

# Acute Severe Ulcerative Colitis

*Optimizing Inpatient Management for Improved Outcomes*



Tauseef Ali, MD, FACG  
Clinical Associate Professor  
Medical Director Crohn's and Colitis Center  
SSM Health Digestive Care  
Oklahoma City, Oklahoma

# Case Scenario

- A 35-year-old male with a 5-year history of moderate UC
- Presents with worsening symptoms over past 7 days, including >10 bloody stools /day and abdominal pain
- Exam: Febrile (101.3°F), HR 110 bpm 95/60 mmHg). Mild abdominal tenderness, no peritoneal signs
- Labs:
  - Hgb: 9.5 g/dL (13.5-17.5 g/dL)
  - WBC: 14,000/ $\mu$ L (4,000-11,000/ $\mu$ L)
  - CRP: 20 mg/dL (<1mg/dL)
  - Serum albumin: 2.5 g/dL (3.5-5.0 g/dL)
  - Stool studies: Negative for infections

**Which of the following is the most appropriate initial management for this patient?**

1. Administer high-dose oral corticosteroids
2. Initiate intravenous corticosteroids
3. Start infliximab immediately
4. Urgent colectomy
5. Administer intravenous fluids and broad-spectrum antibiotics

# ASUC: A Practical Approach



## Chapter 1

Understanding ASUC



## Chapter 2

Workup and Initial  
Management



## Chapter 3

Rescue therapies



## Chapter 4

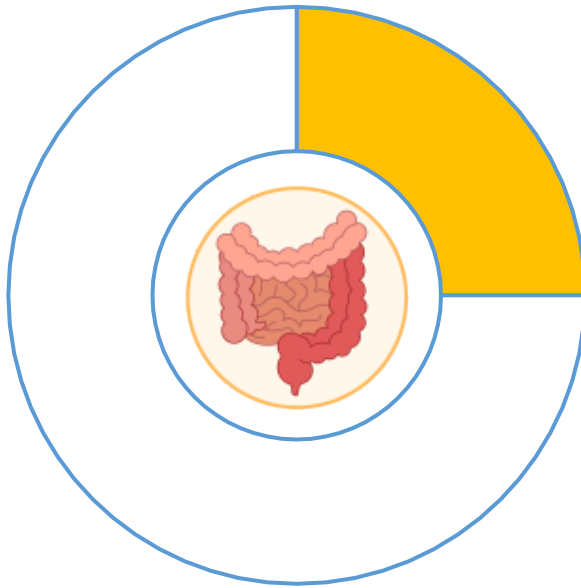
Challenges and  
Proposed algorithm



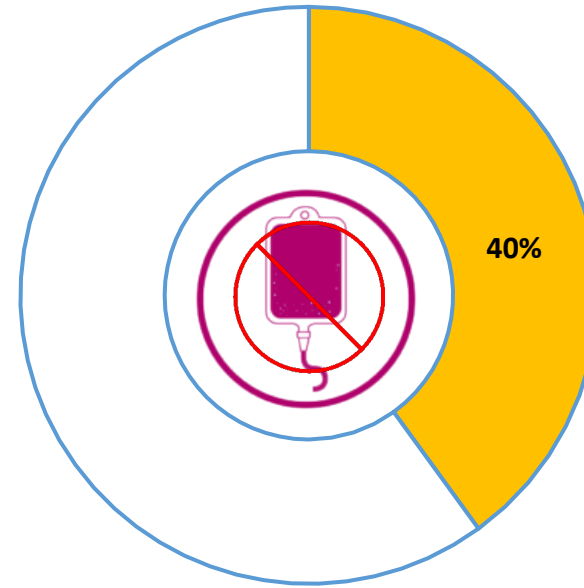
