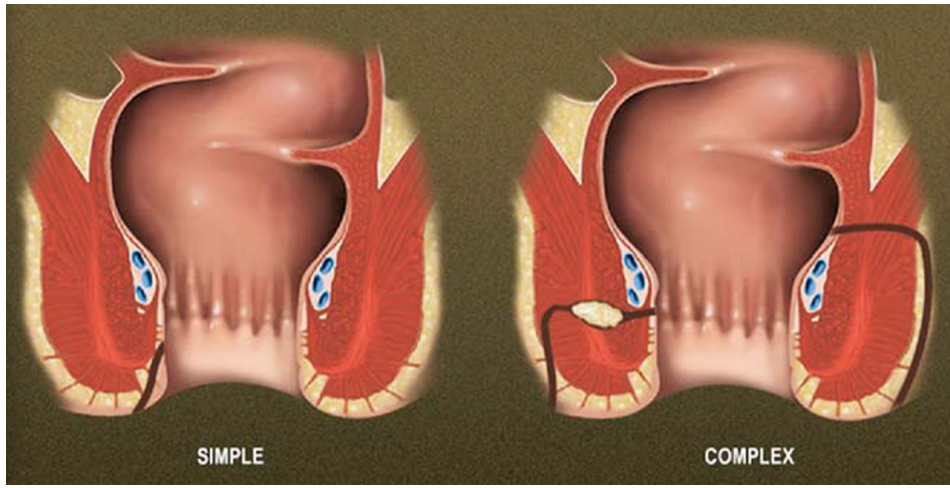
Geldof et al. Lancet Gastro Hep 2022

Causes and Complications of pCD Inform Treatment

- Immune
- Microbiome
- Genetics
- Fibrosis/Scarring

- Immune modulators and anti-inflammatory tx
- Antibiotics
- Surgical Intervention

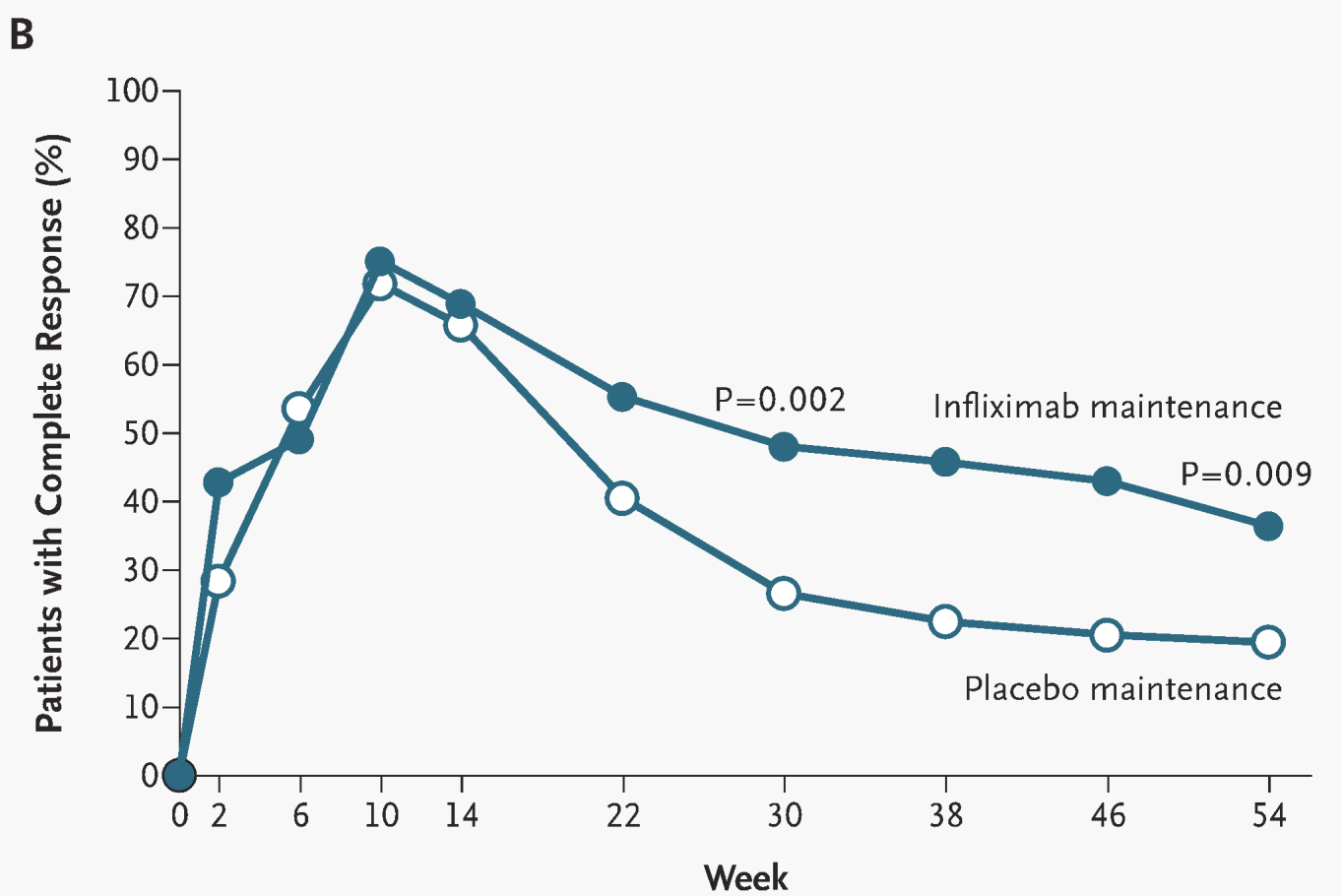
- All patients with IBD should have a careful perianal/digital rectal exam
- Collaboration between gastroenterologists and surgeons
  - Drain all abscesses **before** initiation of advanced therapy
- Presence of rectal inflammation and fistula anatomy guide combined medical and surgical approach.



