The road to change the course of IBD

DR.Hussam Aldeen Alshiekh

Ibnnafees hospital

We knew everything from the beginning!

Burril B. Crohn (1884–1983)

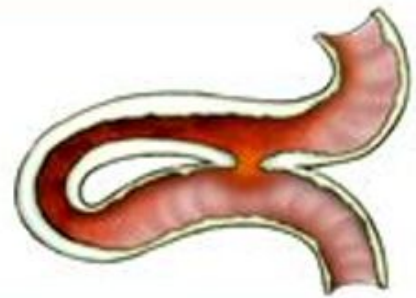
December 11, 1931:

I have an important scientific contribution I would like to present before the AGA next May. I have discovered, I believe, a new intestinal disease, which we have named Terminal Ileitis

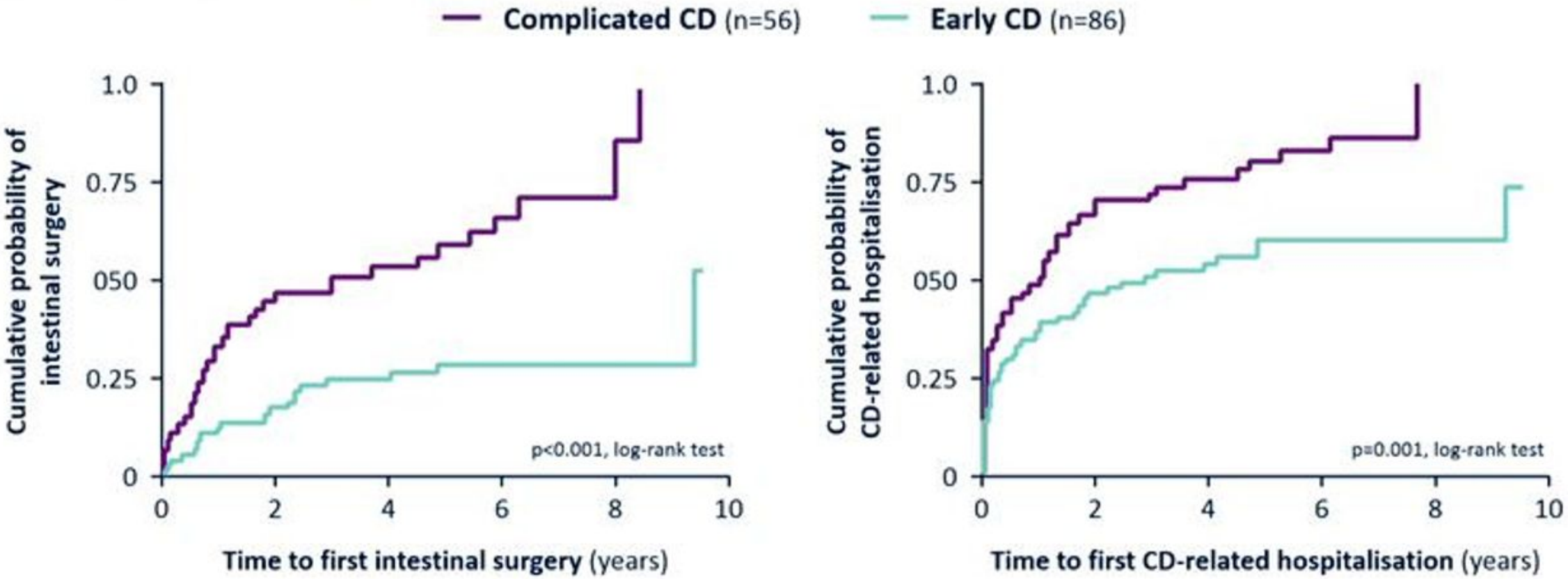
JAMA 1932:99:1323–29:

… The ulceration of the mucosa is accompanied by a disproportionate connective tissue reaction of the remaining walls of the involved intestine, a process which frequently leads to stenosis of the lumen of the intestine, associated with the formation of multiple fistulas …

Bowel damage in CD: lessons from population-based studies

At diagnosis			At 10 years
80%	Inflammation		50%
20%	Stricture		50%
	Fistula		

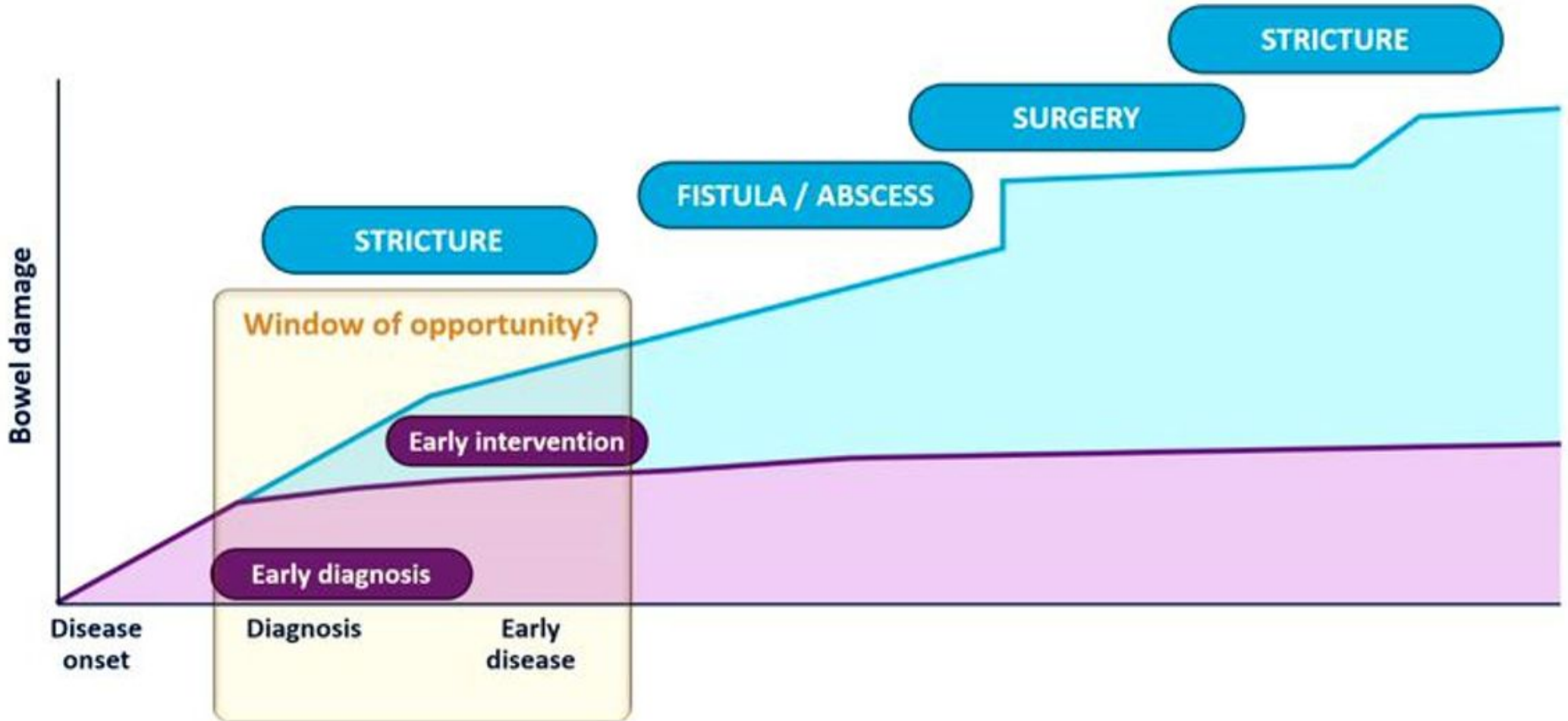
Bowel damage assessed by cross sectional imaging at diagnosis increases the risk of hospitalisation and surgery