**Chapter 1**  
Understanding ASUC

# ASUC: A Practical Approach

# ASUC Burden and Steroid Response

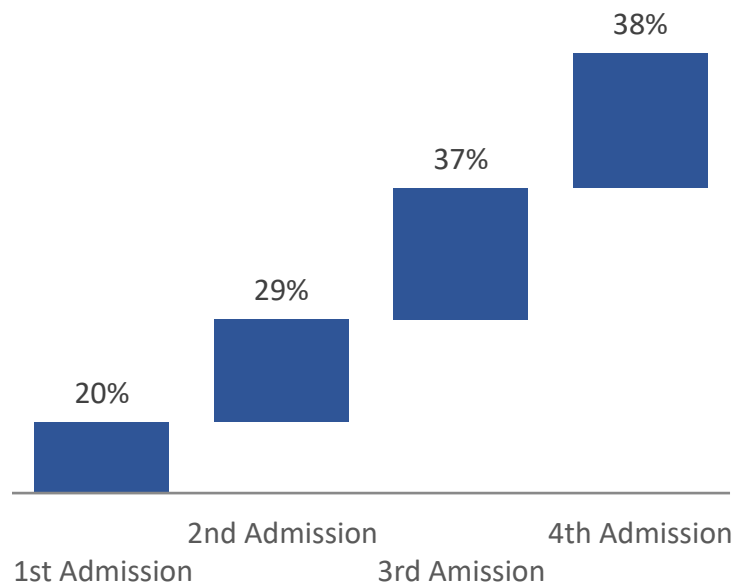


**ASUC at Presentation (25%)**

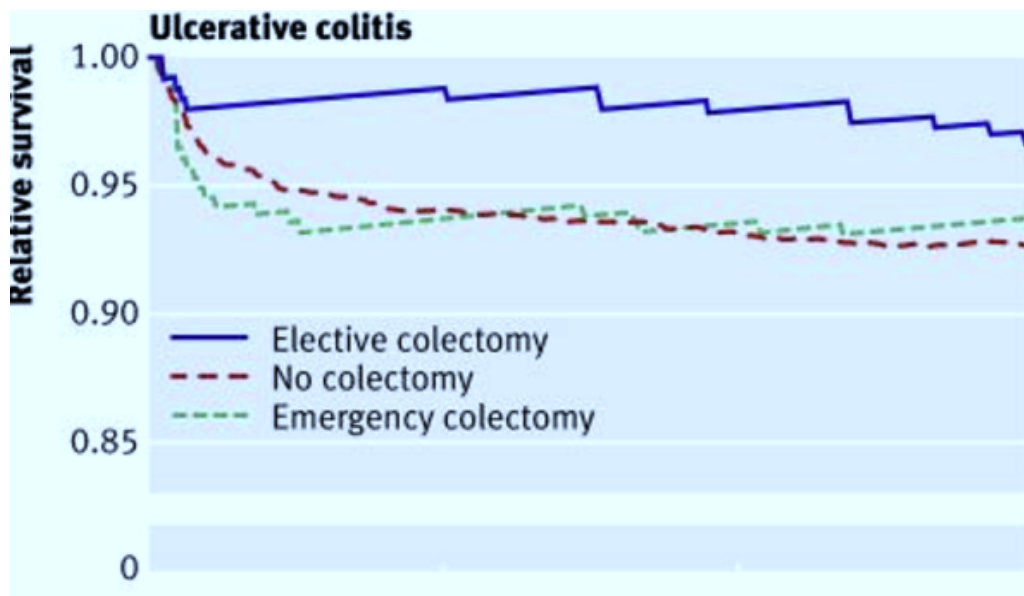


**IV Steroid Non-Response (40%)**

# Colectomy Risk & Survival in ASUC



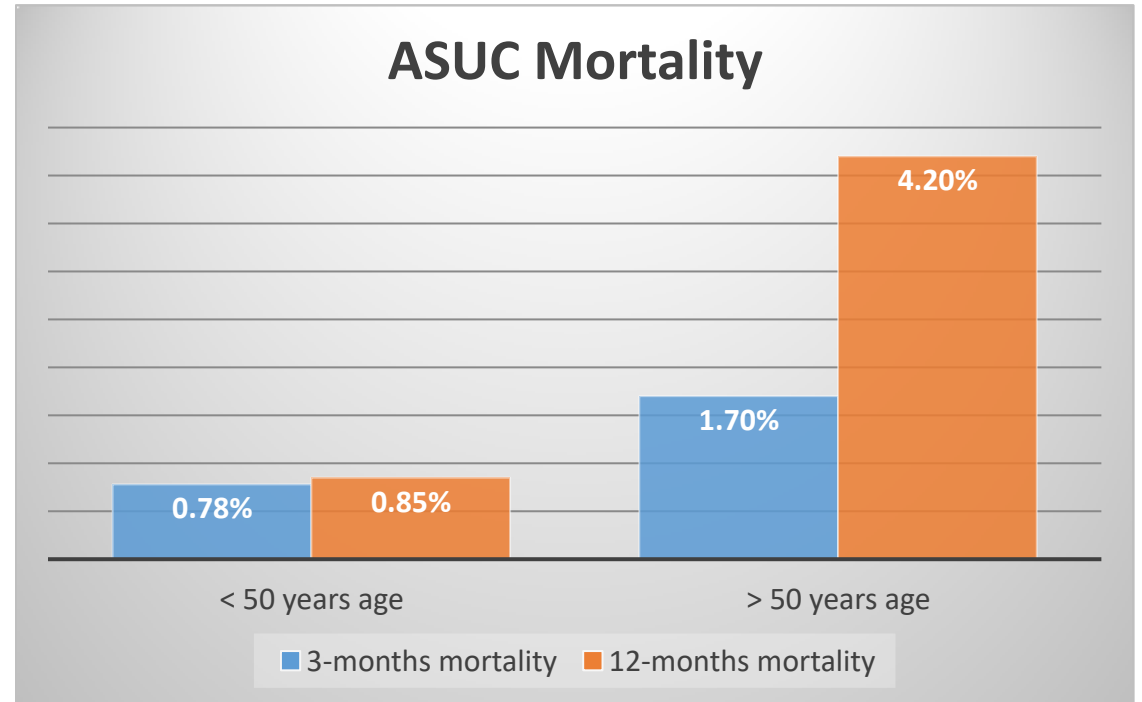
**Colectomy rates for ASUC**



**3-years relative survival (1998-2000)**

# ASUC Mortality: Then and Now

- **Before corticosteroids (pre-1955)**
  - Mortality >30–40% (toxic megacolon, perforation, sepsis)
- **With IV corticosteroids (modern era):**
  - Mortality ↓ to ~1–3% in expert centers



# Defining ASUC: Truelove & Witts Criteria

☞ “≥6 bloody stools/day **plus** ≥1 systemic toxicity marker



Tachycardia **>90bpm**



Fever **>37.8 °C**



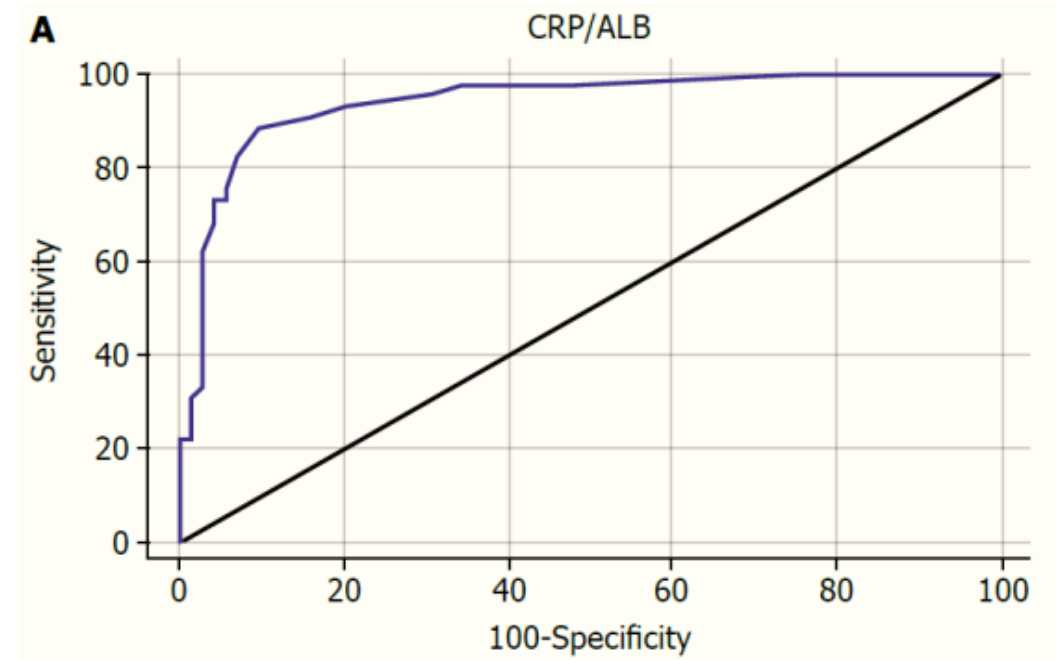
Hemoglobin **<10.5 g/dL**



ESR **>30 mm/h**, CRP **≥ 12 mg/L**

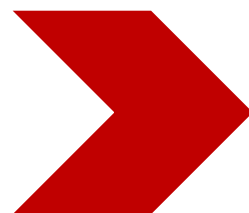
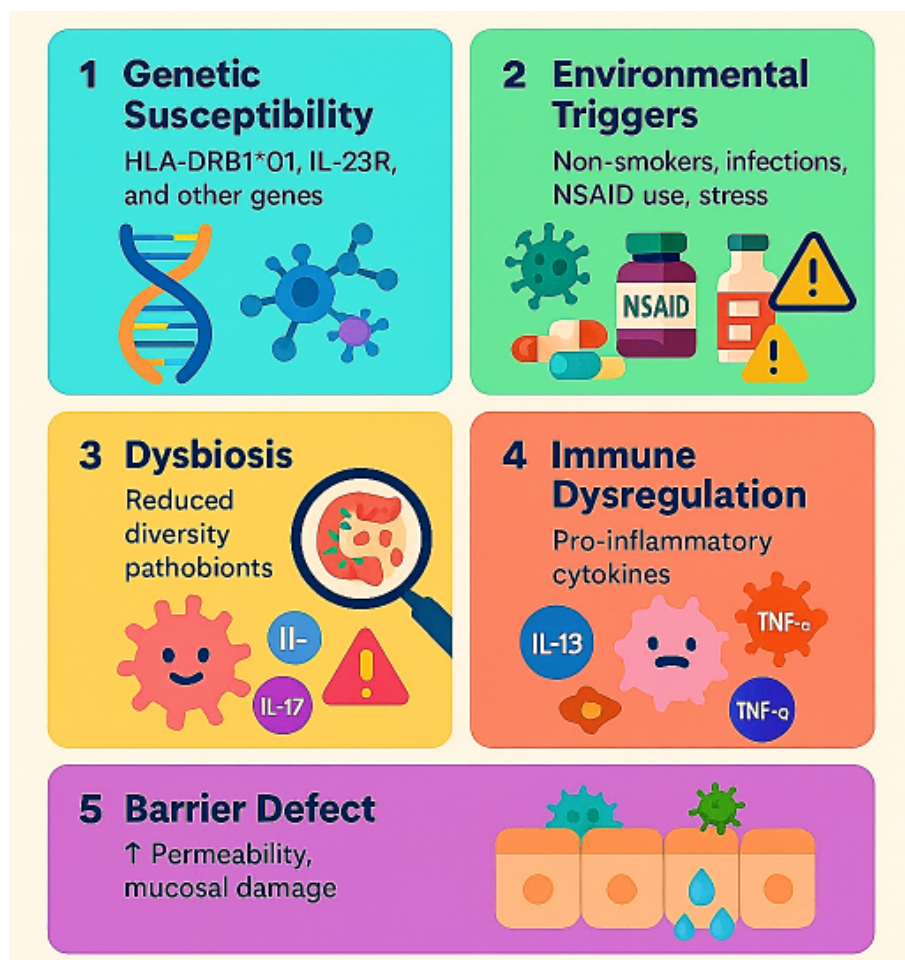
# CRP/Albumin Ratio (CAR): A Simple Prognostic Tool

- **Definition:**  $CAR = CRP \text{ (mg/L)} \div \text{Albumin (g/L)}$
- **Cut-offs:**  $0.6\text{--}0.85 \rightarrow \text{severe disease}$
- **Utility:** Predicts steroid non-response & colectomy risk
- **Limitations:** Non-specific, variable cut-offs

