

The Medical Management of the J-Pouch and Its Complications

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Learning Objectives

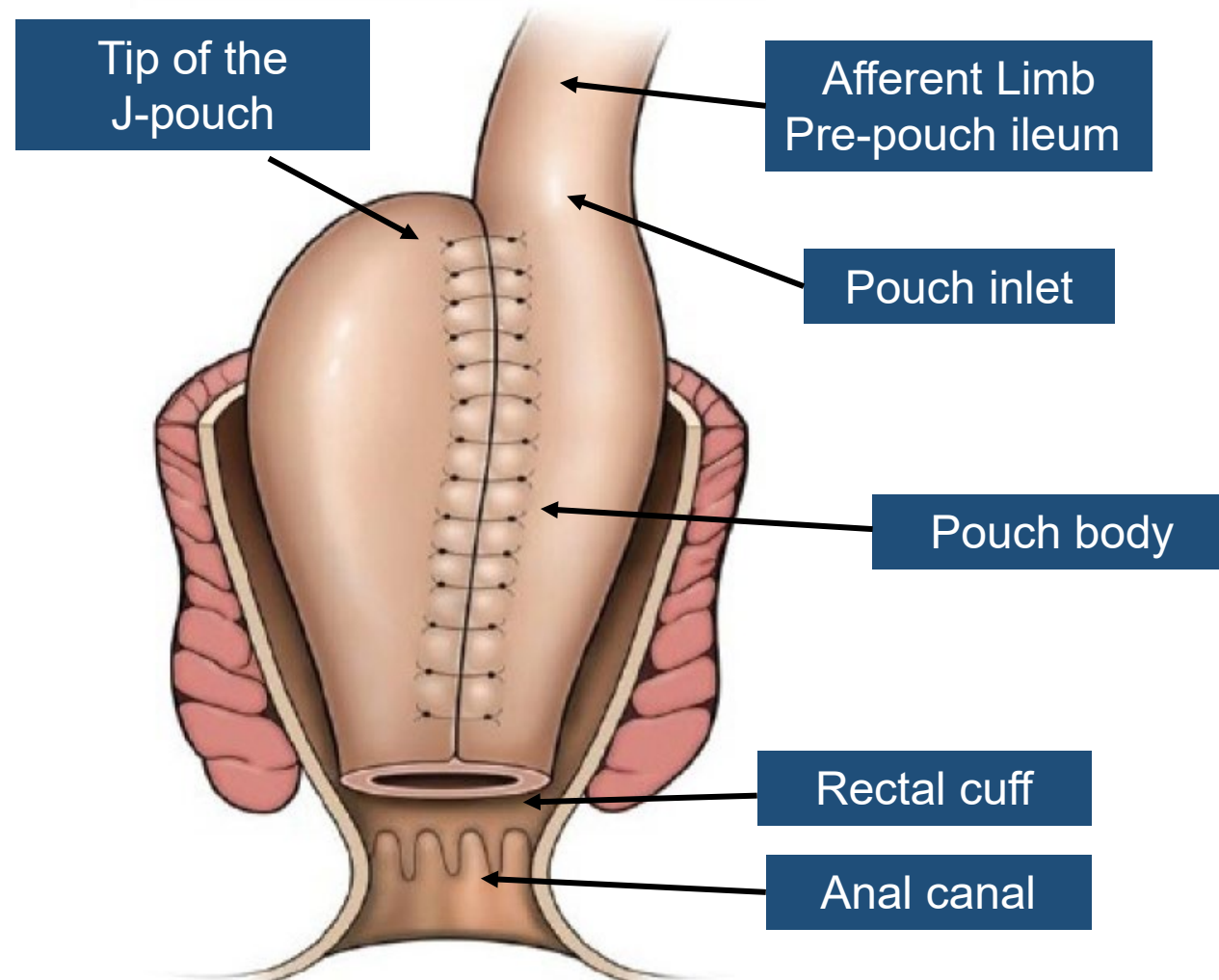
1. Review standard approaches to intermittent pouchitis and supporting data
2. Discuss recent updates in medical management of chronic pouchitis
3. Discuss emerging concepts in the management of chronic inflammatory conditions of the pouch
4. Discuss the concept of prevention in the management of pouch-related disorders

Restorative Proctocolectomy with Ileal Pouch-Anal Anastomosis

Approximately 10% of patients with ulcerative colitis (UC) will require a colectomy within 10 years of diagnosis

In cases of colectomy for refractory colitis due to UC or UC-related dysplasia, restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the preferred surgical intervention

Basics of the J Pouch Anatomy



AGA Guidelines for Pouchitis and Inflammatory Pouch Disorders

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GUIDELINES

AGA Clinical Practice Guideline on the Management of Pouchitis and Inflammatory Pouch Disorders



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GUIDELINES

Standardizing our Approach to Patients with an Ileal Pouch-Anal Anastomosis



Diagnosis and classification of ileal pouch disorders:
consensus guidelines from the International Ileal Pouch
Consortium

Treatment of pouchitis, Crohn's disease, cuffitis, and other
inflammatory disorders of the pouch: consensus guidelines
from the International Ileal Pouch Consortium



Development of the Endoscopic Pouch Score for Assessment
of Inflammatory Conditions of the Pouch



Endoscopic Phenotype of the J Pouch in Patients With Inflammatory Bowel Disease: A New Classification for Pouch Outcomes

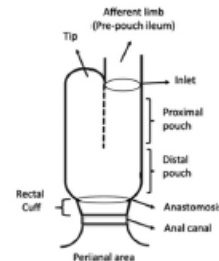
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A New Endoscopic Phenotype Classification for J Pouch Outcomes in IBD The Chicago Classification

N = 426 pts
1,359 pouchoscopies

7 phenotypes



Normal
Afferent limb involvement
Inlet involvement
Diffuse inflammation
Focal inflammation
Cuffitis
Pouch with fistulas

Log-rank test

Inlet stenosis, diffuse inflammation, and
cuffitis significantly increased the risk of
pouch excision.

Cox proportional hazards model

Diffuse inflammation was independently
associated with pouch excision
(HR 2.69; 95% CI 1.34-5.41).

Clinical Gastroenterology
and Hepatology

Pragmatic Definitions of Inflammatory Conditions of the Pouch

Term	Definition
Intermittent Pouchitis	Isolated and infrequent episodes of typical pouchitis symptoms that resolve with therapy (most commonly antibiotics) or spontaneously, followed by extended periods of normal pouch function (typically months to years). Because antibiotics are the most commonly used therapy for symptoms of pouchitis, we anchored our functional definitions of pouchitis around response to antibiotic therapy.
Chronic antibiotic-dependent pouchitis	Recurrent episodes of pouchitis that responds to antibiotic therapy but relapses shortly after stopping antibiotics (typically within days to weeks), and often requires recurrent or continuous antibiotic therapy or other advanced therapies to achieve symptom control. We did not define this entity on the basis of a specific number of pouchitis episodes within a 12- month time period because this is a continuum (some patients may require 3–4 courses of antibiotics per year and others require almost continuous antibiotics) and patients’ and providers’ preferences for treatment approach vary depending on frequency of these episodes.
Chronic antibiotic-refractory pouchitis	Relapsing–remitting or continuous symptoms of pouchitis with inadequate response to typical antibiotic therapy (ongoing symptoms attributable to pouchitis), often needing escalation to other therapies.
Crohn’s-like disease of the pouch	Defined on the basis of the most common and accepted diagnostic criteria for this condition, recognizing variability in prior literature. These diagnostic criteria include presence of a perianal or other fistula that developed at least 12 months after the final stage of IPAA surgery, stricture of the pouch body or pre-pouch ileum, and the presence of pre-pouch ileitis. The panel recognized that pouchitis may often coexist in patients with Crohn’s-like disease of the pouch.