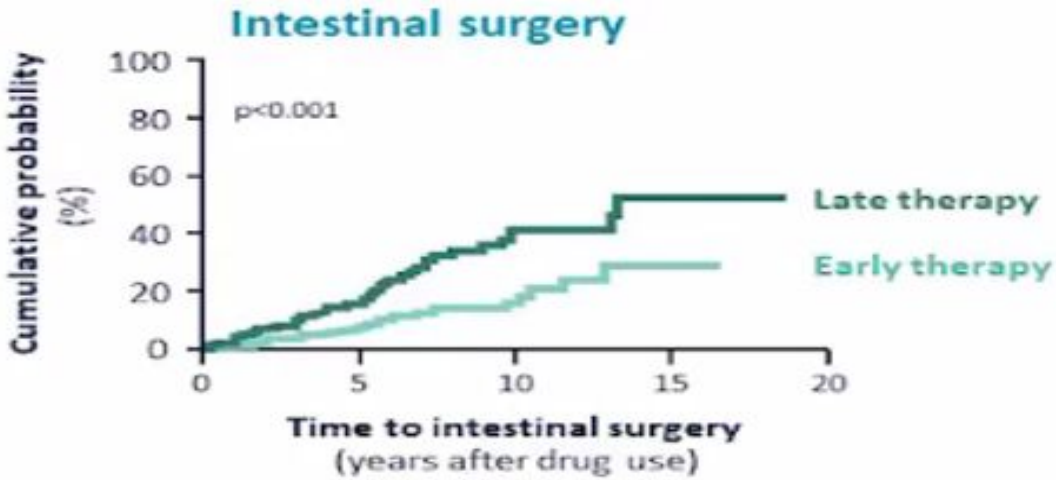
Complicated CD classified as patients with complications at diagnosis, such as strictures, fistulas and abscesses

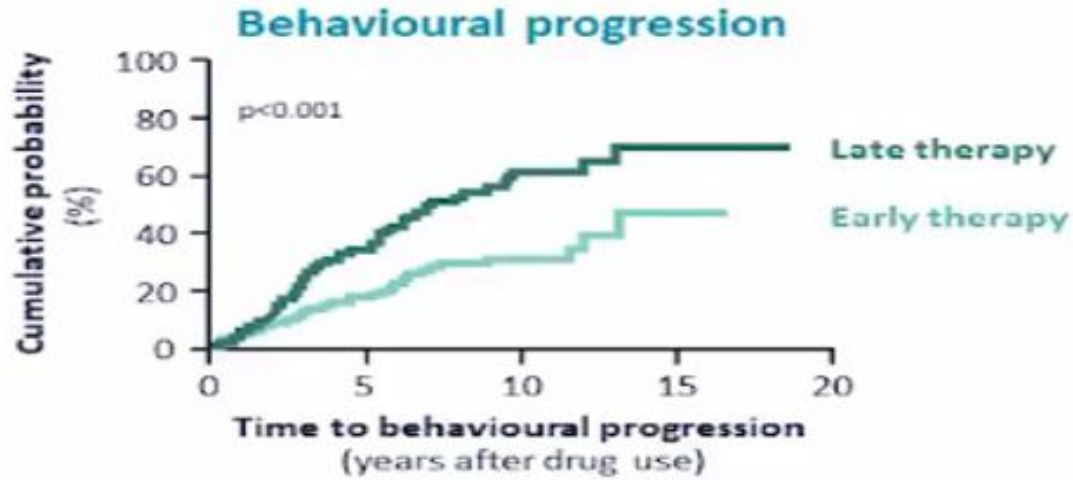
Almost 40% of patients already had bowel damage at diagnosis

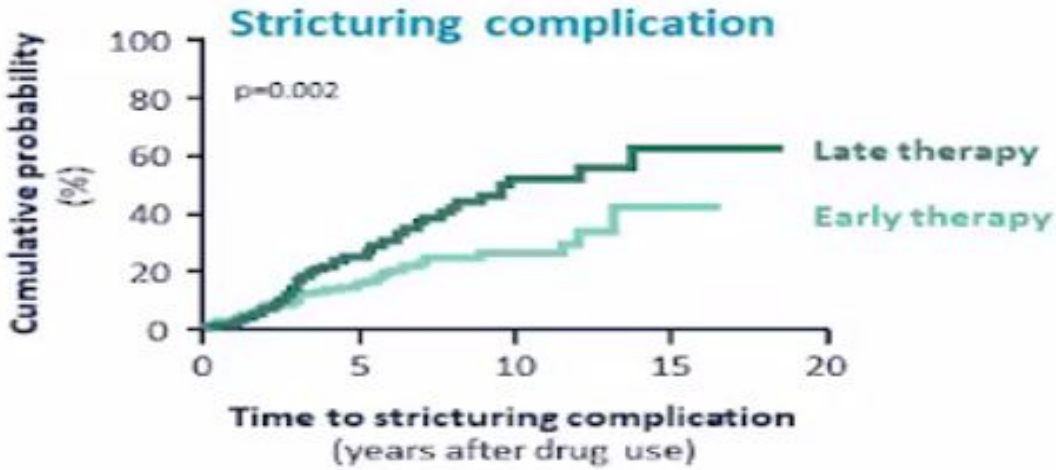
Moving towards disease modification in inflammatory bowel disease

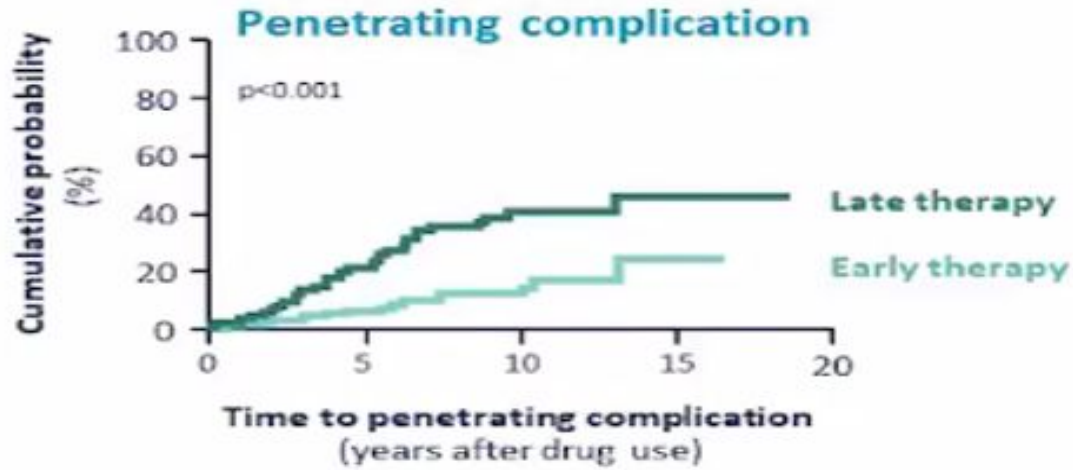


Early anti-TNF / IMM therapy is associated with better long-term clinical outcomes in Crohn's disease