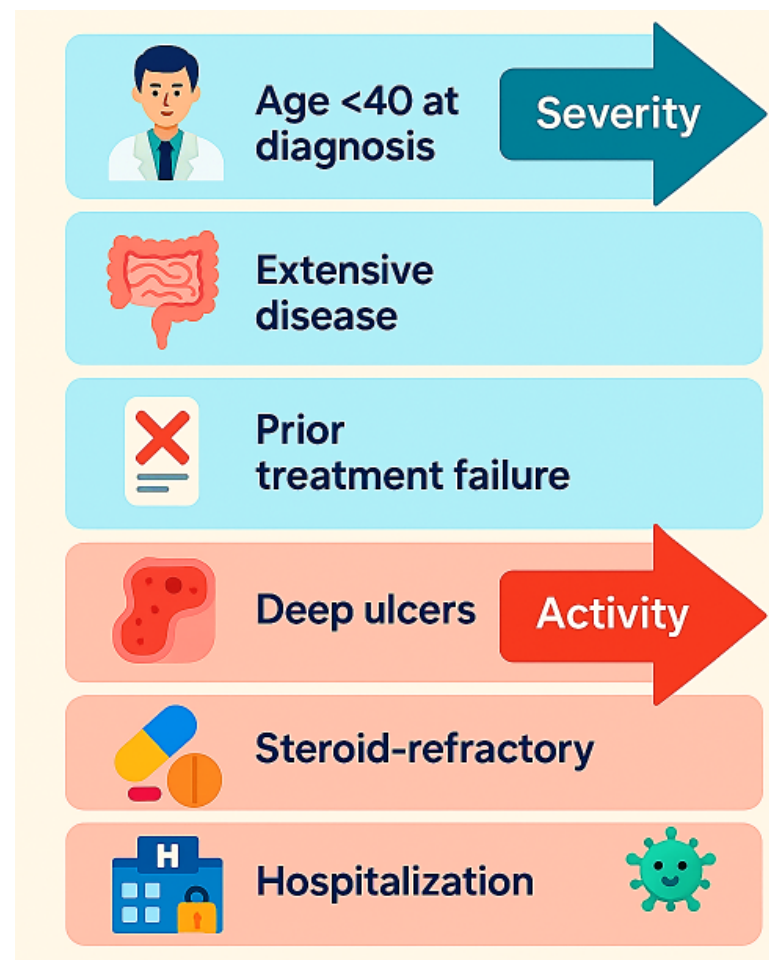


| Parametre | Cut-off | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | AUC   | p            |
|-----------|---------|-----------------|-----------------|---------|---------|-------|--------------|
| CAR       | 0.6     | 88.9            | 90.3            | 85.1    | 92.8    | 0.941 | <b>0.001</b> |