Intermittent Pouchitis (Acute Pouchitis)

Typical symptoms:

- Frequency
- Urgency
- Incontinence
- Abdominal/pelvic cramping or pain

Intermittent pouchitis

- isolated and infrequent episodes of typical pouchitis symptoms
- improve with therapy (most commonly, antibiotics) or spontaneously
- followed by resolution of symptoms and periods of normal pouch function

Intermittent Pouchitis

The typical approach to intermittent pouchitis utilizes a 14-day course of ciprofloxacin or metronidazole

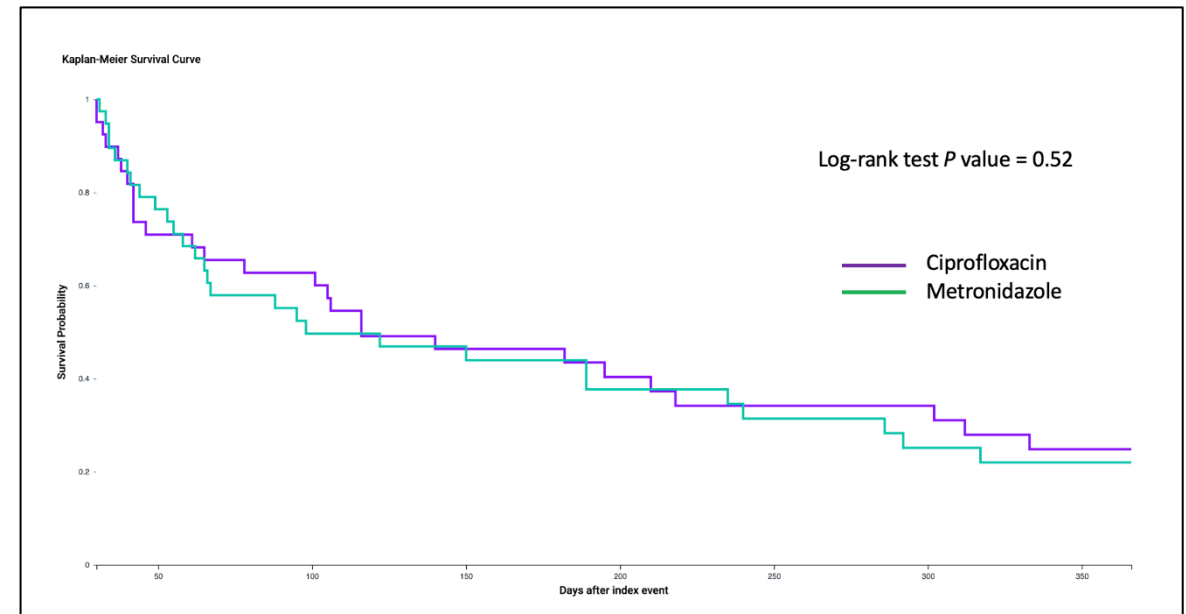
- Ciprofloxacin may be associated with a greater response, with less adverse effects
- Some providers may choose a longer initial course of antibiotics

TABLE 3. Comparison of reduction of the PDAI scores after antibiotic therapy between ciprofloxacin and metronidazole groups

	Post Rx mean reduction		Difference (95% CI)	p value
	Ciprofloxacin (N = 7)	Metronidazole (N = 9)		
Reduction in total PDAI score	6.9 ± 1.2	3.8 ± 1.7	3.2 (1.3–4.6)	0.002
Reduction in symptom score	2.4 ± 0.9	1.3 ± 0.9	1.1 (0.3–2.1)	0.03
Reduction in endoscopy score	3.6 ± 1.3	1.9 ± 1.5	1.8 (0.2–3.2)	0.03
Reduction in histology score	0.9 ± 0.9	0.6 ± 0.5	0.4 (–0.4–1.1)	0.41

PDAI, pouchitis disease activity index; CI, confidence interval.

Time to Recurrent Pouchitis



Nguyen N, et al. Cochrane Database Syst Rev. 2019;5:Cd001176.

Shen B, et al. Inflamm Bowel Dis. 2001;7:301-5.

Barnes EL and Agrawal M, et al. Gastroenterology 2024;166:59-85.

Barnes EL et al. Am J Gastroenterol. 2023;118:1989-1996.

Chronic Pouchitis

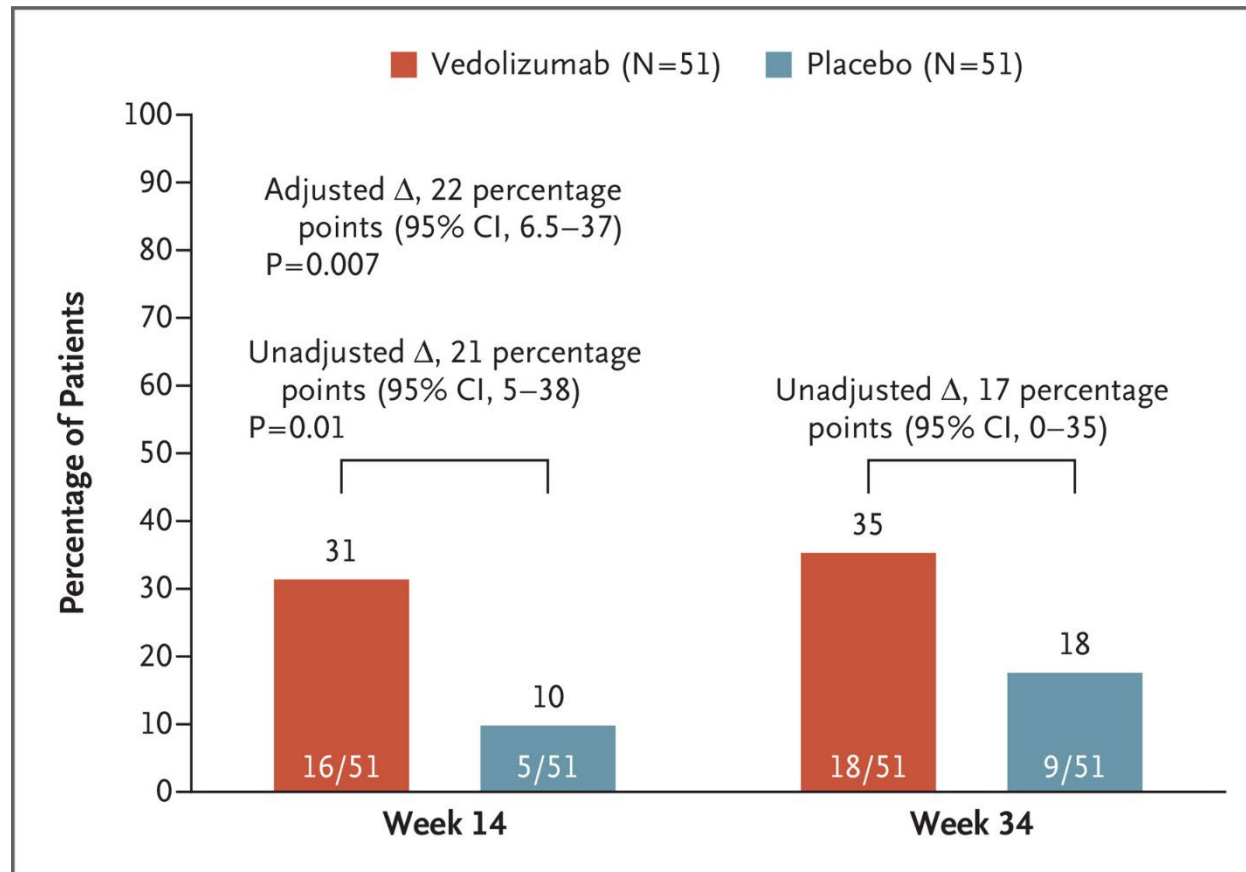
Chronic antibiotic-dependent pouchitis (CADP)

- Symptoms are controlled on antibiotics, but worsen when antibiotics are discontinued
- Traditional definition: Multiple pouchitis episodes per year (>4)
- **Objective of treatment: minimally effective dose of antibiotics that controls an individual patient's symptoms**