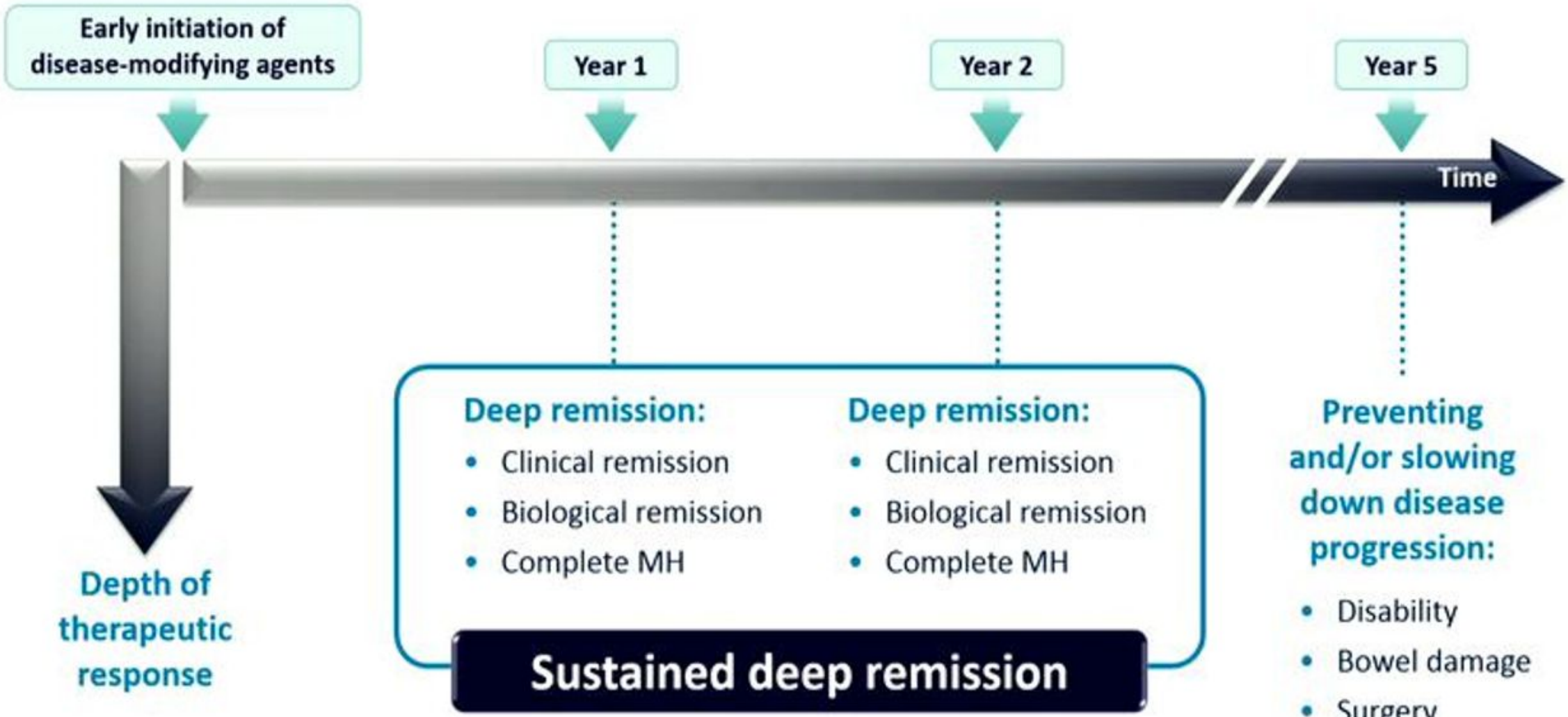






Retrospective analysis of patients with Crohn's disease naive to both intestinal surgery and intestinal complications, and with at least two risk factors for progression.

Targeting early CD *and* achieving sustained deep remission – the best way to change the disease course?



MH, mucosal healing

Is UC a progressive, destructive and disabling condition like CD?

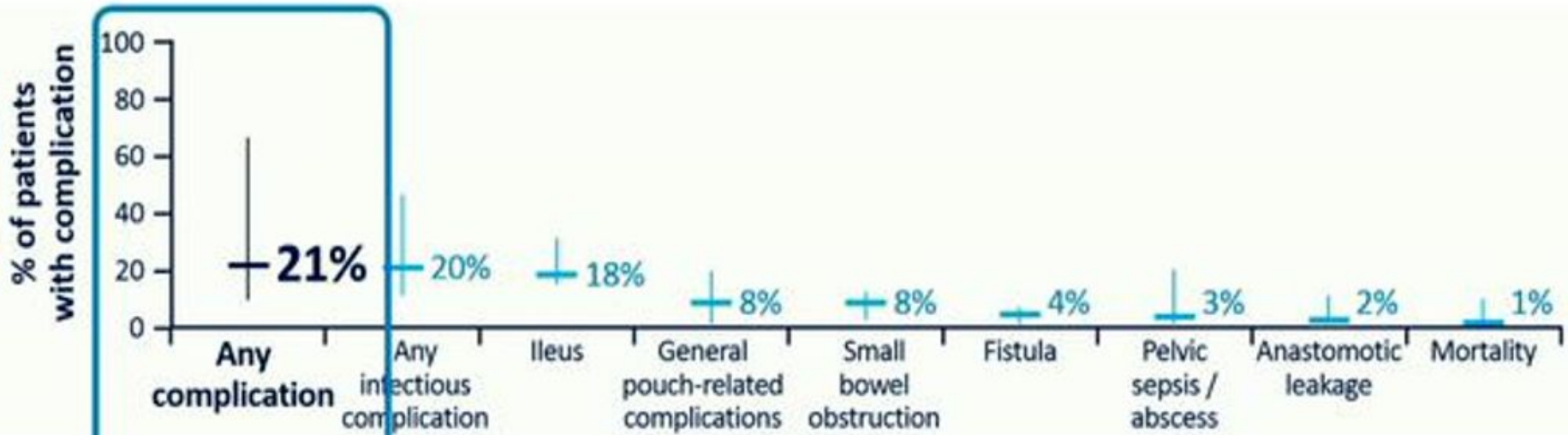
UC patients are often under-treated because of the:

- Possibility to undergo colectomy
- Perception that disease burden is lower in UC than in CD
- Perception that UC is not a progressive disease

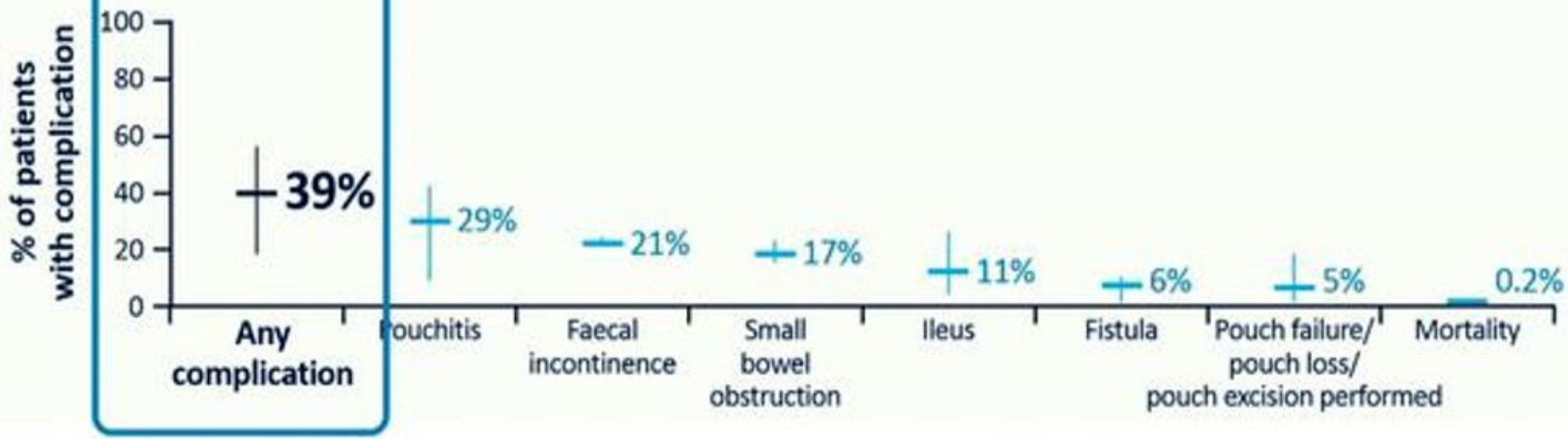
Colectomy is not a cure for UC!