# Pathogenesis and Clinical Risk Factors for ASUC

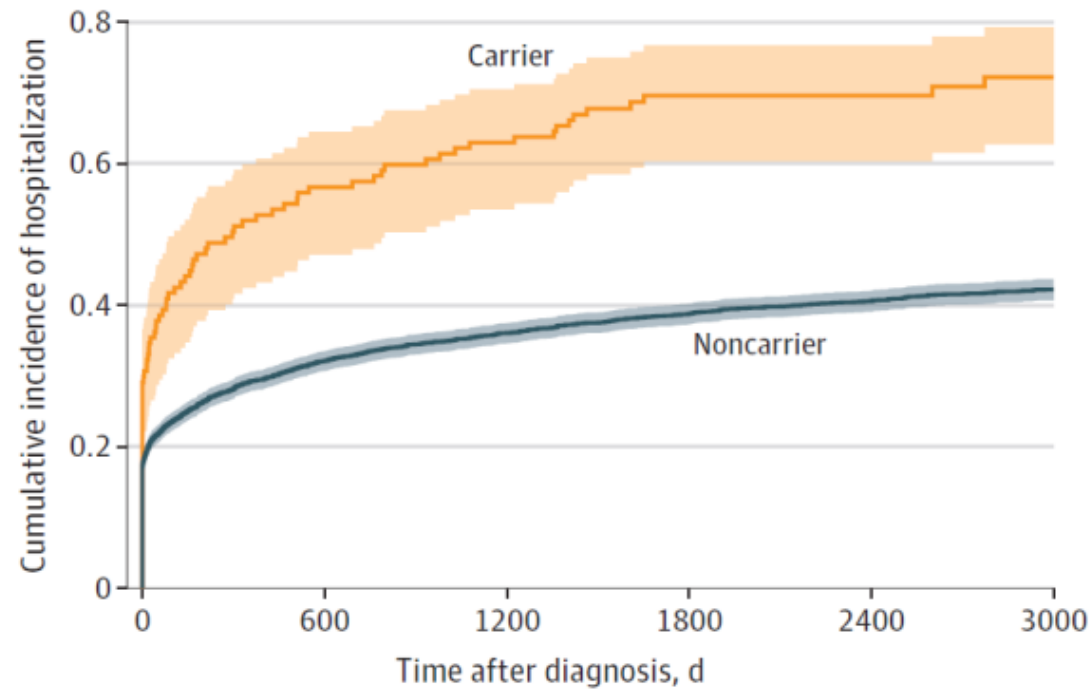


☞ “Translates into clinical risk

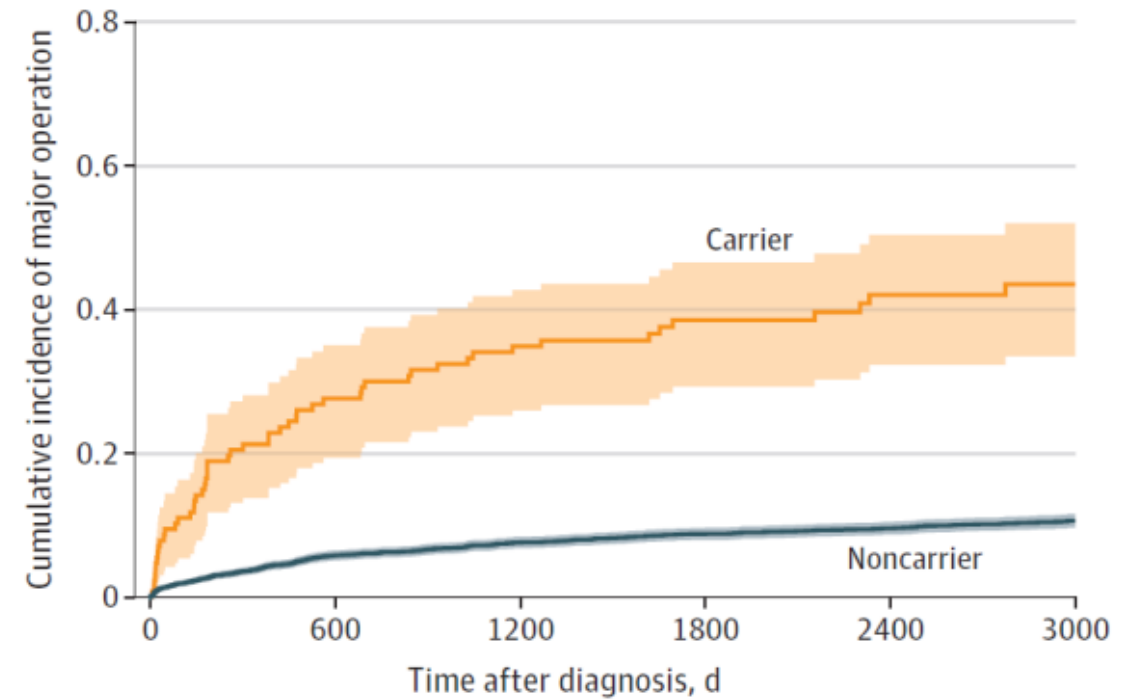


# HLA-DRB1\*01:03 and ASUC

Hospitalization



Major operation



Danish nationwide genome-wide association study

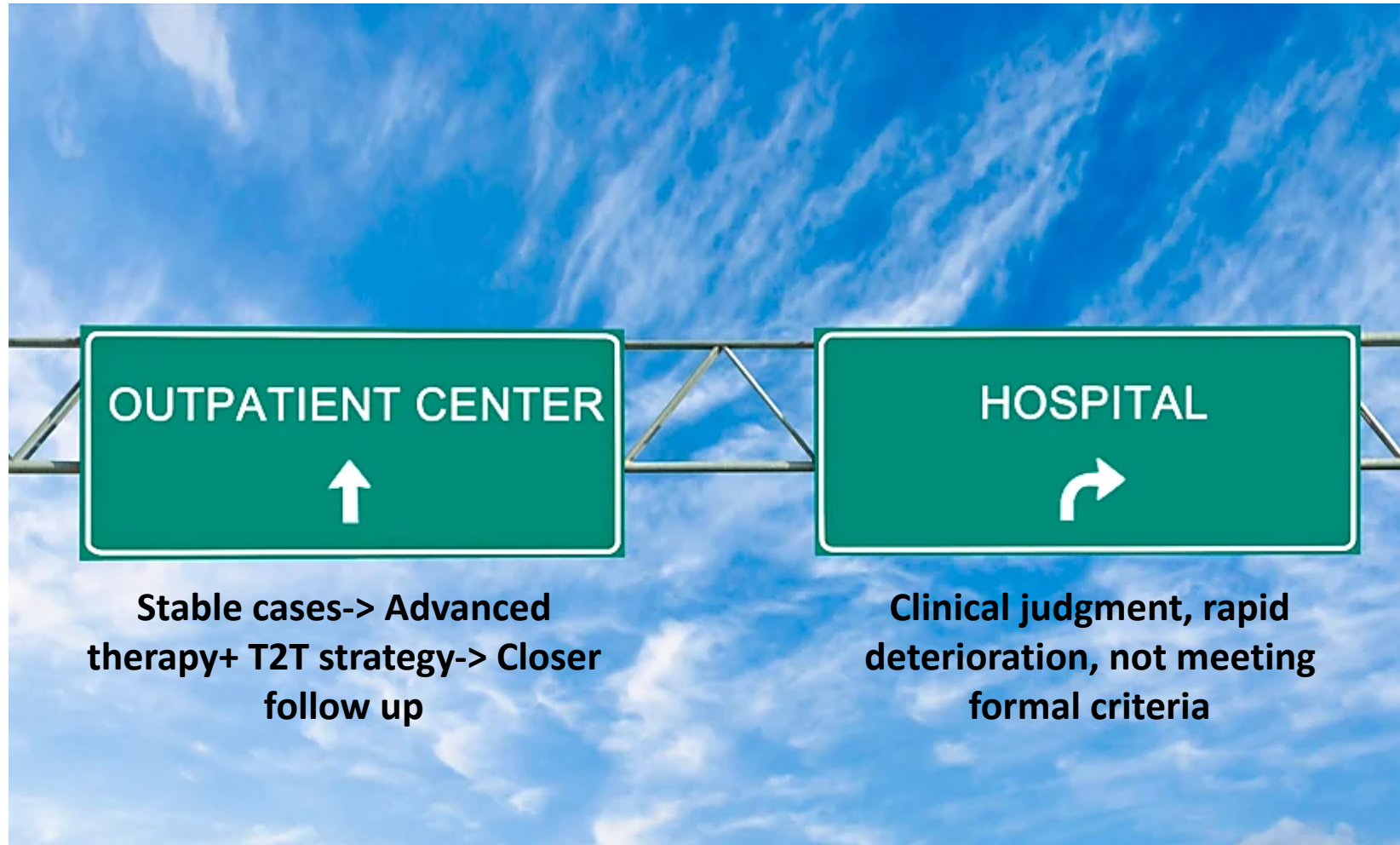


## **Chapter 2**

Workup and Initial  
Management

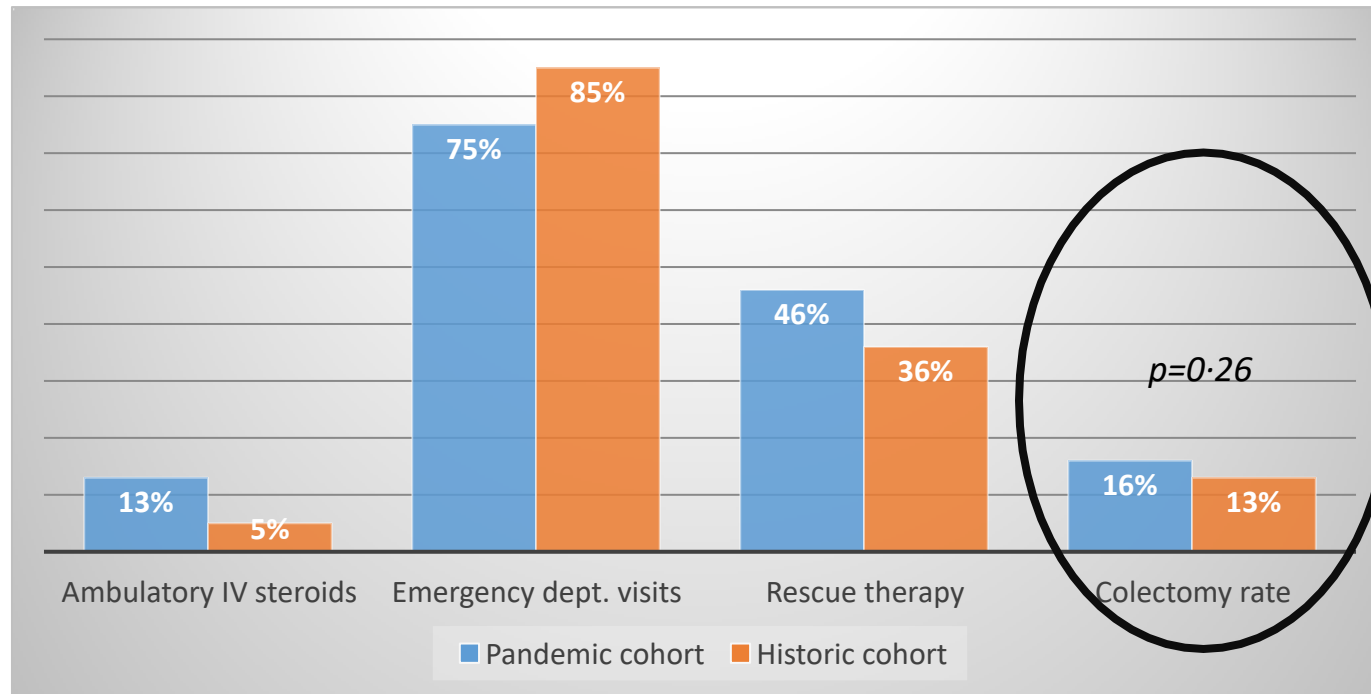
# **ASUC: A Practical Approach**

# ASUC Hospitalization: Changing Thresholds



# Outpatient Salvage Therapy in ASUC: COVID Lessons

PROTECT-ASUC study: Pandemic vs Historic Cohorts



👉 Outpatient salvage feasible—similar colectomy rates despite ↑ ED visits

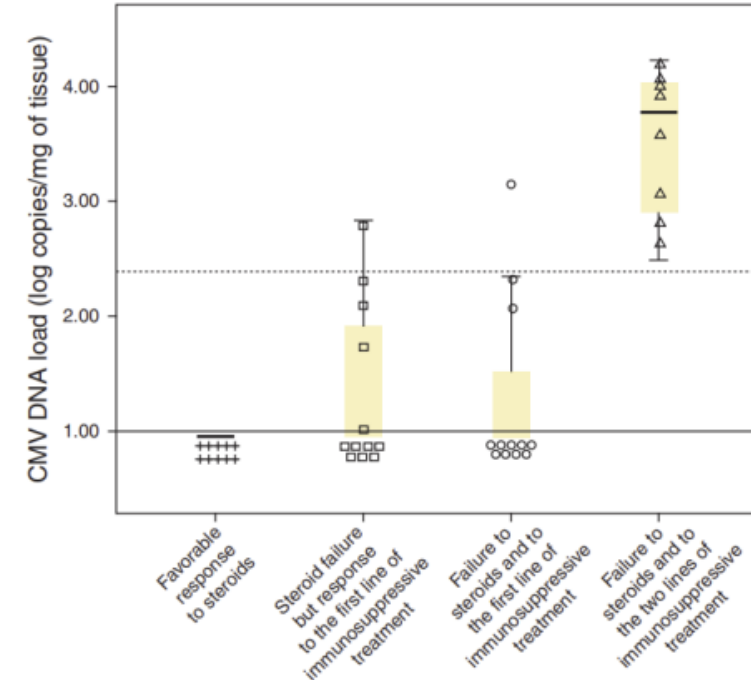
# Concurrent C. Diff Colitis in ASUC

- **5–20%** of ASUC have *concurrent* C. diff
- Increased risk of colectomy and postop complications
- May occur without typical risk factors (hospitalization/antibiotics)
- Pseudo membranes rare
- *Associated* with longer hospital stay and hospital mortality (**4-fold risk**)
- **2-step** testing algorithm is recommended