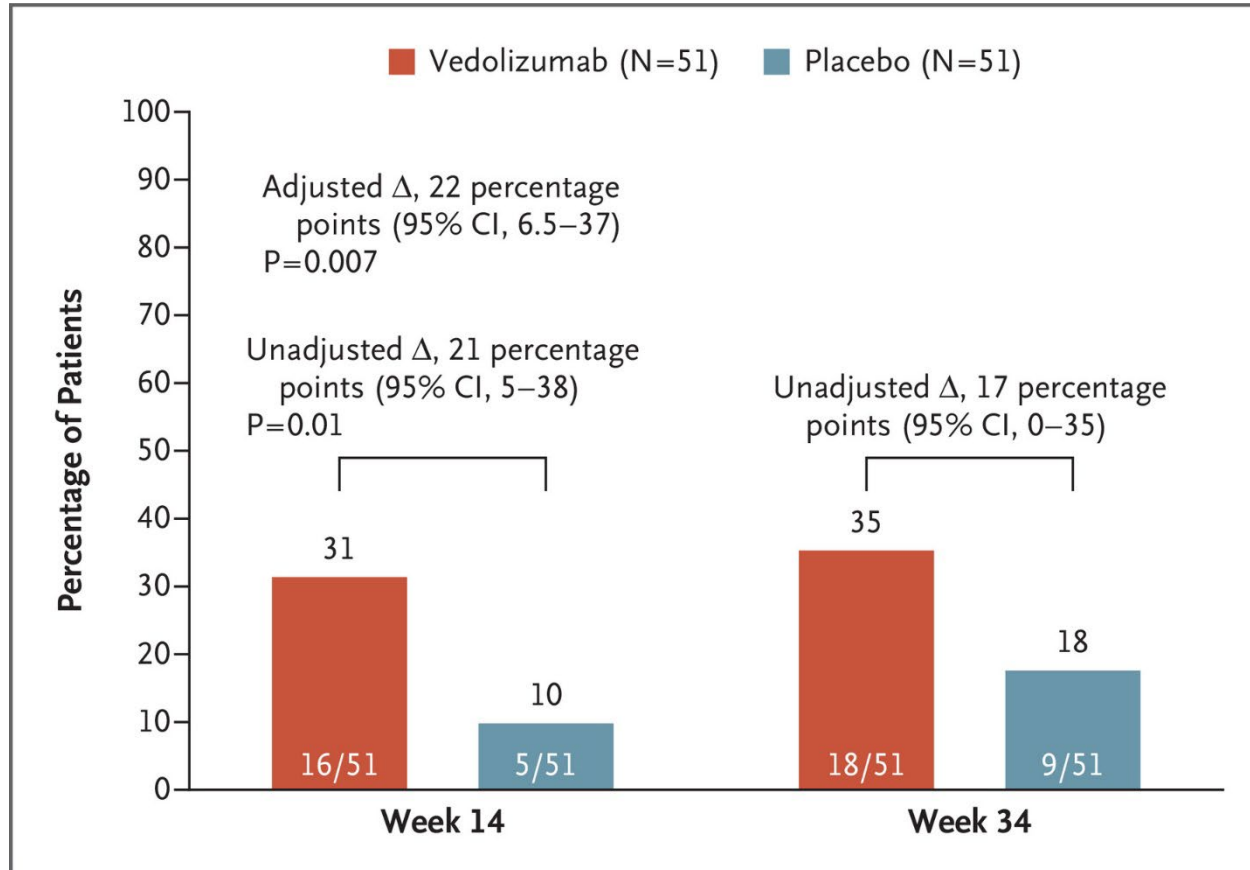
Chronic antibiotic-refractory pouchitis (CARP)

- Relapsing-remitting or continuous symptoms of pouchitis with inadequate response to normal antibiotic regimens
- **Treatment: often requires escalation to other therapies such as biologics or small molecule therapies**

Vedolizumab: The EARNEST Trial



Vedolizumab: The EARNEST Trial

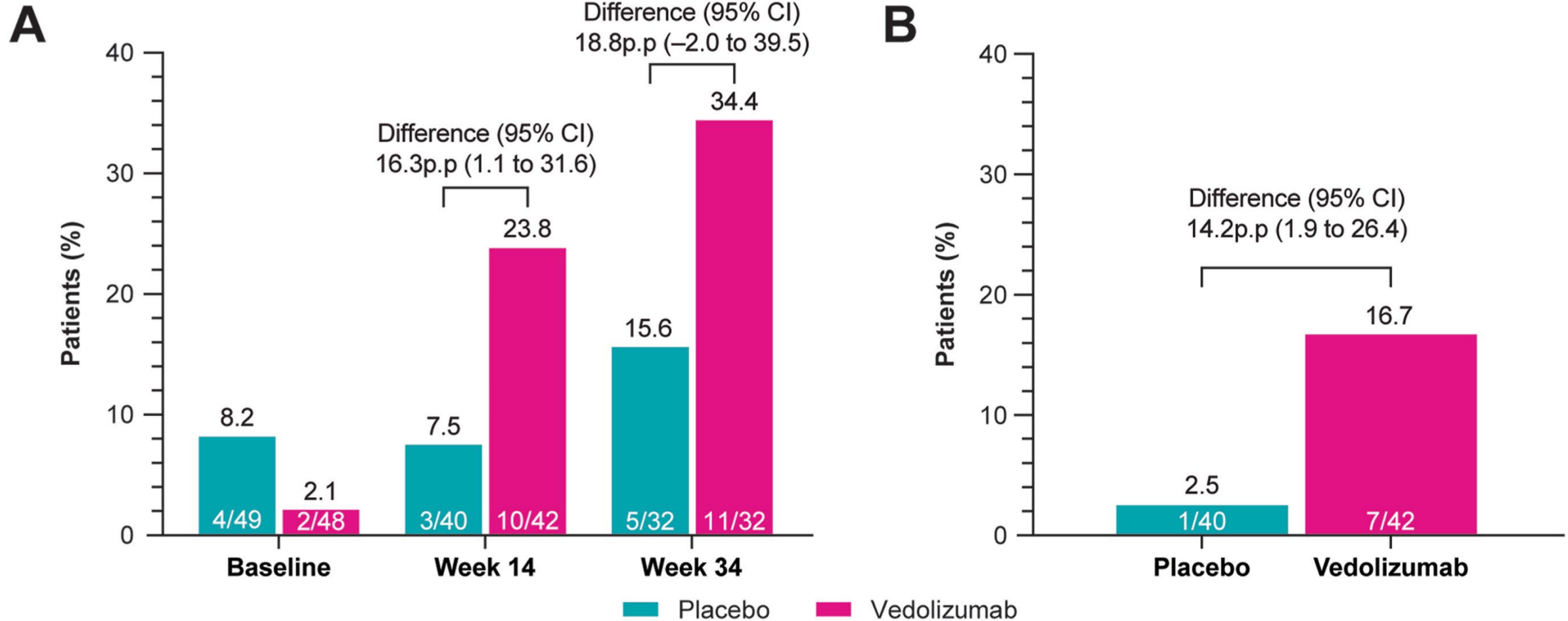


Additional Concomitant Antibiotics for Pouchitis Taken by Visit

Visit, n (%)	Placebo N=51	Vedolizumab N=51
Overall		
N	51	51
Antibiotic use	19 (37.3)	30 (58.8)
No antibiotic use	32 (62.7)	21 (41.2)
Day 1		
N	51	51
Antibiotic use	1 (2.0)	3 (5.9)
No antibiotic use	50 (98.0)	48 (94.1)
Week 14		
N	40	45
Antibiotic use	8 (20.0)	10 (22.2)
No antibiotic use	32 (80.0)	35 (77.8)
Week 34		
N	32	33
Antibiotic use	4 (12.5)	7 (21.2)
No antibiotic use	28 (87.5)	26 (78.8)

All patients received companion antibiotic treatment through week 4, not considered here

Endoscopic Outcomes with Vedolizumab



Proportion of patients with (A) SES-CD remission and (B) mucosal healing at Week 14 (full analysis set). SES-CD remission is defined as a total SES-CD of ≤ 2 .