Wise and Schwartz. CGH 2006
Parian et al. AJG 2023
Shi et al. CGH 2018.

Medical Management of pCD

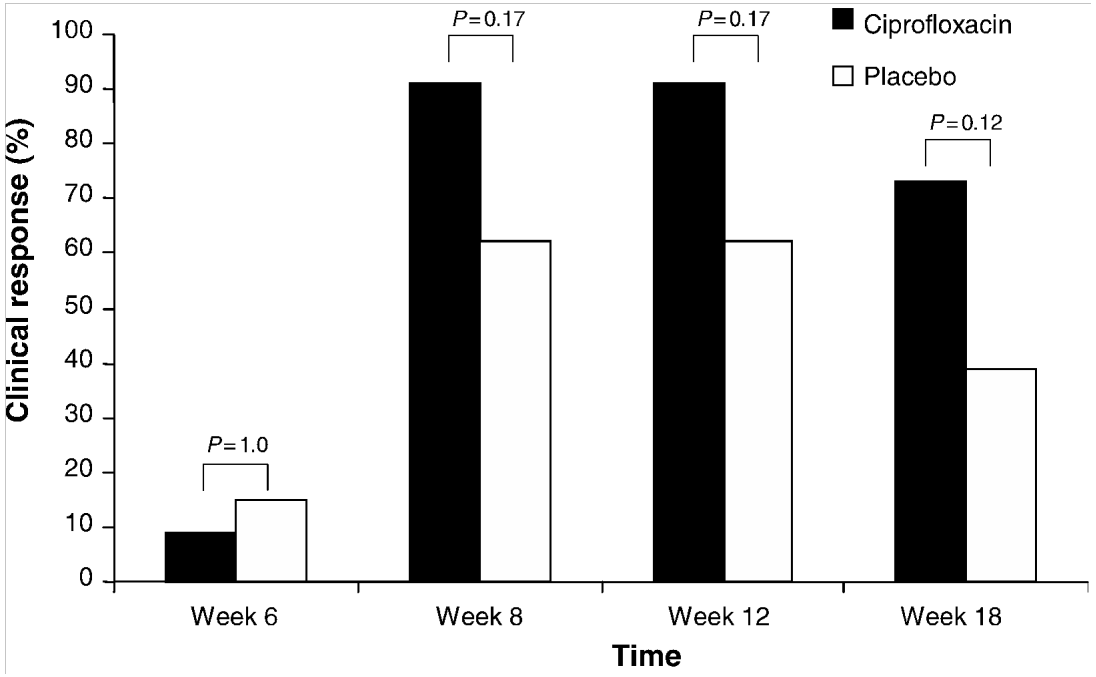
- Infliximab is an effective induction and maintenance agent for pCD
- Subcutaneous infliximab
  - Week 26 clinical remission: 44.6%