Surgical complications

Postoperative short-term (≤30 days)



Postoperative long-term (>30 days)

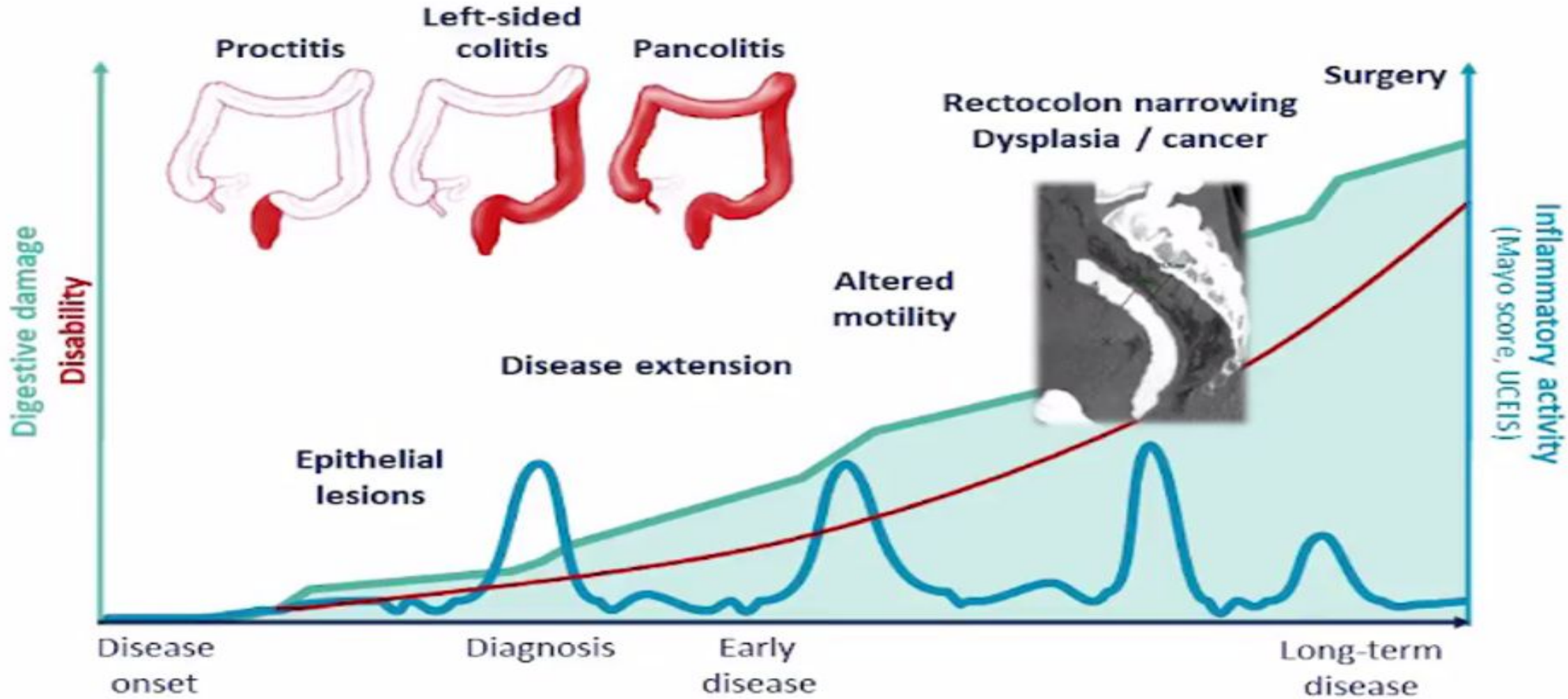


UC has a similar impact on the patient as CD: overall disability

IBD type did not influence IBD-DI (p=0.12)

	Mean ± SD	Min	Max
All IBD (n=200)	**35.3 ± 20.5**	**0**	**91**
Crohn's disease (n=150)	**33.9 ± 19.5**	**0**	**88**
Ulcerative colitis (n=50)	**39.2 ± 23.1**	**0**	**91**

Ulcerative colitis: a progressive disease?



UCEIS, ulcerative colitis endoscopic index of severity.

Colonic strictures in UC should raise concerns about the risk of cancer

Frequency of dysplasia and cancer among patients undergoing surgery for colorectal stricture without preoperative evidence of dysplasia or cancer

	CD (n=248)	UC (n=39)
Low-grade dysplasia, % (n)	**1.2%** (3)	**2.5%** (1)
High-grade dysplasia, % (n)	**0.4%** (1)	**2.5%** (1)
Cancer, % (n)	**0.8%** (2)	**5.0%** (2)
Overall, % (n)	**2.4%** (6)	**10.0%** (4)

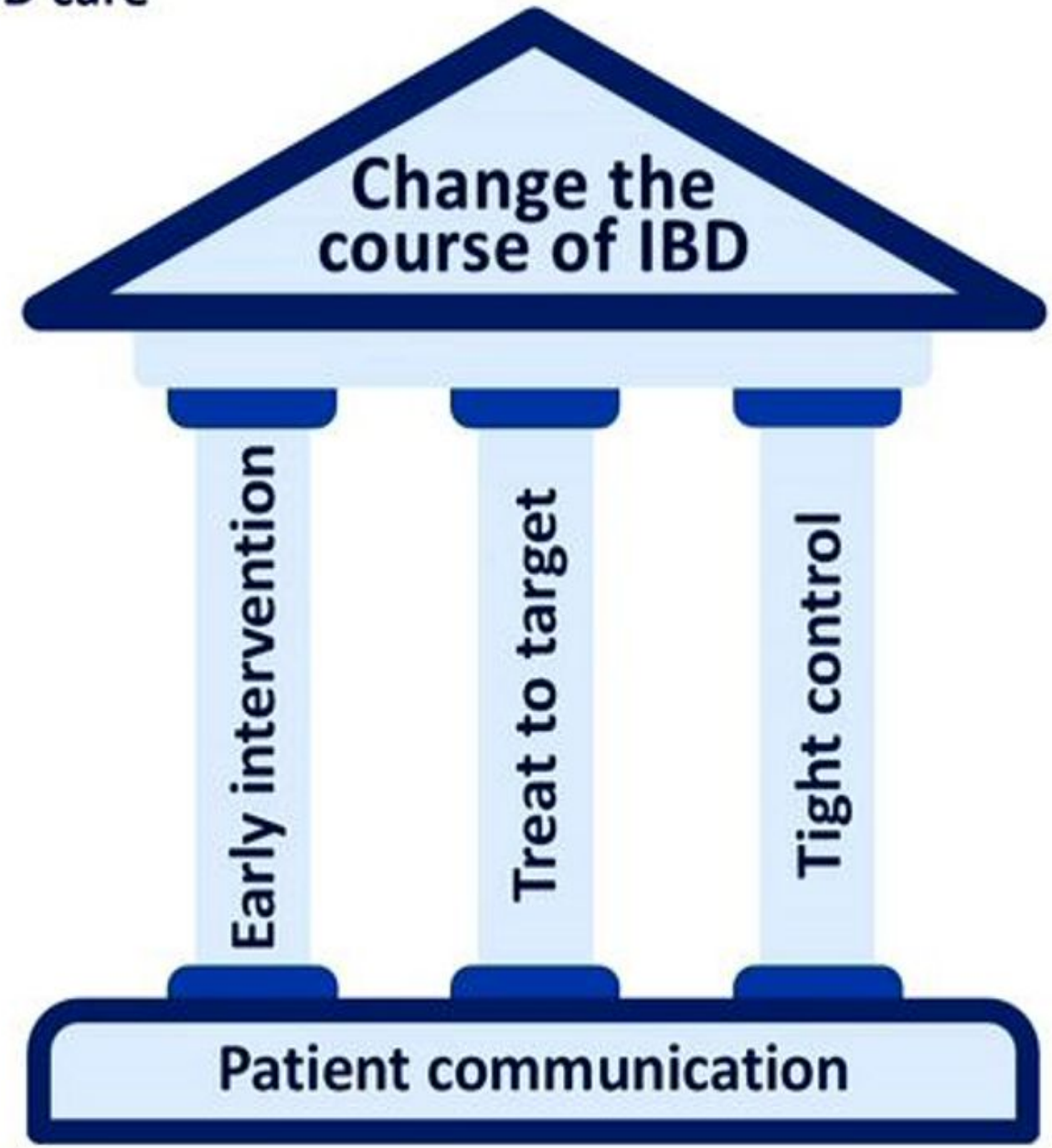
A nationwide study from GETAID:

12,013 patients who underwent surgery for colonic strictures between 1992 and 2014 were screened

GETAID

GETAID, Groupe d'études et thérapeutiques des affections inflammatoires du tube digestif

The three pillars of IBD care



What is treat to target (T2T)?