Ustekinumab: Prospective Data

N=22	Baseline	Week 16	Week 48	P-value
Total mPDAI score (range)	8 (7-10)	7 (4-9)	4 (1.8-7.3)	0.007
Clinical subscore	3.5 (2-4)	2 (1-3)	1 (0-2.3)	0.001
Endoscopic subscore	5.5 (4-6)	4 (3-6)	3 (1.8-4.3)	0.001
Fecal calprotectin mg/kg	357 (199-666)	175 (91-593)	129 (63-333)	0.17
CRP, mg/L	4.1 (1.9-7.2)	3.7 (1.8-9.5)	2.5 (1.3-4.4)	0.09

Previous treatment for pouchitis included topical or systemic 5-aminosalicylic acid (n=6), topical or systemic steroids (n=17), immunomodulators (n=8), anti-tumor necrosis factor agents (anti-TNF; n=9), vedolizumab (n=7), or tofacitinib (n=1)

Crohn's-like Disease of the Pouch

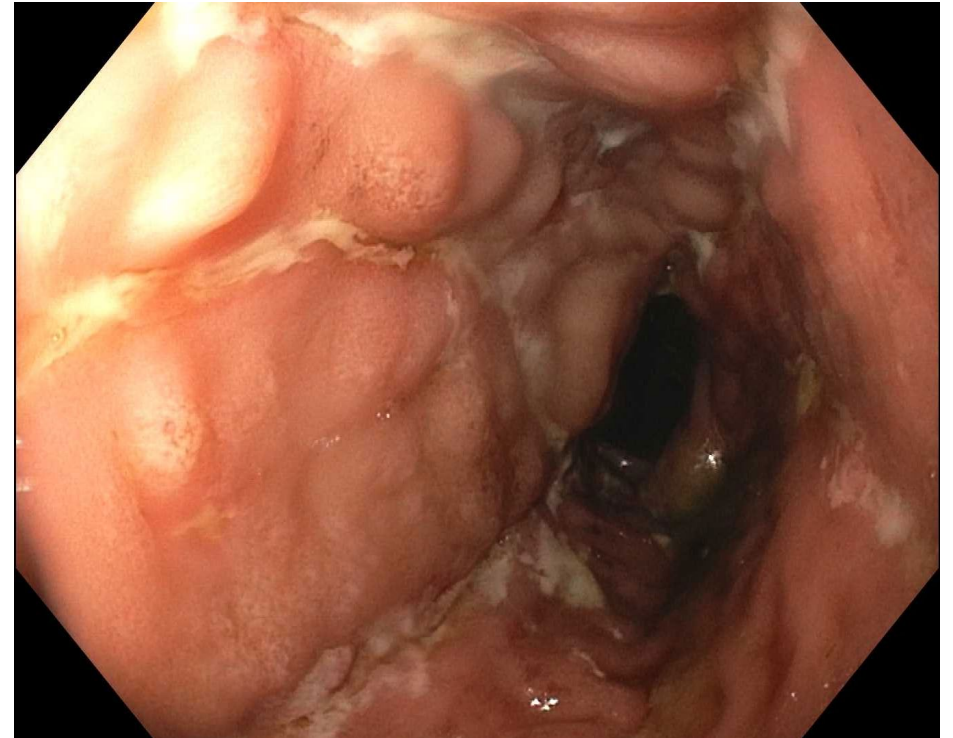
Characterized by fistulae development, pouch and afferent limb strictures, and pre-pouch ileitis

Meta-analysis of 11 Studies

Incidence Range: 5% - 21%

Pooled Incidence:

10.3% (95% CI: 6.1% – 15.4%)



Efficacy of Biologic Therapy for Crohn's-like Disease of the Pouch

Anti-TNF Therapy: Systematic review and meta-analysis

- Rate of short-term clinical remission: 0.64 (0.50 – 0.77)
- Rate of long-term clinical remission: 0.57 (0.43– 0.71)

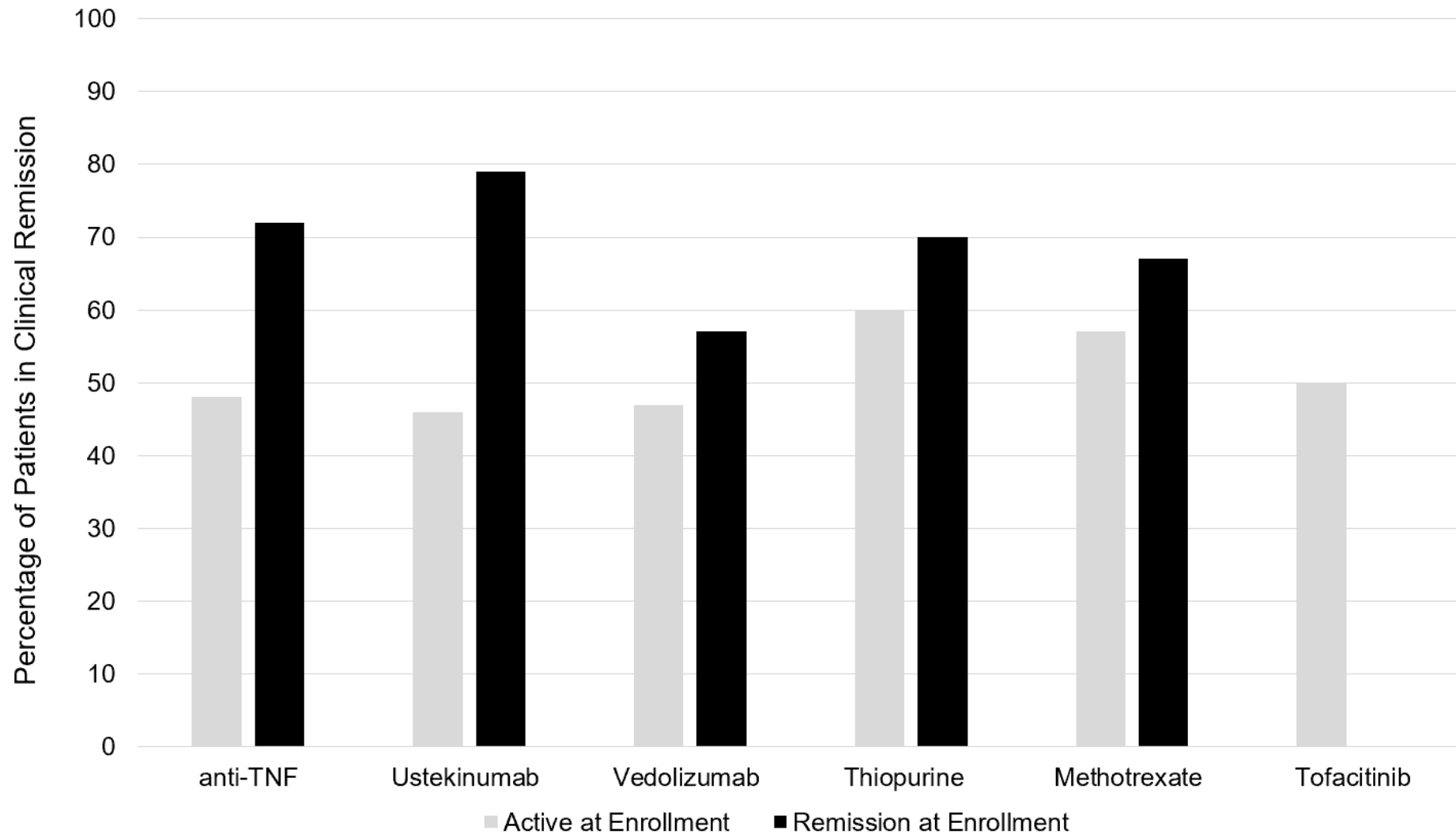
Vedolizumab: Multicenter study from 5 academic IBD centers

- 71% clinical response
- 19% clinical remission
- 36% discontinued vedolizumab
- 60% continued antibiotics