Lichtenstein et al. AJG 2025
Sands et al. *NEJM* 2004
Andre et al. AJG 2025

Medical Management of pCD

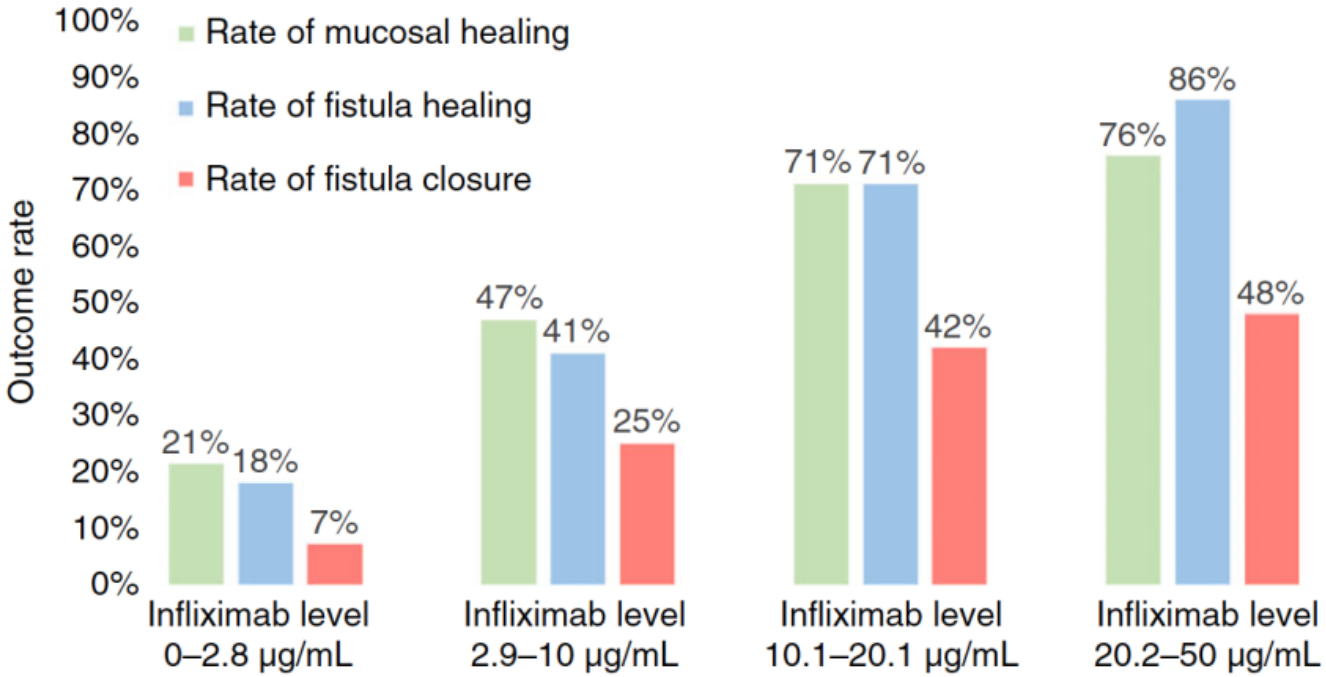
- Combination therapy with abx improves response
  - N=24 received **infliximab** 5mg/kg at wk 6, 8, 12 and were followed for 18 weeks
  - Randomized to ciprofloxacin 500 mg bid or placebo for 12 weeks
  - Trended towards better **clinical response** with IFX+Cipro (OR = 2.37, 95%CI = 0.94-5.98, P = 0.07)
  - **PDAI at Wk 18** only improved with IFX+Cipro (P = 0.008)
  - Similar data with adalimumab + ciprofloxacin



West RL, et al. *Aliment Pharmacol Ther.* 2004;20:1329-36
Dewint et al. *Gut* 2014

Medical Management of pCD

- Higher infliximab trough levels associated with perianal fistula healing
  - Cross sectional study of 117 CD patients with active fistulas on IFX for >24 weeks
  - **Patients with FH had a significantly higher IFX trough levels** (using HMSA) than those with active fistulas (15.8 vs. 4.4 µg/mL, p<0.0001)
  - Patients with antibodies to IFX had a lower chance of FH
  - IFX trough levels >10.1 µg/mL were an independent factor for predicting FH



Yarur A, et al. *Aliment Pharmacol Ther*. 2017;45(7):933-40.