Aim	Concept	Strategy	Additional principles
To avoid development of serious complications and disability in patients with chronic conditions	Treating to a pre-defined treatment target that is associated with optimal long-term outcomes (goal-oriented approach)	Ongoing and regular monitoring of the target and/or surrogate marker, with optimisation of treatment when the target is not met	All components – target, treatment and monitoring – are tailored to the needs of the individual patient De-escalation of therapy may be considered when treatment goals are achieved

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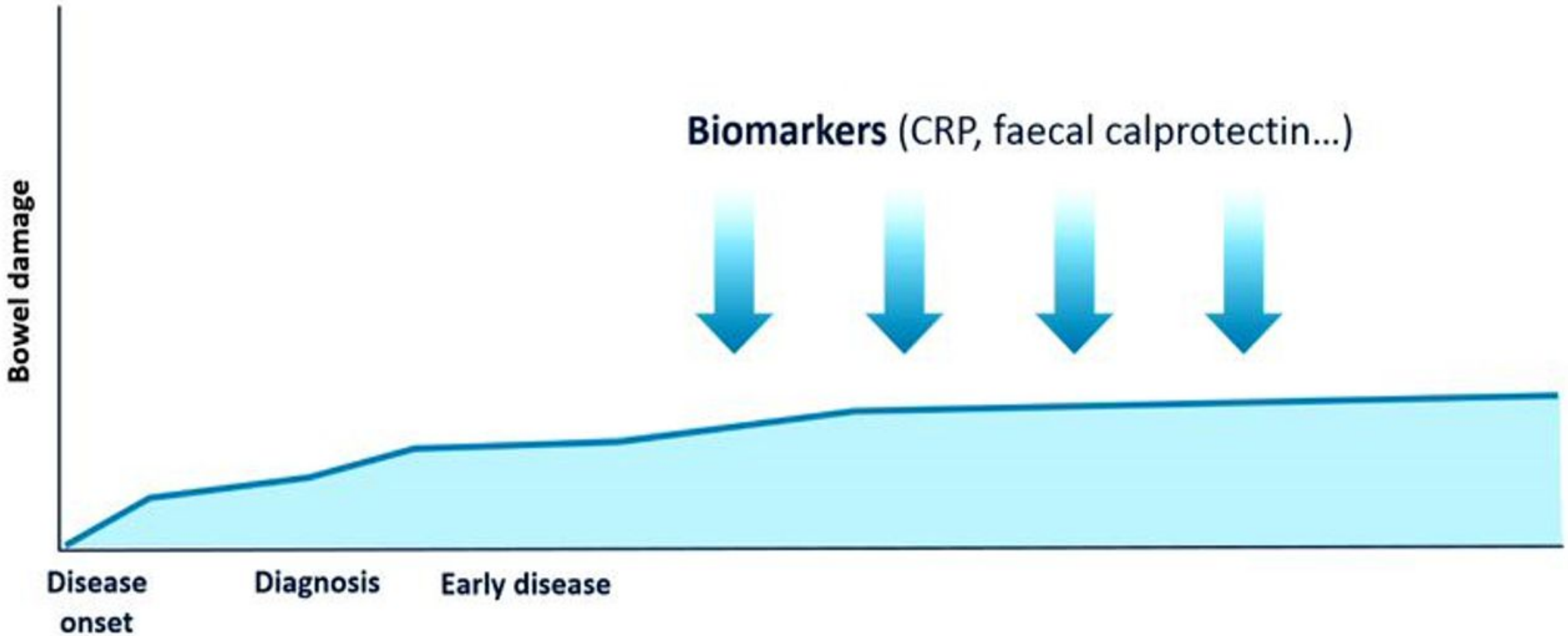
A T2T approach involves pre-defining a treatment target, in consultation with the patient, continuously monitoring disease activity, and modifying treatment until the target is reached

STRIDE: Treat-to-target recommendations in IBD

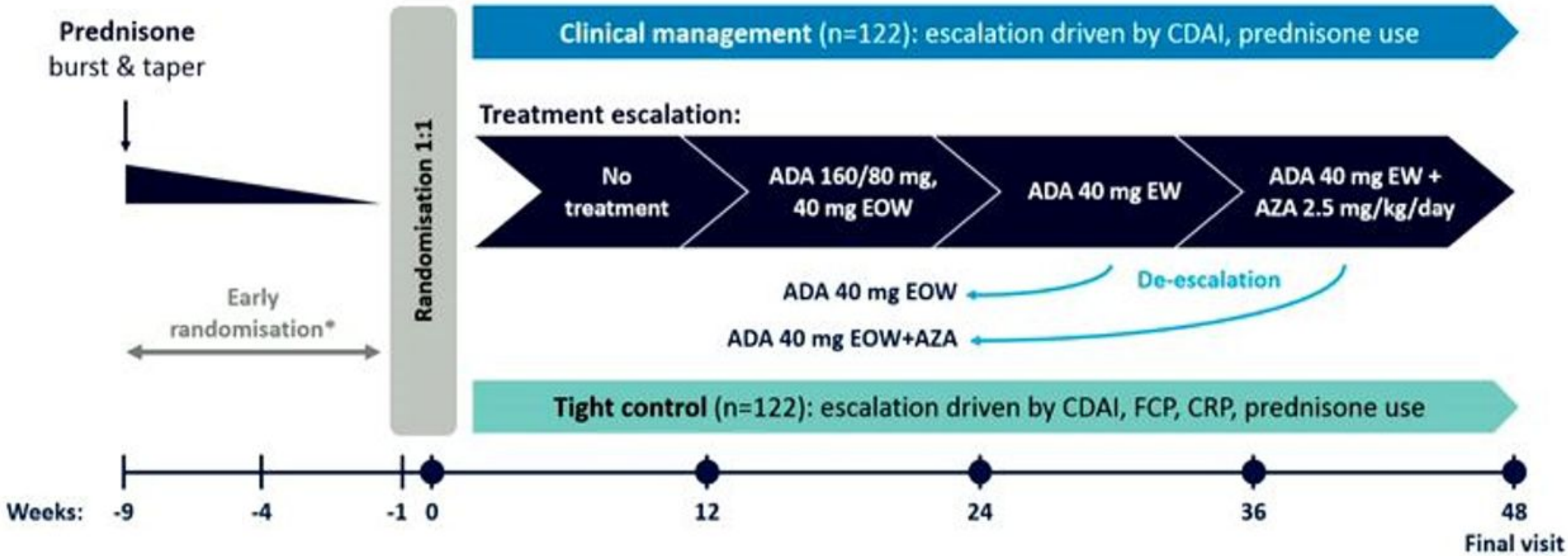
		Crohn's disease	Ulcerative colitis
Clinical	1	Resolution of abdominal pain and normalization of bowel habit should be the target (PRO)	Resolution of rectal bleeding and normalization of bowel habit should be the target (PRO)
	2	**Resolution of symptoms alone is not a sufficient target**. Objective evidence of inflammation of the bowel is necessary when making clinical decisions	**Resolution of symptoms alone is not a sufficient target**. Objective evidence of inflammation of the bowel is necessary when making clinical decisions
Endoscopic	3	**Absence of ulceration is the target**	A Mayo endoscopic subscore of 1 should be a minimum target. **A Mayo endoscopic subscore of 0 is the optimal target.**
	4	Endoscopic or, where endoscopy cannot be performed, cross-sectional imaging assessment should be performed 6–9 months after the start of therapy	Endoscopic assessment should be performed 3–6 months after the start of therapy for a patient with symptoms