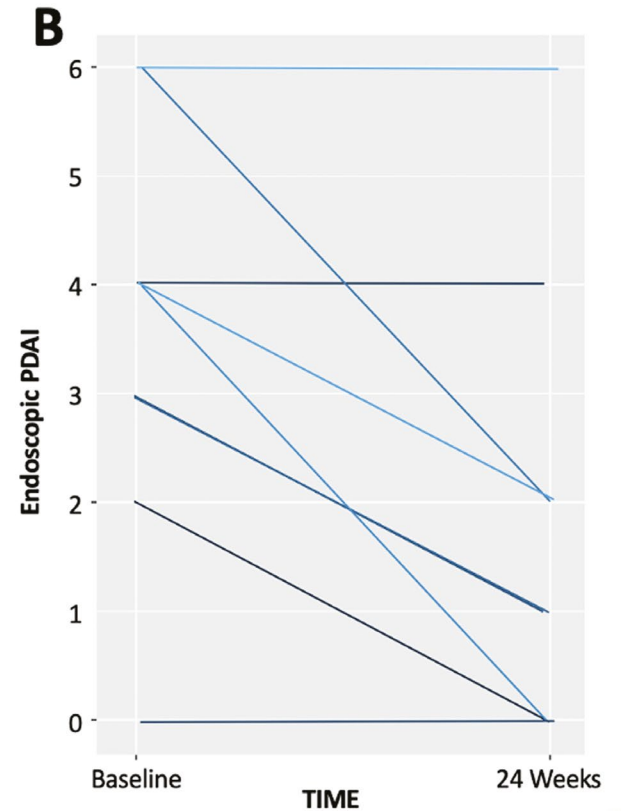
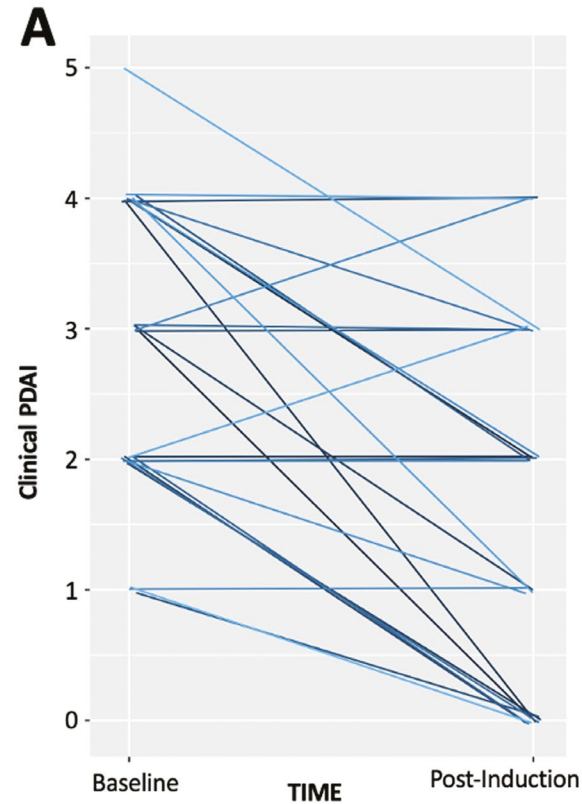
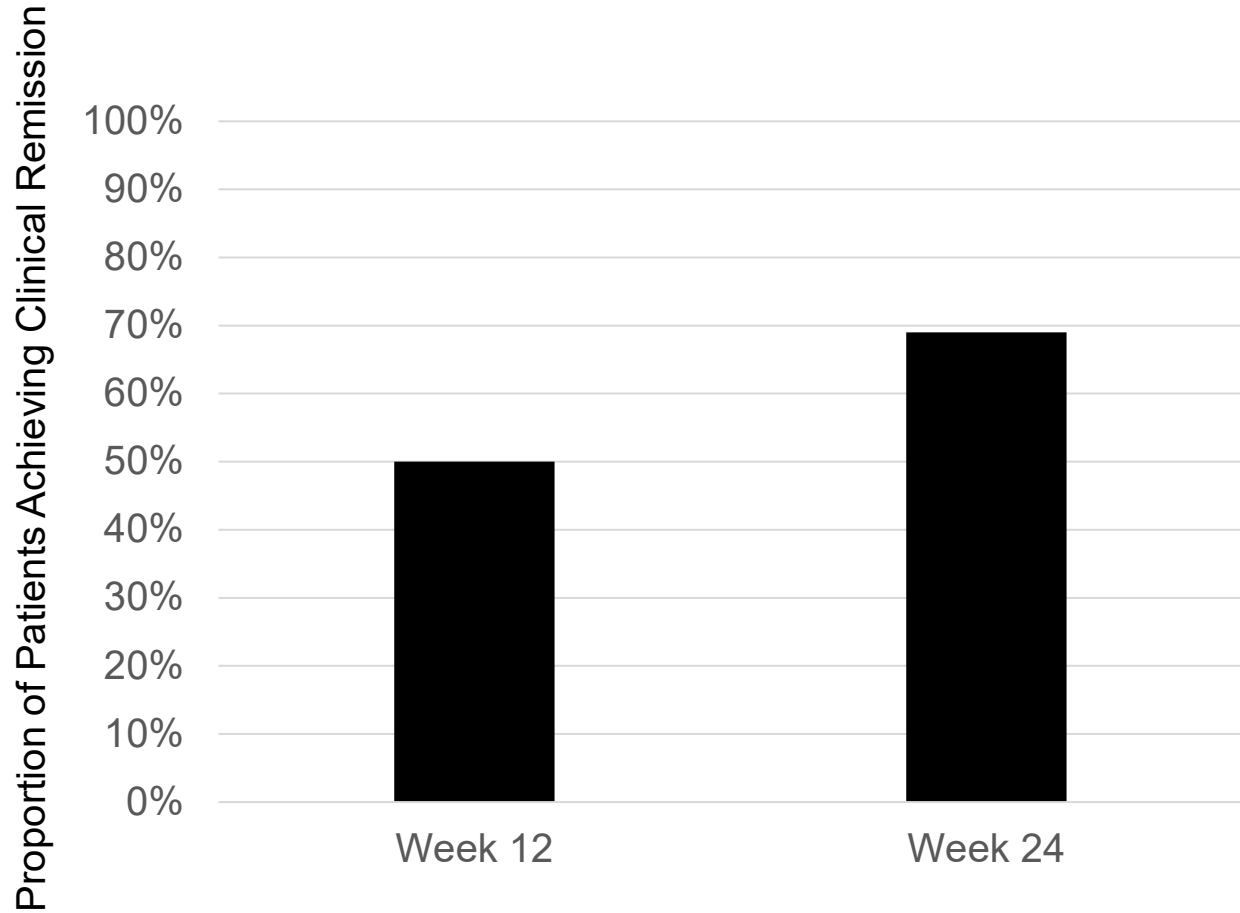
Ustekinumab: Multicenter study from 4 academic IBD centers

- 83% clinical response (6 months after induction)
- Responders demonstrated significantly less pouch inflammation compared with non-responders (29% vs. 100%, $p=0.023$)

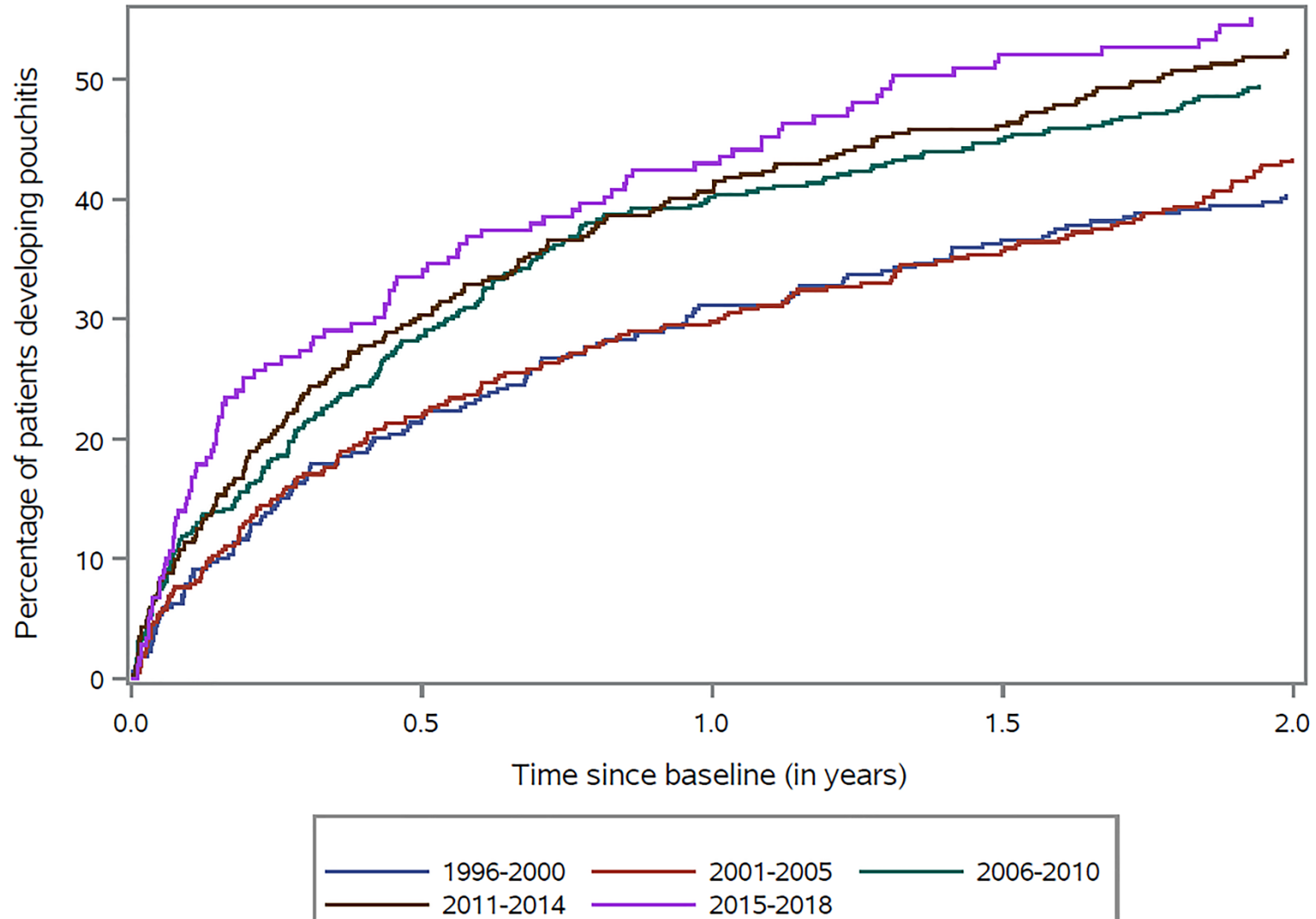
Clinical Remission at 6 months after enrollment (CD pouch)