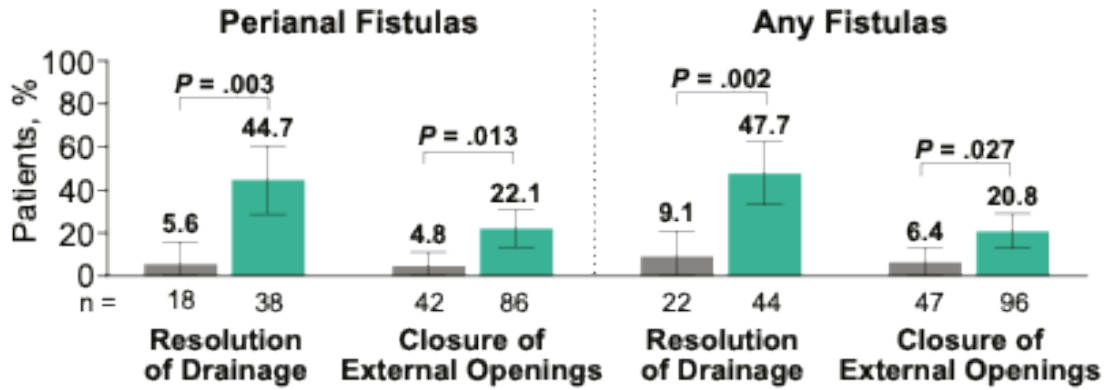
Medical Management of pCD

- Upadacitinib after anti-TNF failure
  - Post-hoc analysis of patients from U-EXCEL, U-EXCEED, and U-ENDURE

12-week induction

Placebo n = 47

Upadacitinib 45 mg n = 96

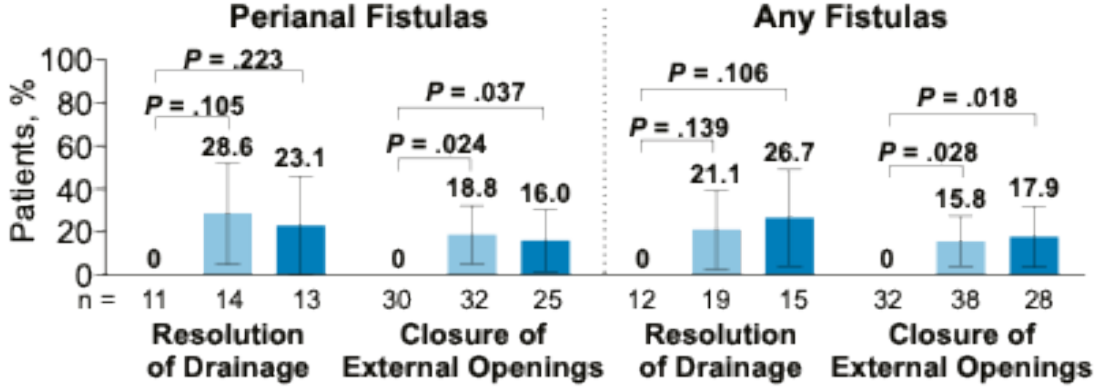


52-week maintenance
(among responders to induction)