"Tight control"



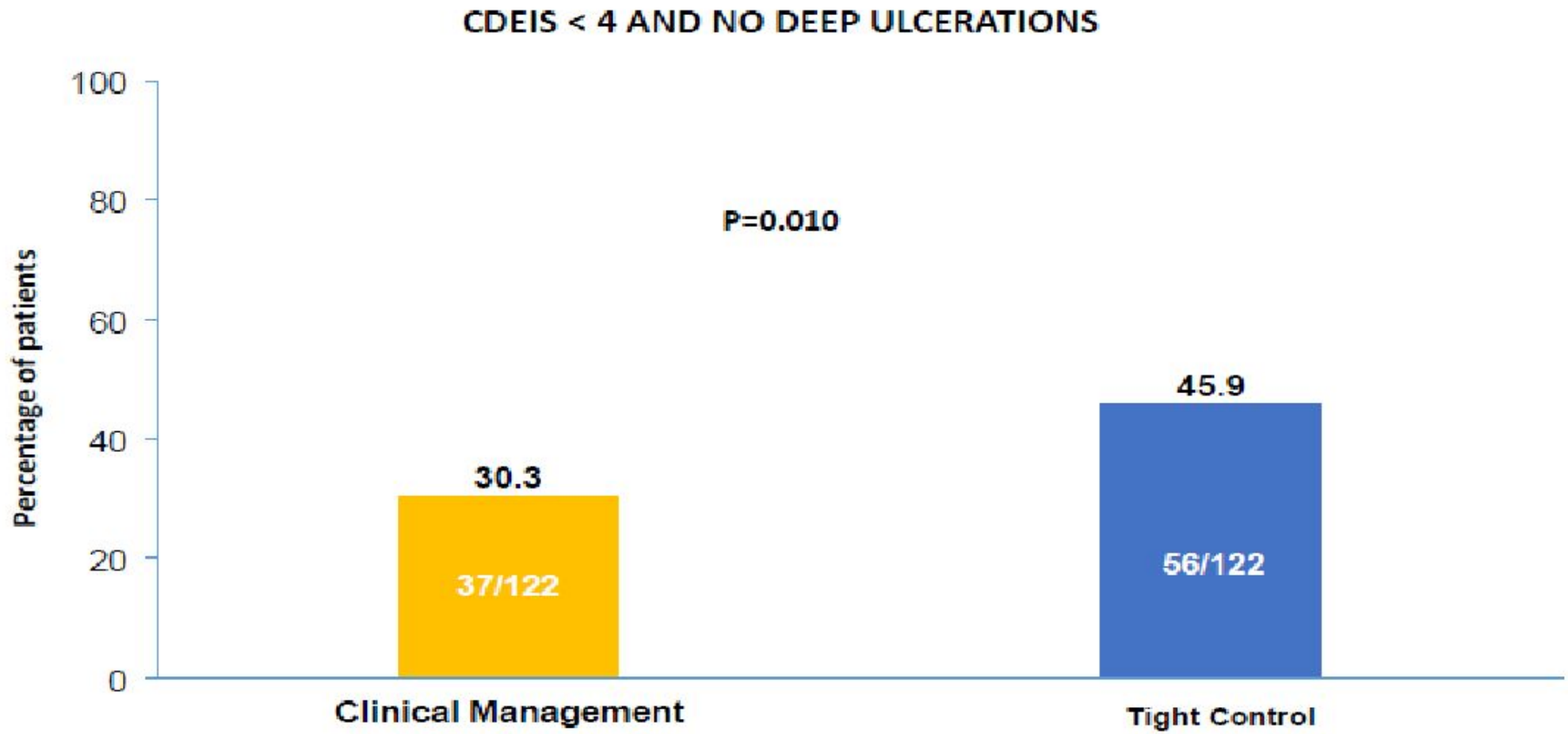
CRP, C-reactive protein

CALM: study design and treatment algorithm



*CDAI >220 AND one of the following: steroid therapy >4 weeks and best to taper per investigator assessment, intolerant/contraindication for steroid therapy, best interest of the patient per investigator assessment.
**CDAI >300 for 2 consecutive visits 7 days apart or per investigator discretion [elevated CRP/FC, ulceration taken into consideration]; moved to T2T group.
ADA, adalimumab; AZA, azathioprine; CDAI, Crohn's Disease Activity Index; CRP, C-reactive protein; EOW, every other week; EW, every week; FCP, faecal calprotectin; T2T, treat to target

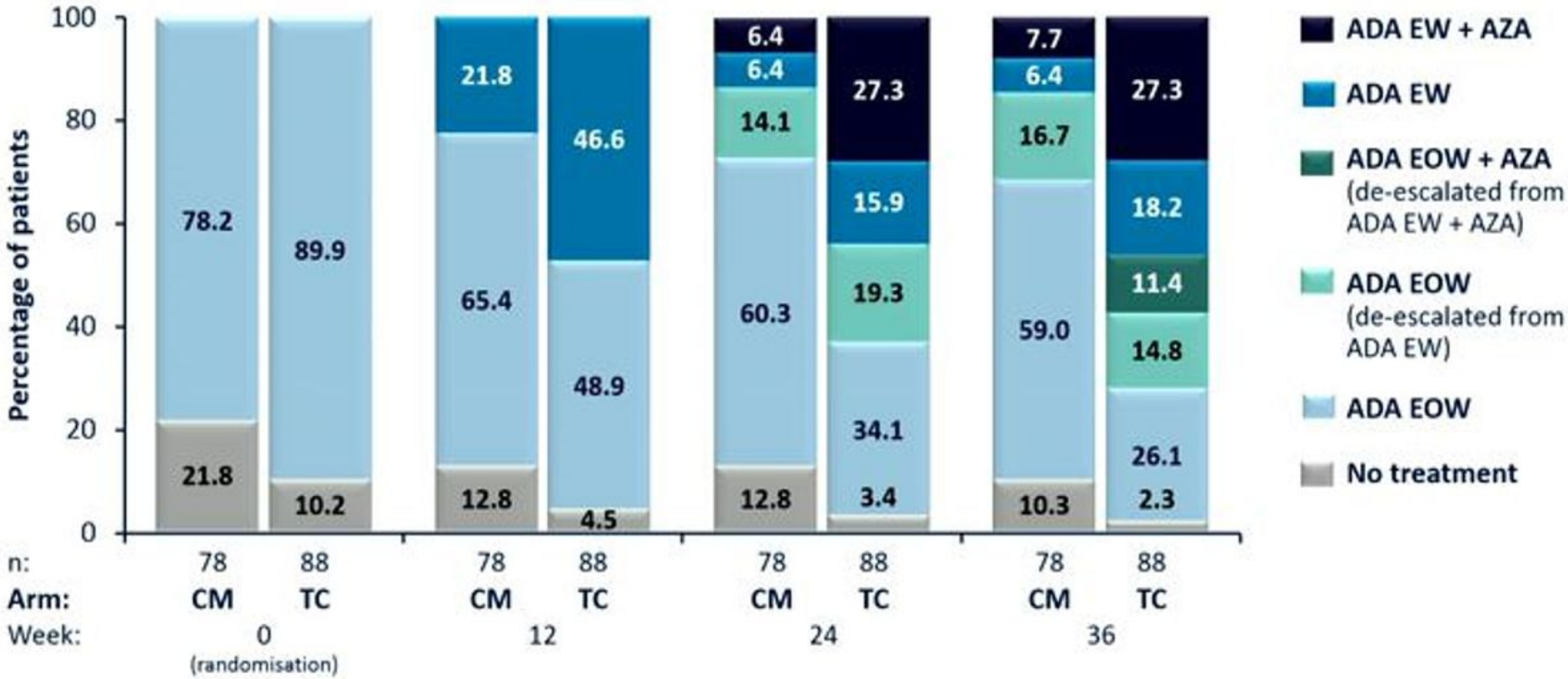
CALM Results:
Primary endpoint 48 weeks after randomization