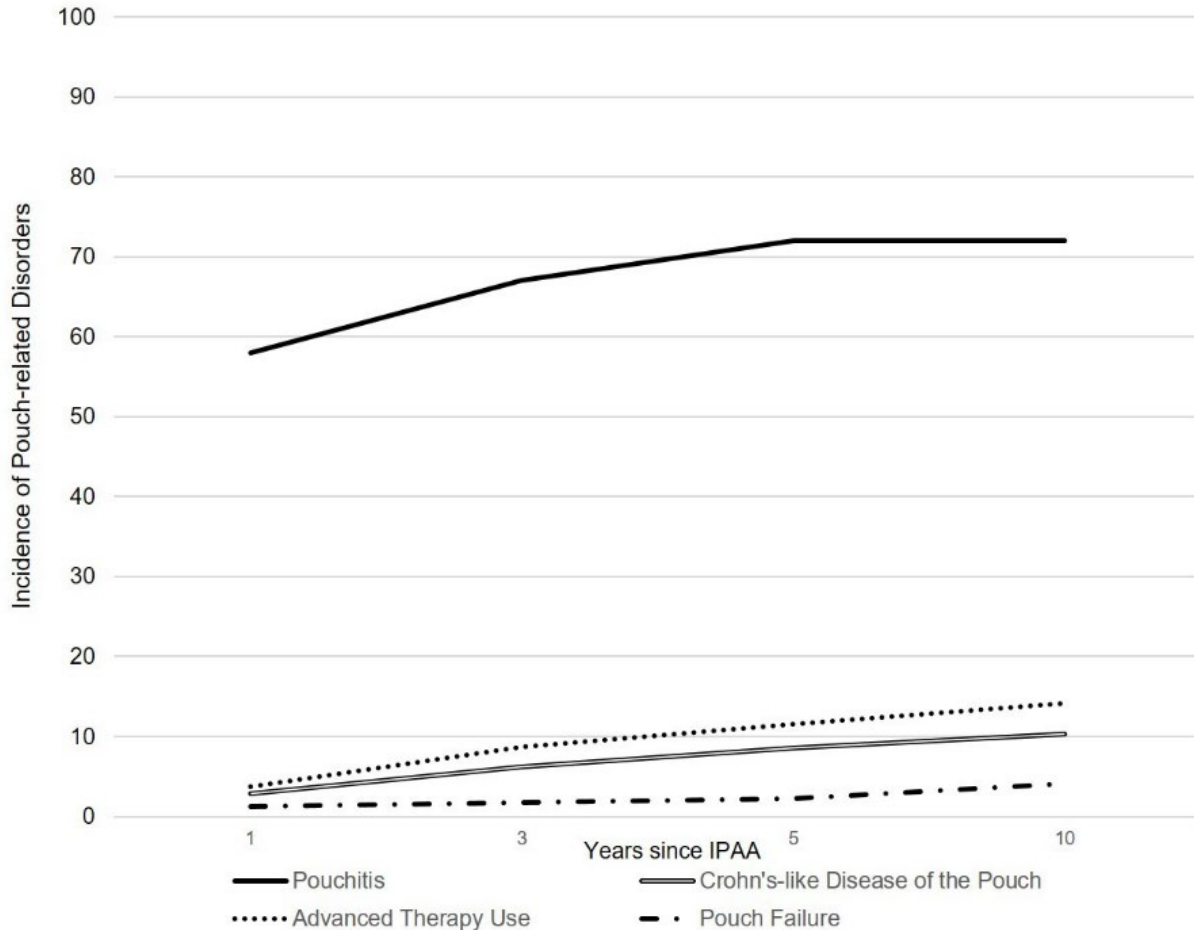
Risankizumab in the treatment of Crohn's-like Disease of the Pouch



Changing Incidence of Pouchitis Over Time



Current Epidemiology in the United States (using TriNetX)



Cumulative Incidence Rates

Pouchitis

- 10 year: 72%

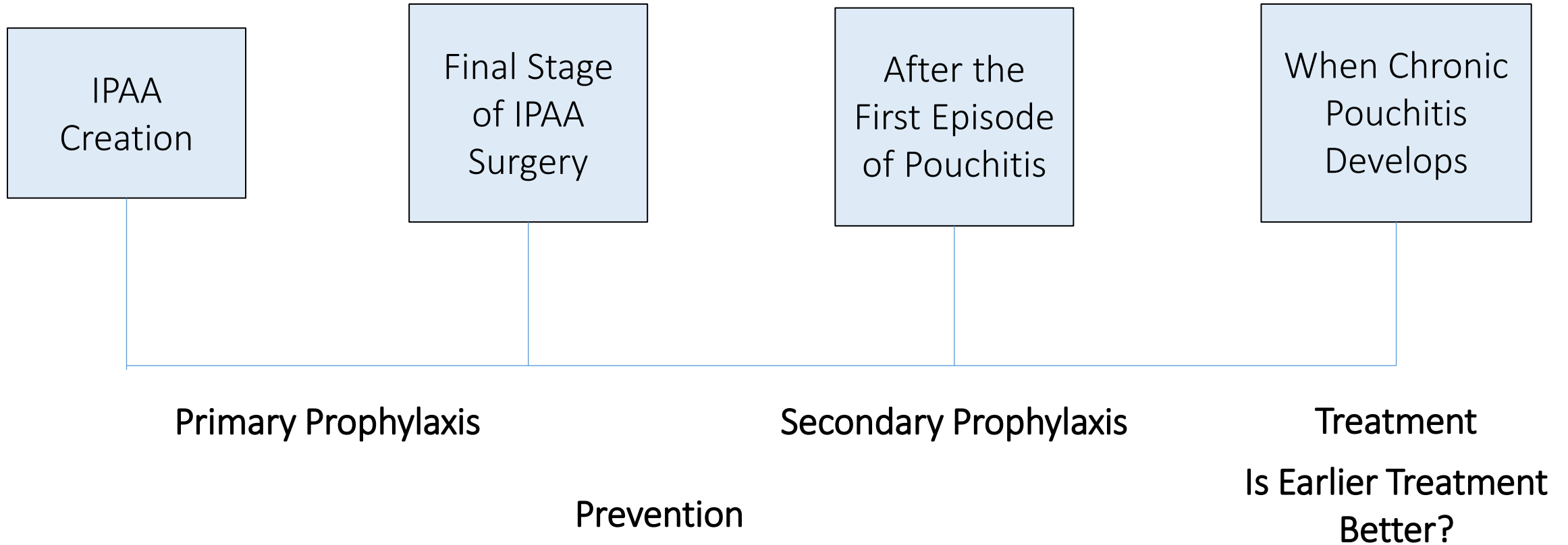
Crohn's-like disease of the pouch

- 5-year: 8.6%
- 10-year: 10.3%

Advanced therapy use

- 5 year: 11.8%
- 10 year: 14.4%

When Do We Intervene? Is There an Optimal Time to Intervene?