Placebo n = 32

Upadacitinib 15 mg n = 38

Upadacitinib 30 mg n = 28



Colombel et al. CGH 2025

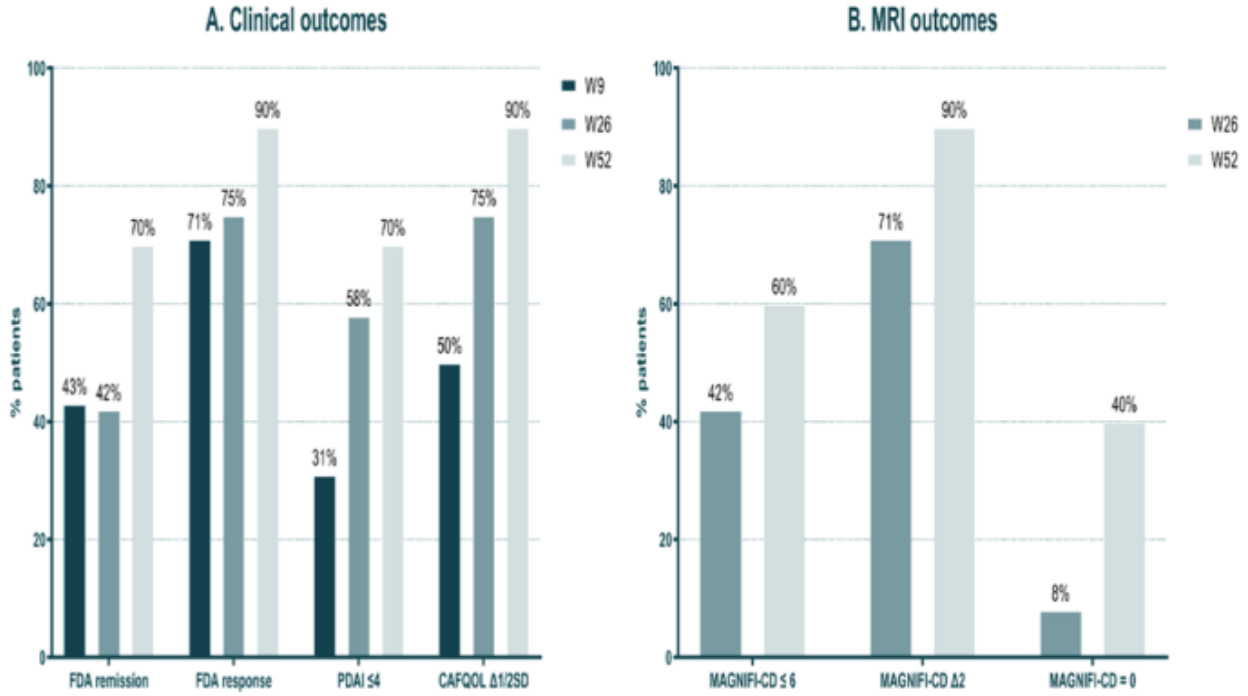
Medical Management of pCD

Therapy	Recommendation	Level of Evidence
Infliximab (IV)	Strong	Moderate
Infliximab (SC)	---	---
Adalimumab	Conditional	Low
Upadacitinib	Conditional	Very Low
Ustekinumab	Conditional	Very Low
Vedolizumab	Conditional	Very Low

Lichtenstein et al. AJG 2025

Other Management of pCD

- Hyperbaric oxygen therapy (HBOT) may be a complementary approach to fistula management
  - Not FDA approved
  - Active pCD→6 months medical therapy→seton placement→20 HBOT sessions→seton removal and closure of internal opening→20 HBOT sessions