Colombel J-F et al. *Lancet* 2017 [epub ahead of print]

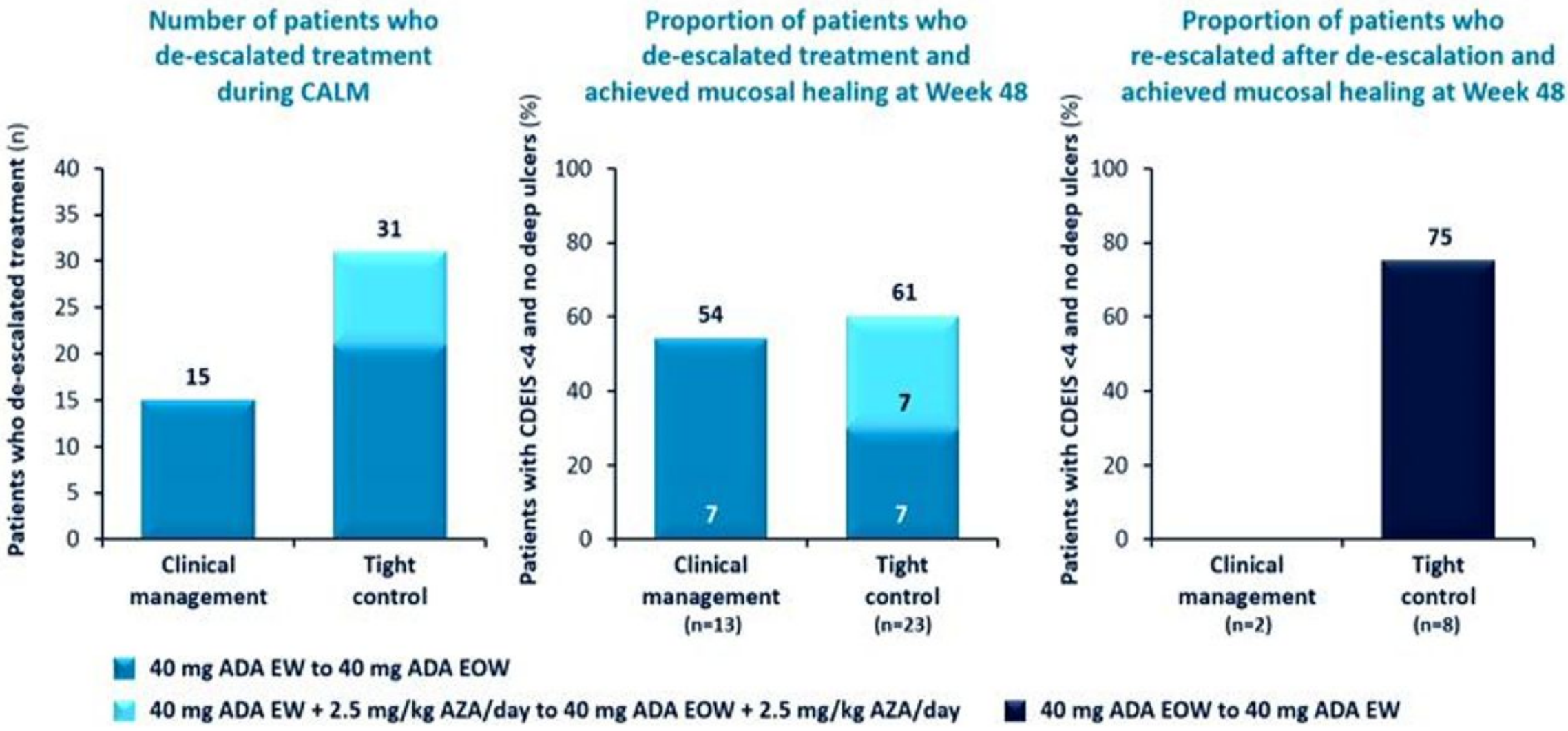
CALM: treatment options over time

Patients who completed the study and did not move to the rescue group



ADA, adalimumab; AZA, azathioprine; CM, clinical management; EOW, every other week; EW, every week; TC, tight control

CALM: treatment optimisation

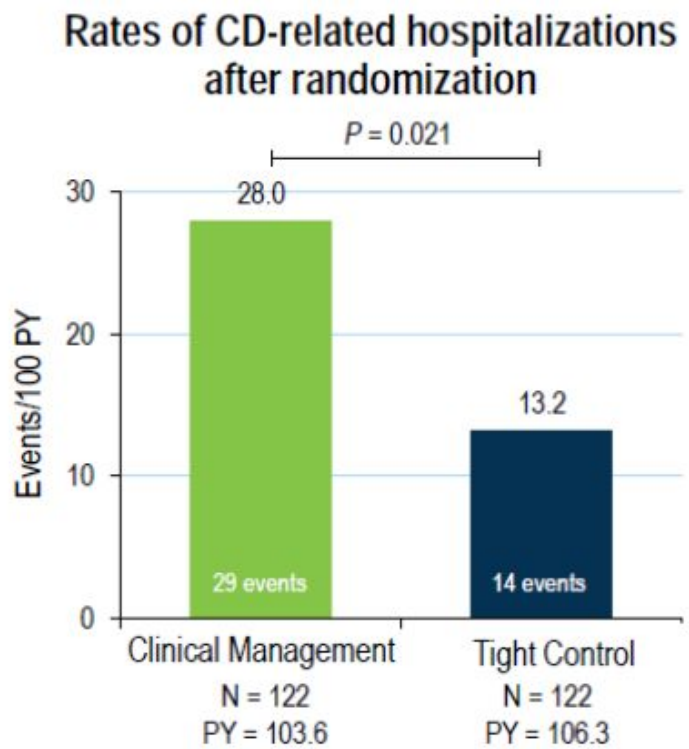


ADA, adalimumab; AZA, azathioprine; CDEIS, Crohn's Disease Endoscopic Index of Severity; EOW, every other week; EW, every week

CALM: Post-hoc analyses

- Compared with clinical management, treat to target was associated with significant reductions in:
  - CD-related hospitalizations
  - Time to CD-related flare
- No significant difference:
  - CD-related surgical procedure
  - CD-related hospitalizations or serious complications

- TC had £669 higher total direct medical costs and 0.032 higher QALYs
- ICER was £20,913 per QALY, which is below the UK NICE threshold of £30,000



CD: Crohn's Disease
*CD-related hospitalization, other than CD-related major surgery, on or after randomization and ≤ 70 days after last dose.