Primary Prevention: Probiotics

Question 1. In patients who undergo IPAA for UC, what is the effectiveness of probiotics for the primary prevention of pouchitis?

Recommendation 1. In patients with UC who undergo IPAA, the AGA makes no recommendation in favor of, or against, the use of probiotics for primary prevention of pouchitis. (*No recommendation, knowledge gap*)

Comment: There is a need for better evidence from clinical trials to inform the use of probiotics as a primary prevention strategy for pouchitis, especially given the potential cost and burden of long-term use with limited data on potential benefits.

8-strain probiotic formulation as primary prophylaxis

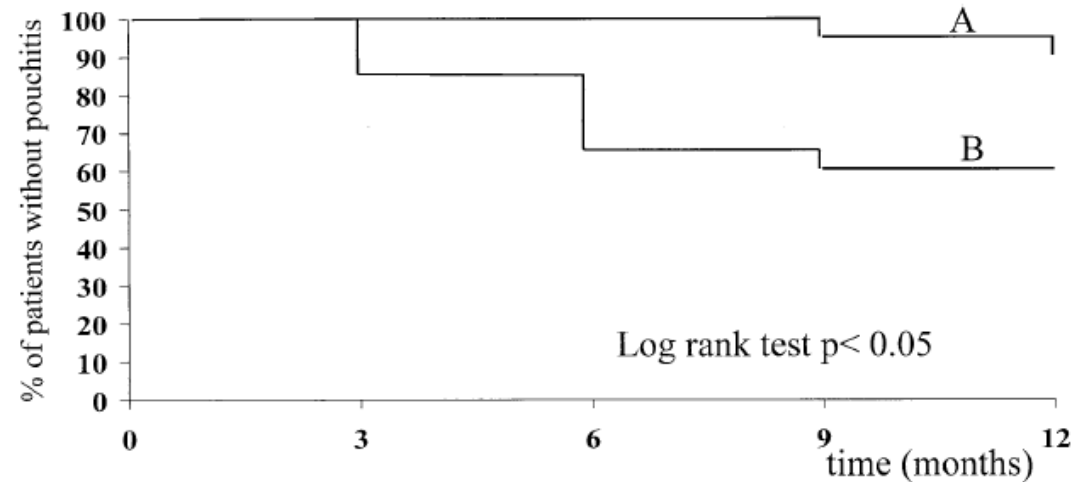


Figure 2. Kaplan–Meier estimates of cumulative rates of pouchitis during treatment with (A) VSL#3 or (B) placebo.

Secondary Prevention: Probiotics

Question 5. In adult outpatients with pouchitis, what is the effectiveness of probiotics for the prevention of recurrent pouchitis?

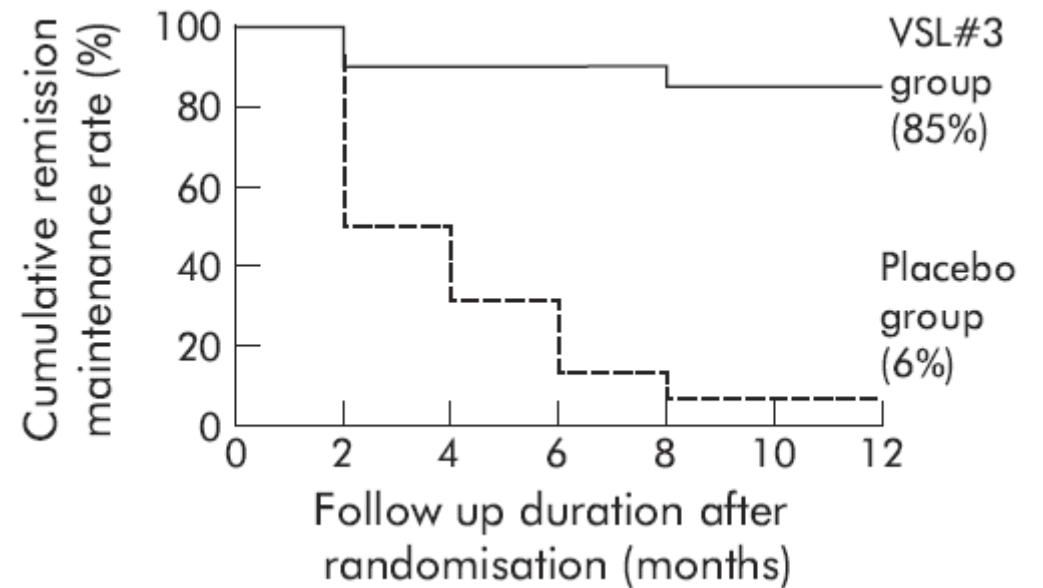
Recommendation 5. In patients with UC who have undergone IPAA and experience recurrent episodes of pouchitis that respond to antibiotics, the AGA suggests using probiotics for preventing recurrent pouchitis. *(Conditional recommendation, low certainty of evidence)*

Comment: Patients, particularly those with infrequent episodes of recurrent pouchitis or when the burden of long-term probiotic treatment is excessive, may reasonably choose avoiding any treatment to prevent recurrence of pouchitis.

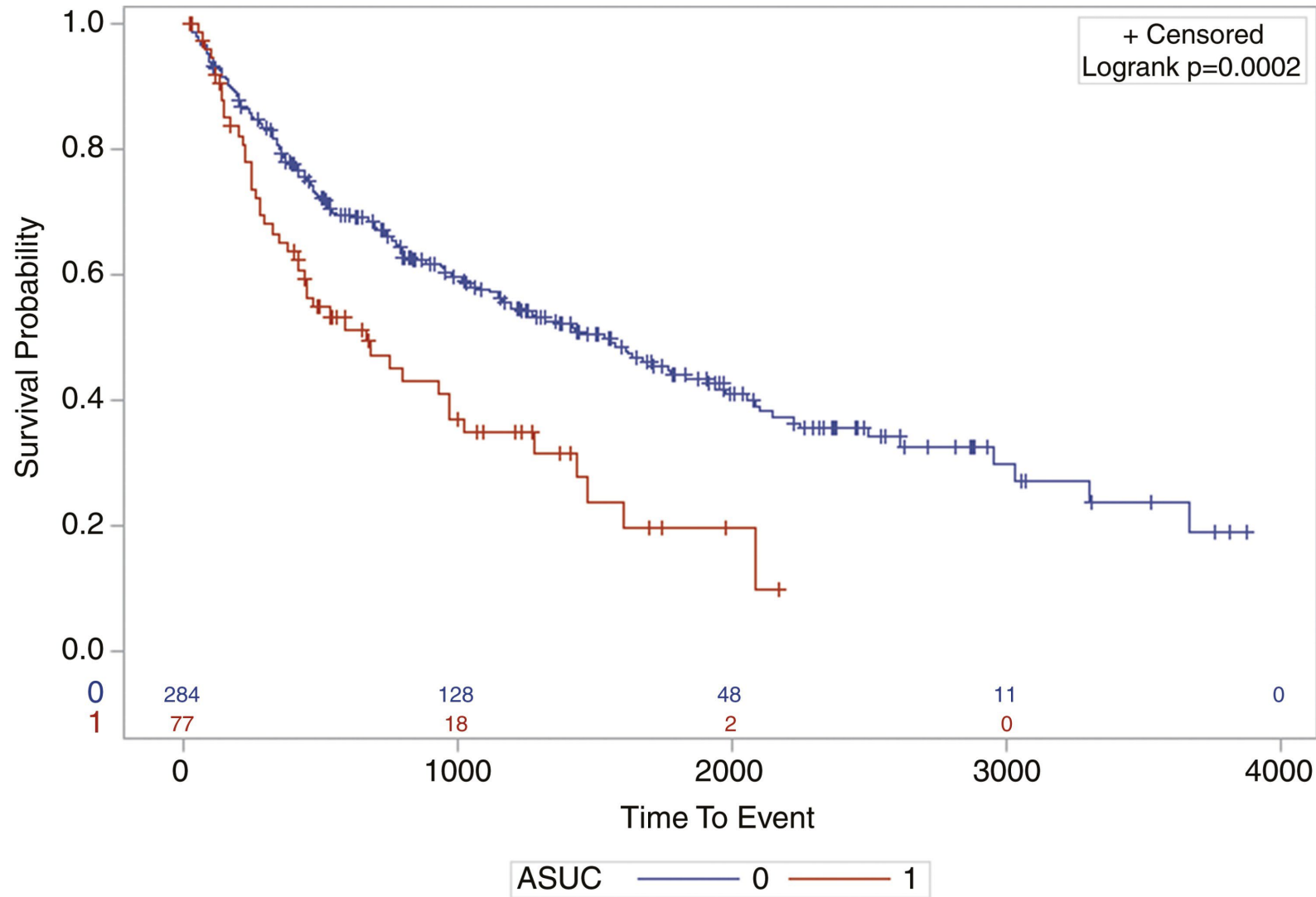
Implementation Consideration

- De Simone formulation of multistrain probiotics was used in clinical trials of prevention of pouchitis.