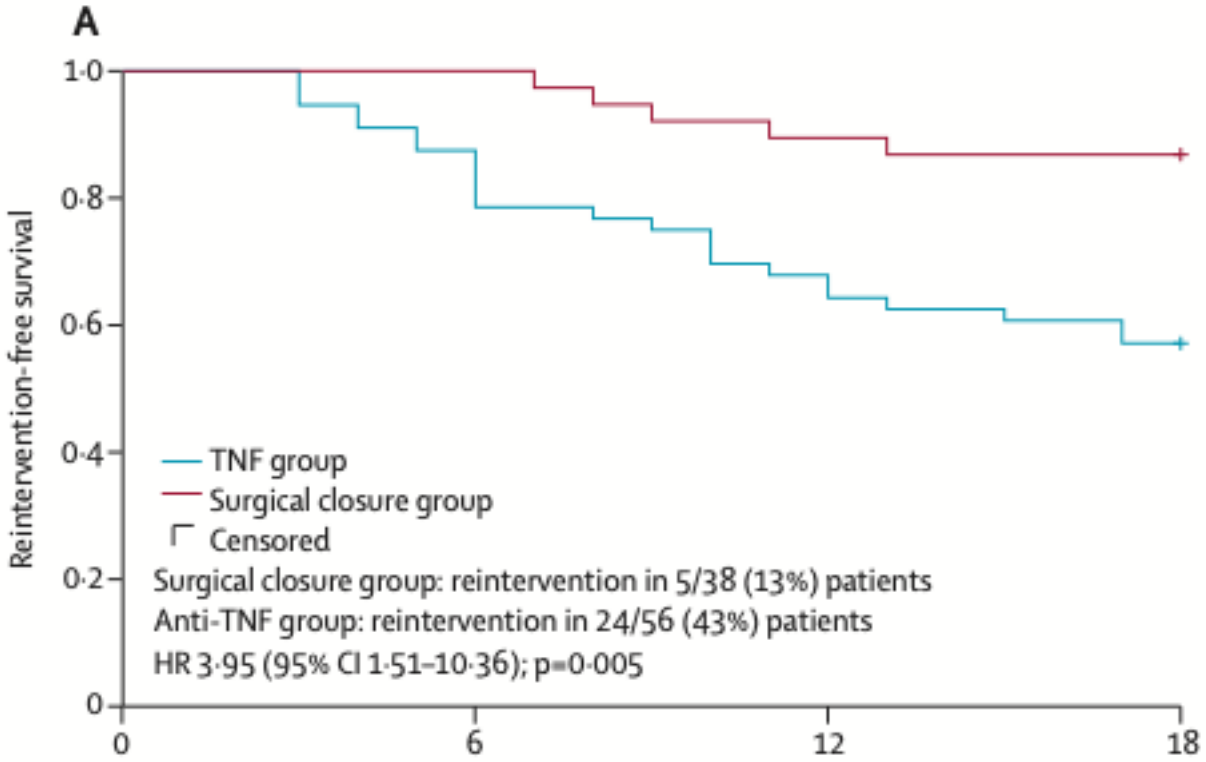
Mulders et al. JCC 2025
Piotrowicz et al. JCC 2025
Lansdorp et al. UEGJ 2022

Surgical Management of pCD

- Seton placement and removal
- Fistula curettage
- LIFT
- Advancement flap
- VAAFT
- FiLaC
- Diversion

PISA-II

- Fewer re-interventions in patients that received short-term anti-TNF + surgical closure vs chronic anti-TNF



Meima-van Praag et al. Lancet Gastro Hep 2022

Surgical Management of pCD

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ADMIRE-CD II—Phase 3 trial of darvadstrocel (DVS) for pCD

- ALL patients had **fistula curettage** and **seton placement** followed by additional curettage and **internal opening closure** prior to receiving DVS or placebo.
- Combined remission at week 24
  - DVS 48.8%
  - PBO 46.3%

Serclova et al. JCC 2024

Treat to Target in pCD?

- Clinical targets and trial endpoints are variable and poorly defined
- Focus on evidence-based, objective endpoints is required to improve research and clinical care

Table 2. Recommendation of MRI-based Activity Index to Define Healing of Fistulae in Perianal Crohn's Disease

A radiologically improved fistula on MRI in perianal Crohn's disease can be defined by a 50% reduction in the score of any of the following MRI-based activity indices:	% Level of agreement (either strongly agree or somewhat agree)
• MAGNIFI-CD	98.7% (75/76)
• mVAI	98.7% (73/74)
• VAI	98.6% (73/74)
• PEMPAC	98.6% (70/71)
A radiologically healed fistula can be defined by a score of 0 in any of the following MRI-based activity indices:	
• MAGNIFI-CD	96.1% (73/76)
• mVAI	98.6% (72/74)
• VAI	97.3% (73/74)
• PEMPAC	98.6% (70/71)

Anand et al. CGH 2025

Can pCD be Prevented?

- 10-30% of adult and pediatric CD patients have asymptomatic (subclinical) sinus tracts identified by pelvic MRI
- Subclinical pCD patients are >3x more likely to develop clinical pCD
- New pediatric CD patients treated with anti-TNF were 82% less likely to develop perianal fistula
- Adult patients treated with anti-TNF as first biologic vs vedolizumab were less likely to develop perianal fistula (HR 0.88; P=0.0045)

Adler et al. Gut 2025
McCurdy et al. CGH 2024
Kim et al. CGH 2020
Kim et al. JCC 2021
Antaya et al. AJG 2025
Zhi et al. Gastro 2019