Colombel J., Panaccione R., Bossuyt P., et al. UEGW 2017

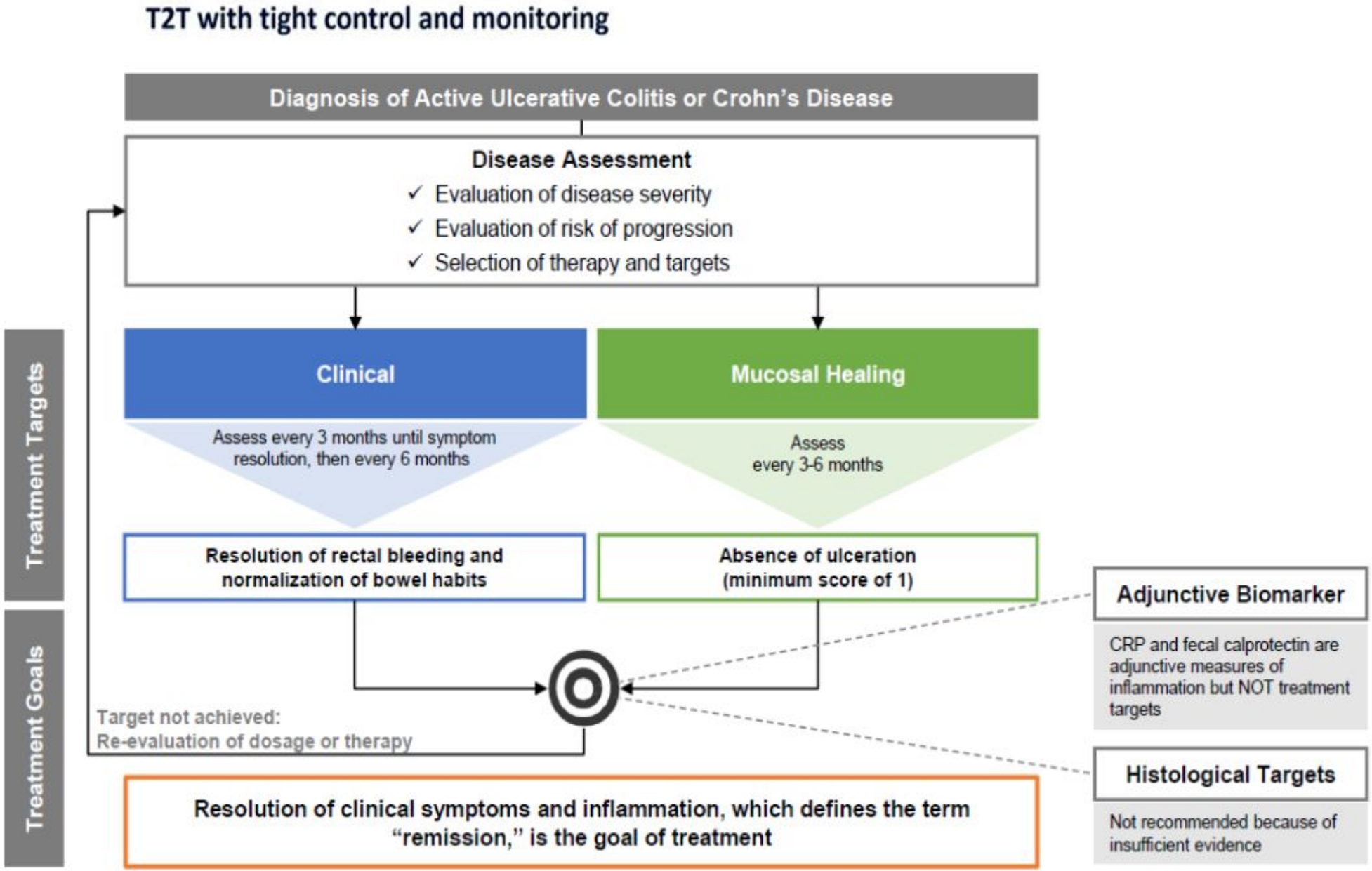
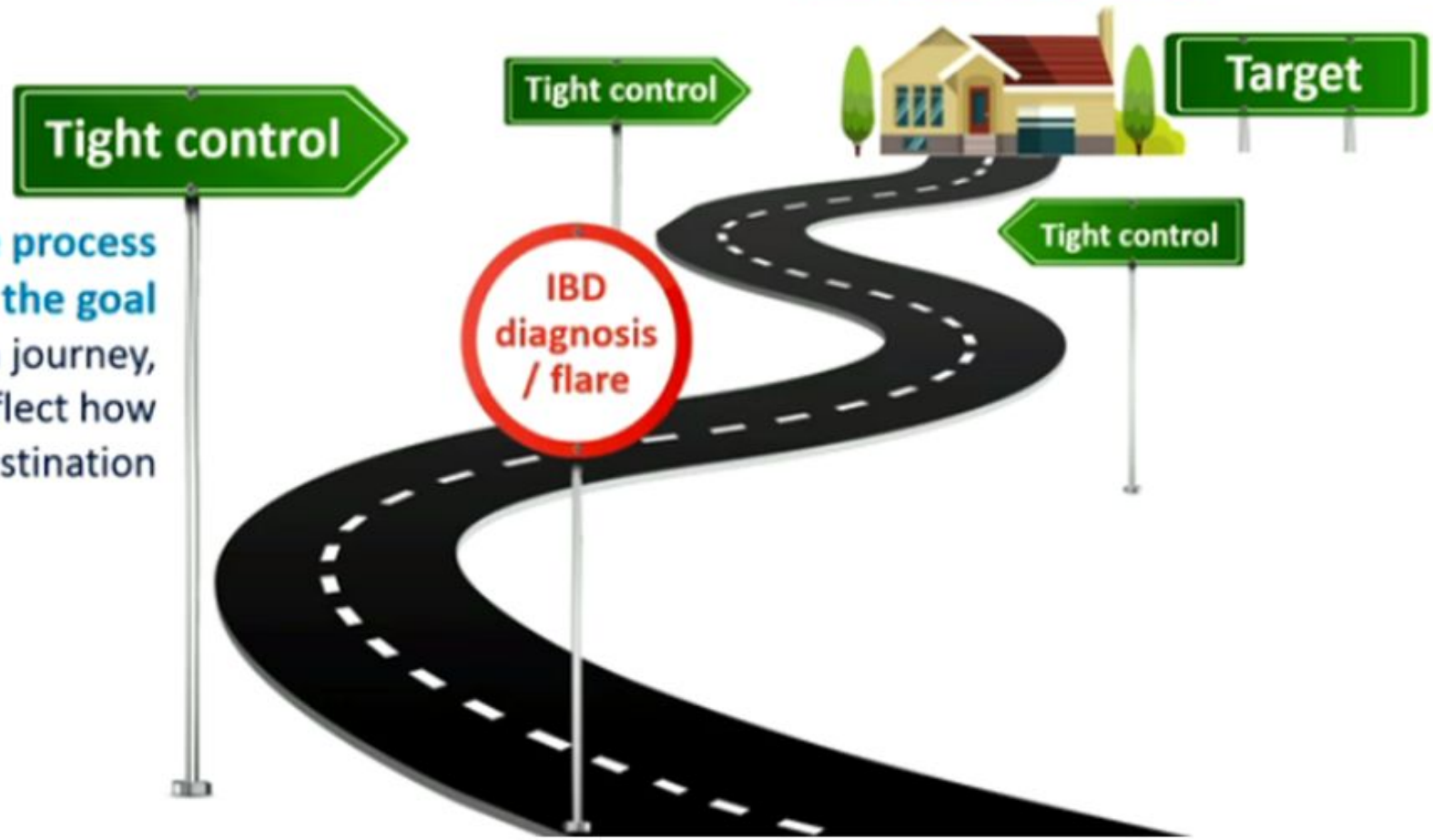


Figure 1. STRIDE recommendations for patients with CD and UC. *Adapted from Peyrin-Biroulet et al*[4] *and Ungaro et al*.[16]

What it looks like at the end !!

This is the destination



This is the process to achieve the goal

If you were on a journey, this would reflect how we get to our destination

The messages .....

UC and CD are progressive diseases, and have same clinical burden

Treating early improves clinical outcomes

T2T and TC are complementary and should be tailored to the individual patient

biomarkers are an important bridge that helps to achive the best possible results