8-strain probiotic formulation as secondary prophylaxis (maintenance of remission)



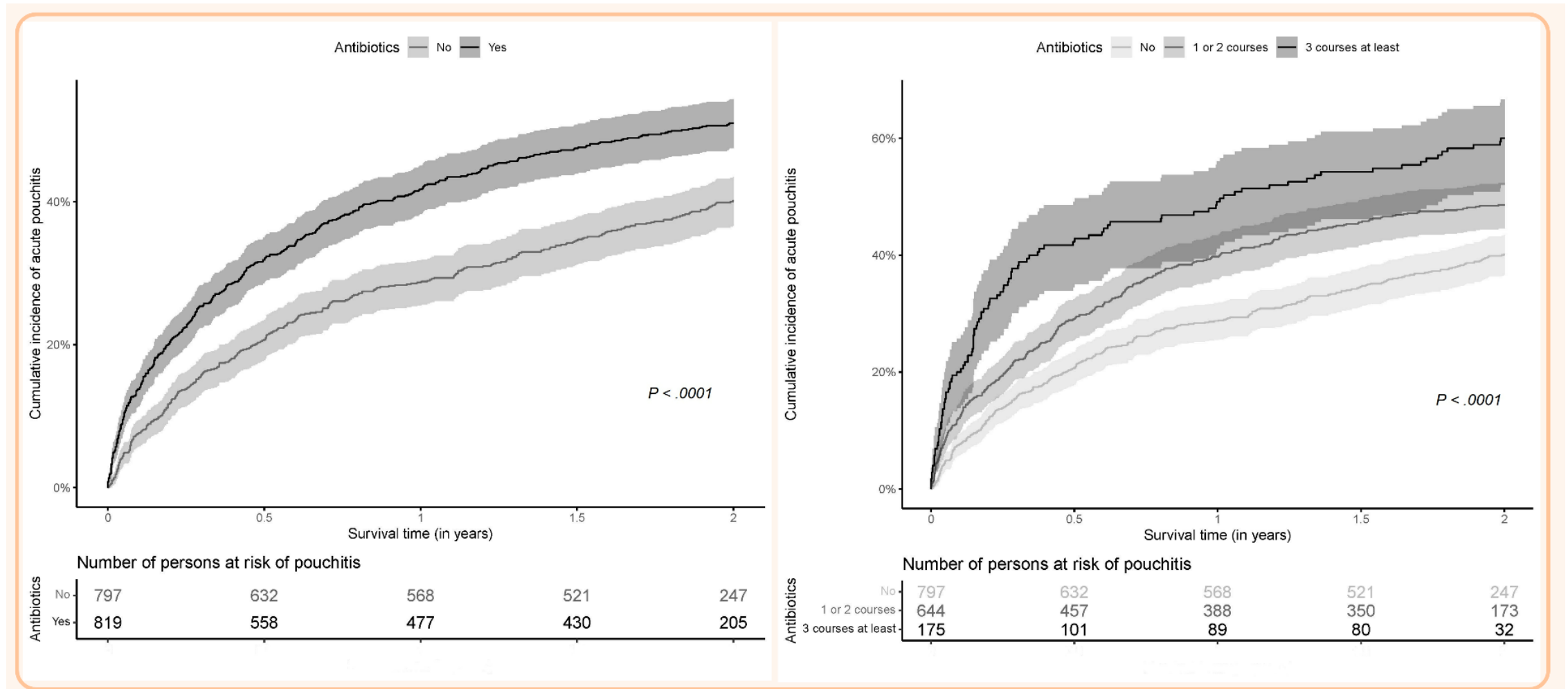
Patients with Acute Severe Ulcerative Colitis are at Increased Risk for Pouchitis



Probability of Pouchitis

- Acute severe ulcerative colitis
HR 1.50, 95% CI 1.04-2.17
- Greater number of biologics
pre-colectomy
HR 1.57, 95% CI 1.06-2.31

Antibiotic Use as a Risk Factor for Pouchitis



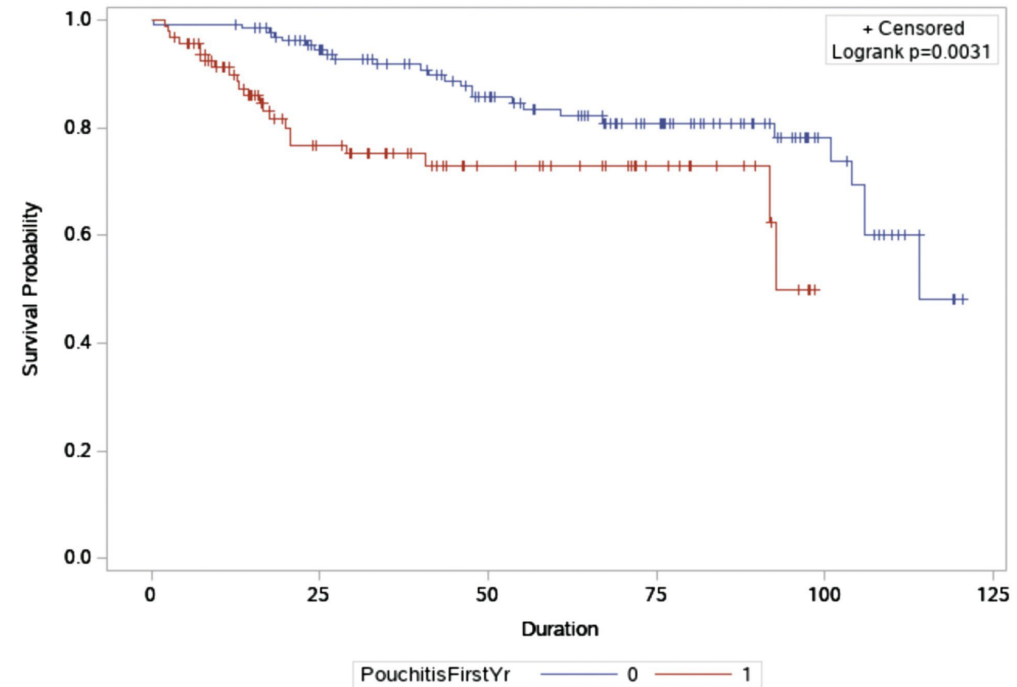
Early Pouchitis is Associated with Chronic Inflammatory Conditions of the Pouch

Among 626 patients undergoing IPAA, 137 developed pouchitis within the first 180 days after IPAA

- CADP: aOR 3.97, 95% CI 2.19-6.10
- Crohn's-like disease of the pouch: OR 2.77, 95% CI 1.54-4.98

Among 412 patients, pouchitis within 12 months of IPAA was associated with increased risk for Crohn's-like disease of the pouch

- HR 2.43, 95% CI 1.32-4.45



Summary and Conclusions

There are indications of an increasing burden of pouchitis and chronic inflammatory conditions of the pouch

Ciprofloxacin and metronidazole remain the first-line antibiotic therapies for intermittent pouchitis

The EARNEST study demonstrated the efficacy of vedolizumab in the treatment of chronic pouchitis in a phase 4, randomized, placebo-controlled, trial

Other biologics and small molecules are being studied using rigorous methodology to demonstrate effectiveness in this population

Earlier opportunities for intervention may exist; whether this decreases the burden of pouch-related disorders is unknown



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