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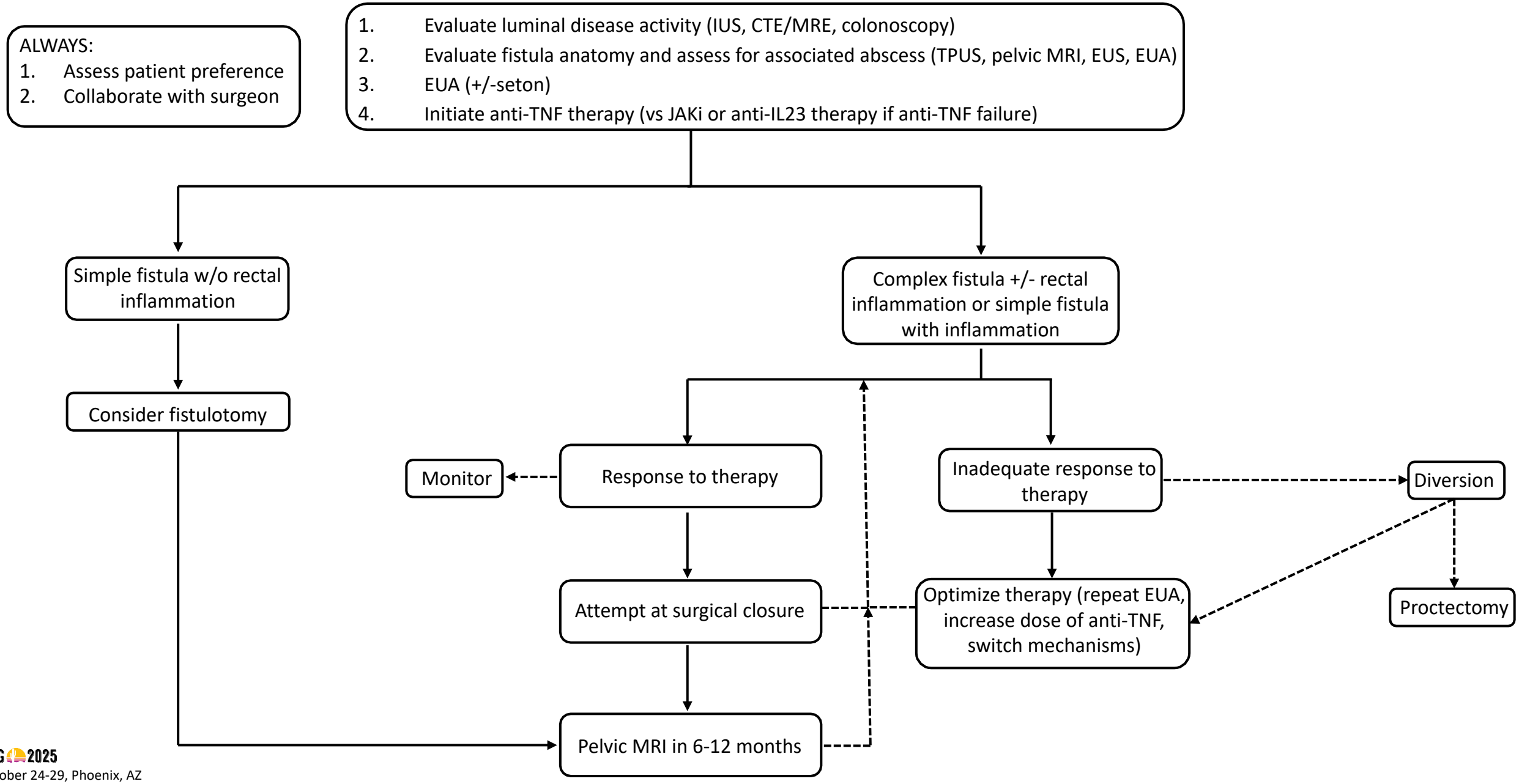
- How can we screen for subclinical pCD?
- How can we identify patients at greatest risk of progressing to clinical pCD?
- Can we modify risk with currently available therapies?
- Do subclinical lesions resolve with therapy and should that be a treatment target?

Adler et al. Gut 2025
McCurdy et al. CGH 2024
Kim et al. CGH 2020
Kim et al. JCC 2021
Antaya et al. AJG 2025
Zhi et al. Gastro 2019

Approach to New Perianal Fistula



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