☞ **Do not stop Immunosuppressive IBD therapy (continue therapy)**

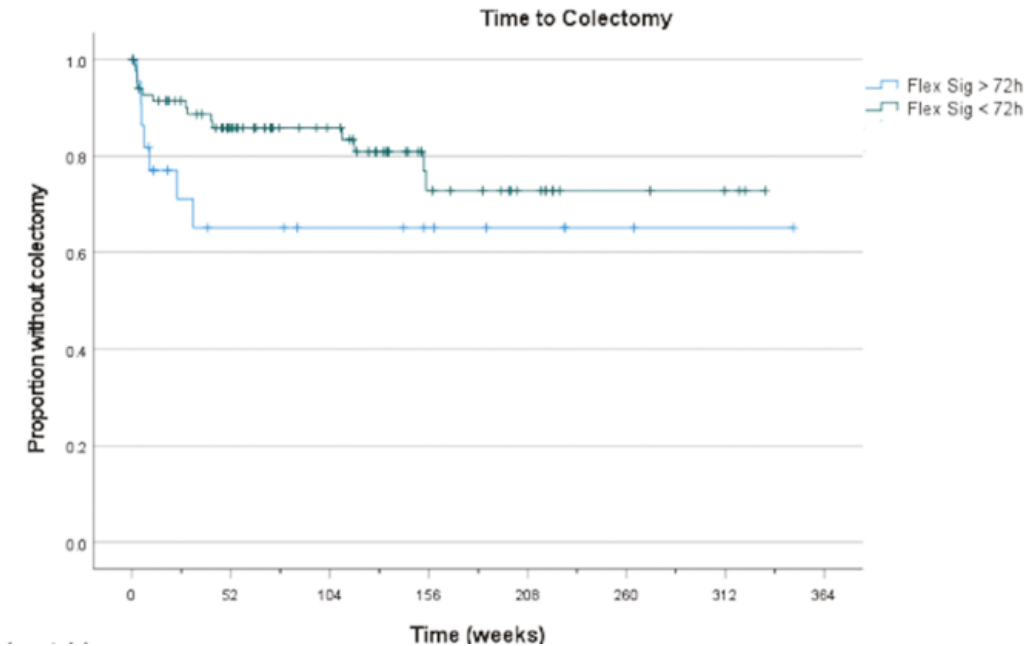
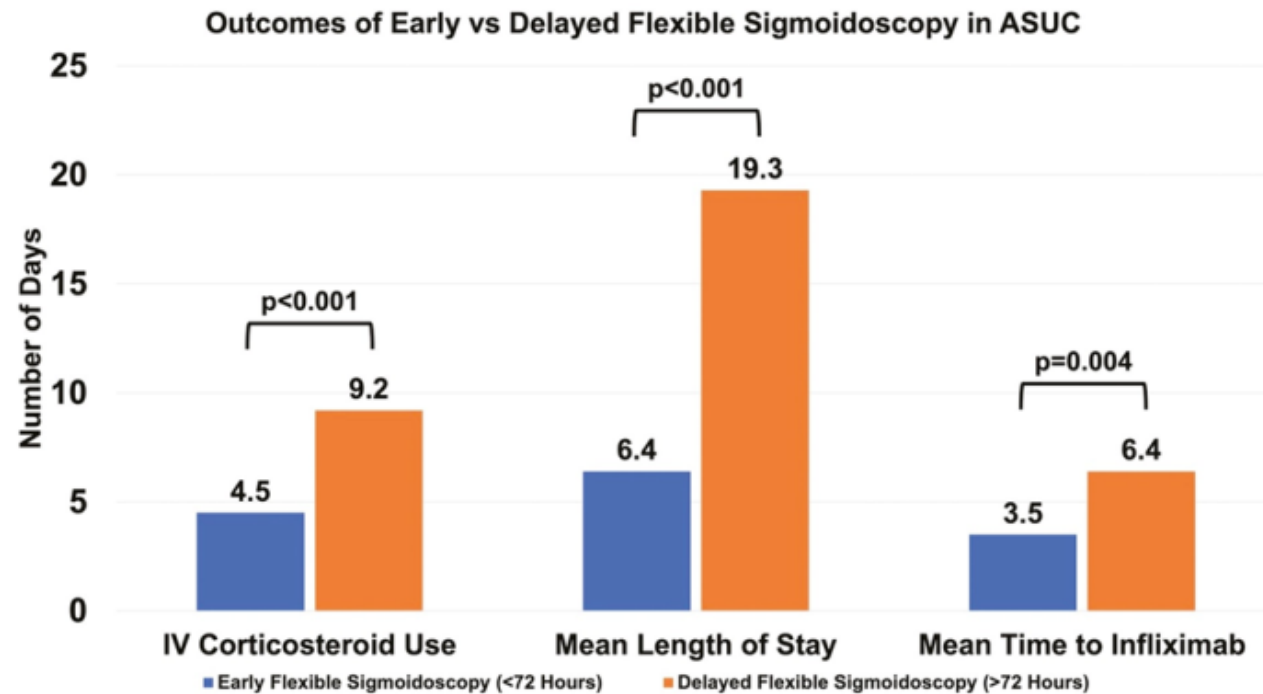
# CMV Reactivation in ASUC

- **10–30%** of hospitalized steroid-refractory ASUC have CMV
- Linked to steroid refractoriness and colectomy risk
- **>250 copies/mg** → drug resistance (RR 4.7)
- **>2000 copies/mg** → colectomy predictor (OR 17.2)
- Assay variability between centers = limitation
- **Antivirals benefit** steroid-refractory cases



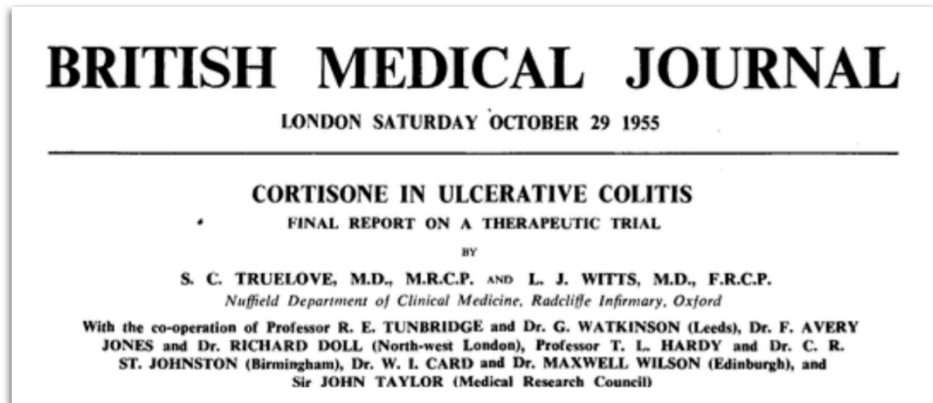
👉 Check CMV in steroid-refractory ASUC—high viral load predicts colectomy, antivirals can help

# Early Sigmoidoscopy Improves Outcomes

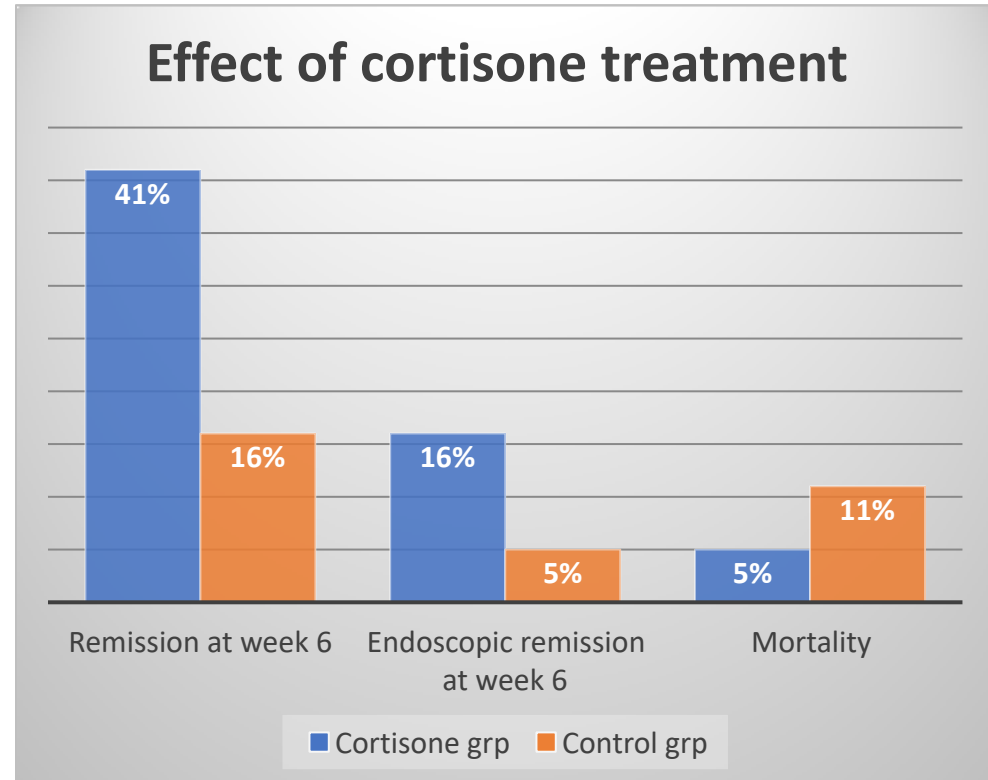


☞ Early sigmoidoscopy reduces LOS, cost, colectomy, and mortality

# Truelove & Witts 1955: Steroids Transform ASUC Care



Landmark BMJ trial, 1955

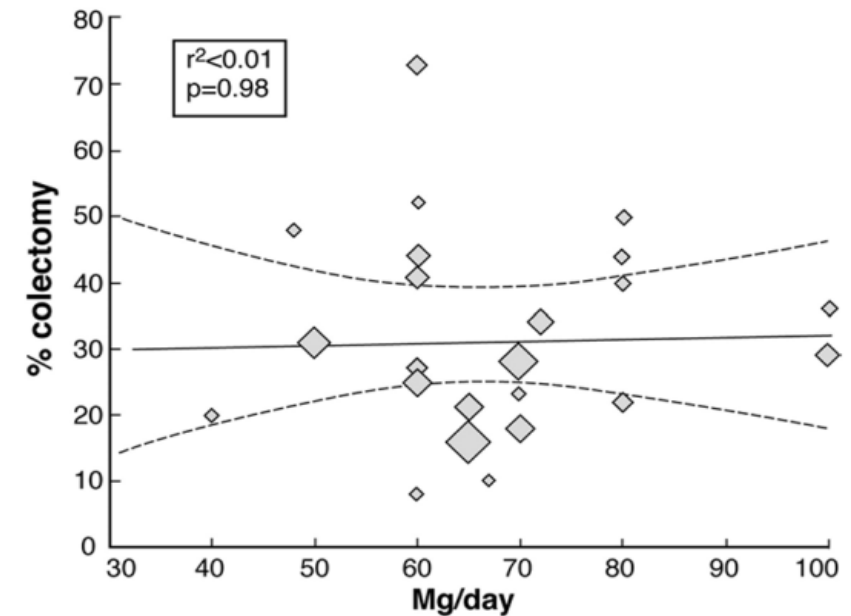


☞ Steroids increased remission, reduced mortality — still first-line for ASUC

# IV Steroids in ASUC: Dose & Duration

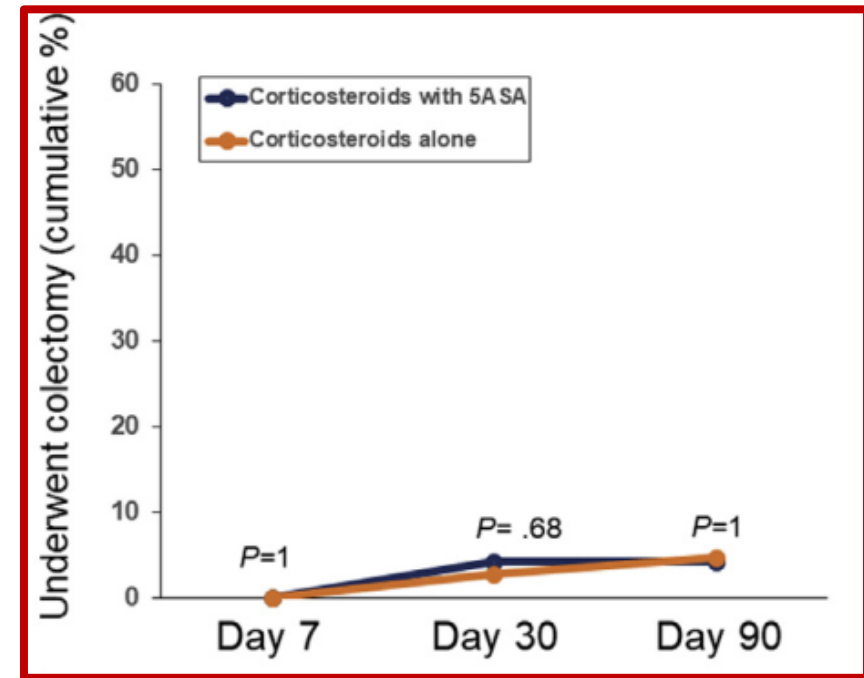
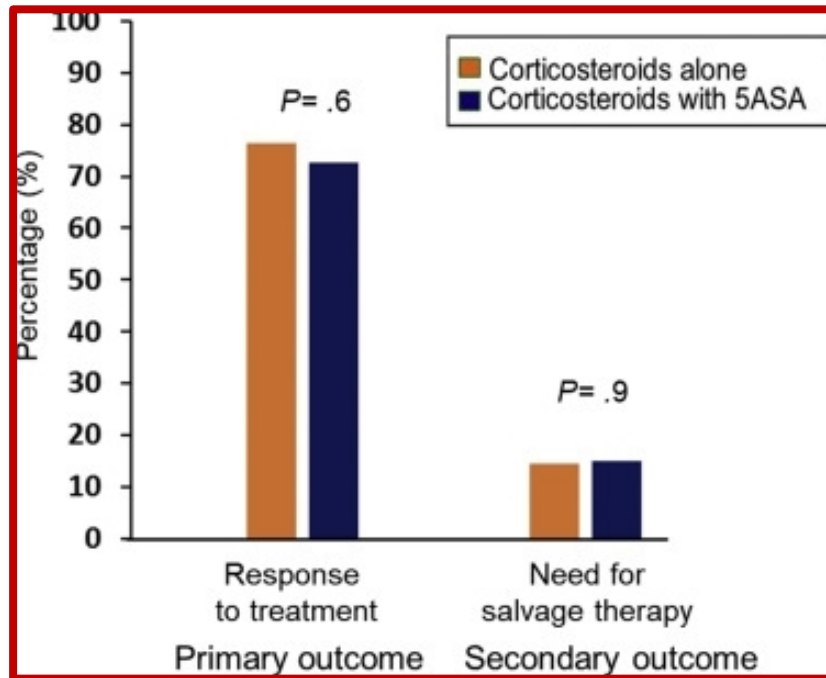
- No studies comparing different dosing regimens
- No significant difference between continuous vs. bolus administration
- No benefit beyond 60 mg/day methylprednisolone
- Trial of 3–5 days adequate
- Continued use beyond 7 days ineffective

👉 **Optimal: 60 mg/day × 3–5 days**



Meta-regression controlled for disease severity at baseline-  
no correlation of the dose used with colectomy rate

# Adding Mesalamine to Corticosteroids



👉 Do not continue or add 5-ASA in hospitalized ASUC patients already on IV steroids

# Day 1 Predictors of Steroid Failure in ASUC

## ADMIT ASC

- CRP of  $\geq 100$  mg/L (1 point)
- Albumin of  $\leq 25$  g/L (1 point)
- UCEIS  $\geq 4$  (1 point) or  $\geq 7$  (2 points)
- Scoring of  $\geq 3 \rightarrow$  **84%** risk of steroid failure

## ACE Index

- CRP  $\geq 50$  mg/L
- Albumin  $\leq 30$  g/L and
- Mayo Endoscopic Score = 3
- **78 %** nonresponse to IV steroids

# Day 3 Predictors of Steroid Failure in ASUC

## Oxford Index

- > 8 BM on day 3 OR
- 3–8 BM + CRP > 45 mg/L
- **85% required colectomy**
- 40% partial responders and 5% responders required colectomy

## Edinburgh score

- Stool frequency (< 4: 0 points, 6–9: 2 points, > 9: 4 points)
- Albumin  $\leq 30$  g/L day 1 (1 point)
- Colonic dilation > 5.5 cm day 3 (4 points)
- Score of  $\geq 4 \rightarrow$  **85% medical therapy failure**

☞ Both indices: ~85% failure prediction

# Predictors for Colectomy in ASUC



## Highest Risk Predictors

- Oxford criteria – OR 4.4
- ESR (↑) – OR 2.9
- CRP (↑) – OR 2.6
- UCEIS (↑) – OR 2.4
- Hemoglobin (↓) – OR 2.0

## ⚡Moderate Risk Predictors

- Sarcopenia – OR 1.9
- Extensive colitis – OR 1.8
- Prior steroid use – OR 1.7



## Protective Factor

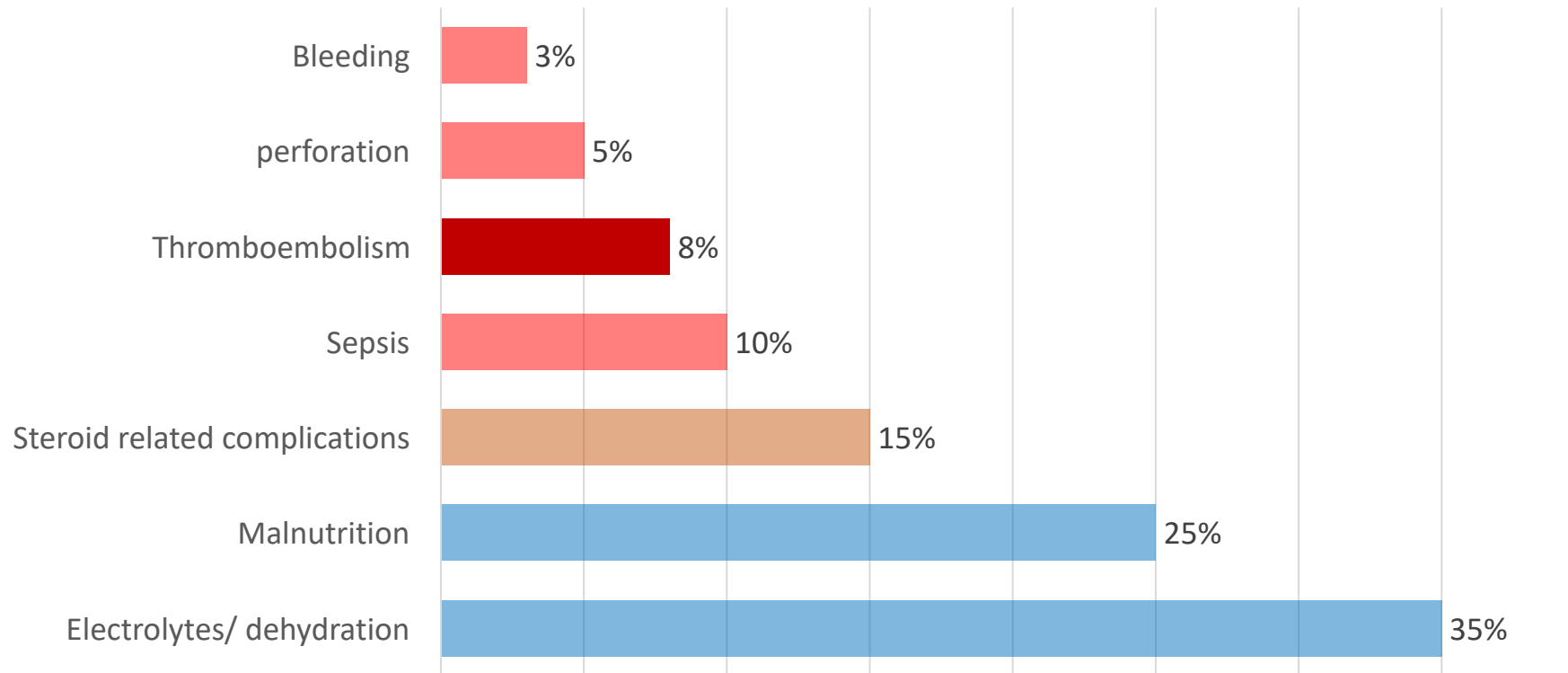
- Albumin – OR 0.3  
(per 1 g/dL increase)

👉 Early risk stratification = lower colectomy rates

## Day 3- The Decision Point



# Complications of Acute Severe UC



**⚠ Thromboprophylaxis is essential in all hospitalized ASUC patients**

# VTE Risk in Acute Severe UC

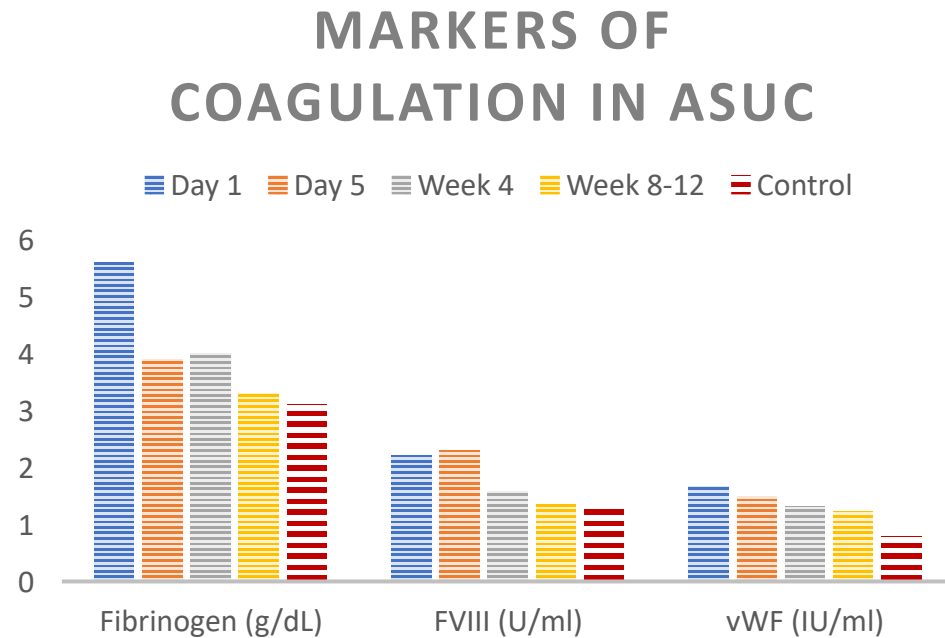
- **2-fold higher risk of VTE** (IBD vs general population)
- **10-15 fold higher risk** (hospitalized IBD vs matched controls)
- **2-fold higher mortality** from inpatient VTE



**VTE Risk Factors**

# VTE Risk in ASUC: Beyond Hospitalization

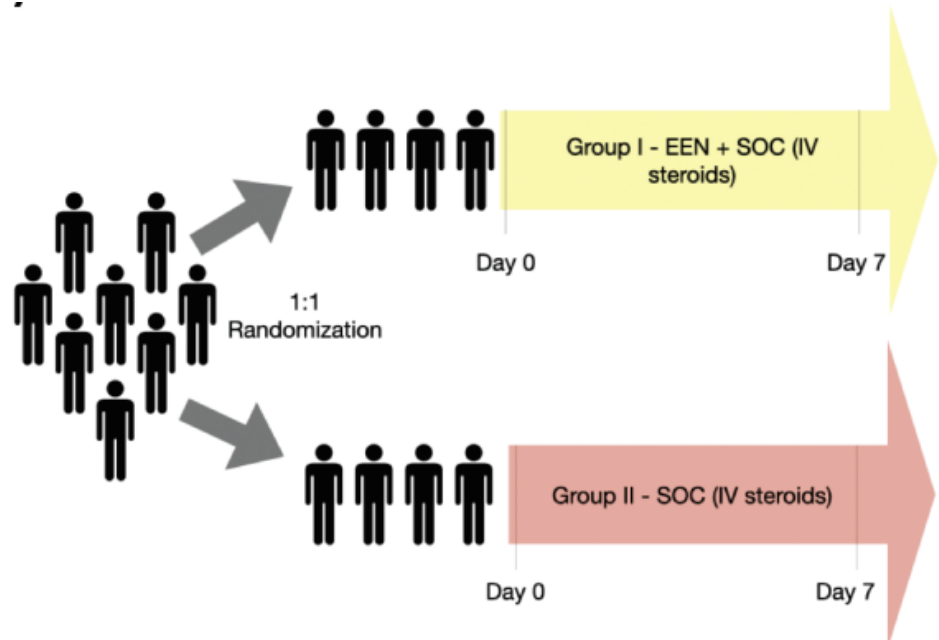
- VTE risk remains high **post-discharge**
- Hypercoagulability persists after discharge
- Pharmacologic prophylaxis reduces VTE
- Potential benefit of **extended prophylaxis** after discharge



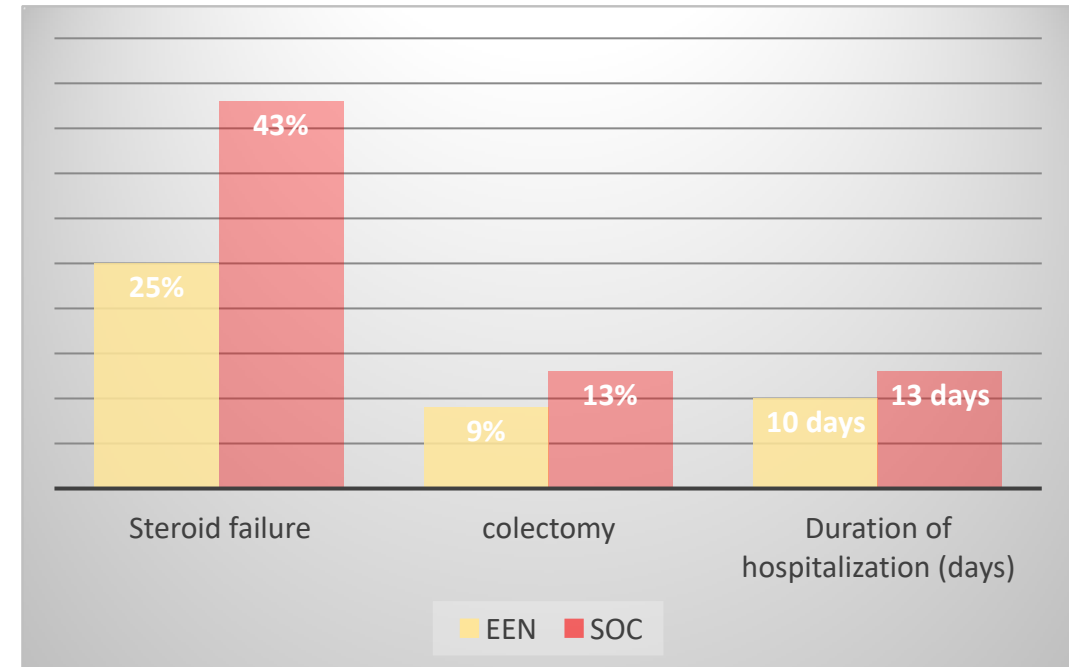
# Nutrition in Acute Severe UC

- Improved nutritional status improves bowel motility and intestinal permeability as well as reduce inflammatory reactions
  - ✓ *Recommended* → Enteral nutrition
  - ✗ *Not recommended* → Parenteral nutrition (TPN)
- Key Risks (for TPN)
  - ⚠ Higher mortality
  - ⛶ Longer hospital stay
  - \$ Increased costs

# Exclusive Enteral Nutrition as Adjunctive Therapy



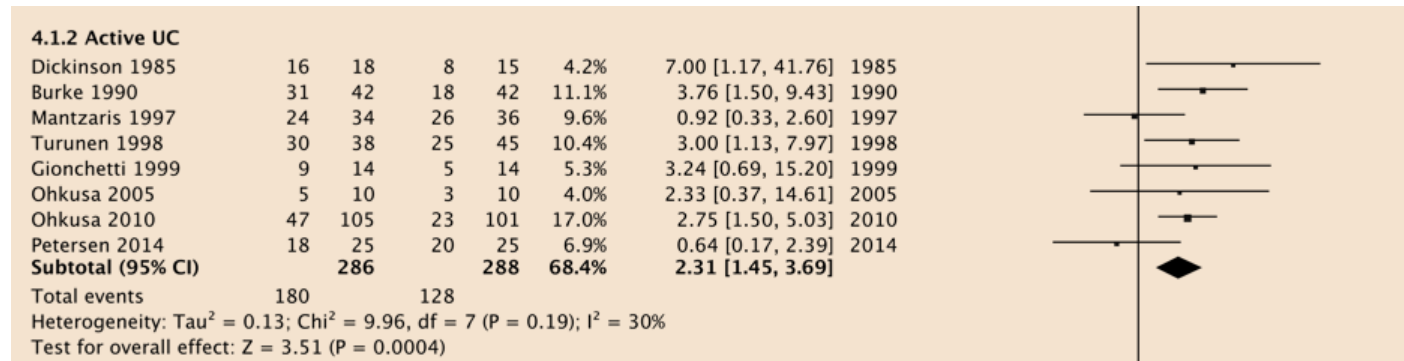
⚠ 16% patients did not tolerate exclusive enteral nutrition  
(Peptamen- caloric requirement calculated from BMI)



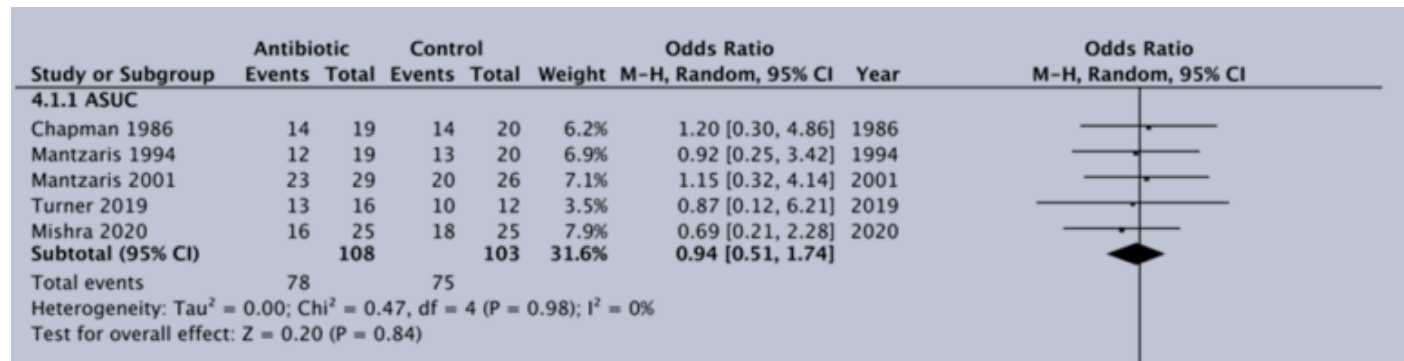
➡ EEN may reduce steroid failure and shorten hospitalization, but tolerance remains a challenge (16%)

# Antibiotics in ASUC: Do They Help?

Clinical response for antibiotics compared to placebo in ASUC vs. non ASUC patients- Meta-analysis



Active UC (non-ASUC):  
**Some benefit**



ASUC:  
**No benefit (OR ~1, NS)**

👉 Meta-analysis shows no added benefit of antibiotics in ASUC. Some effect seen in non-severe UC



## **Chapter 3**

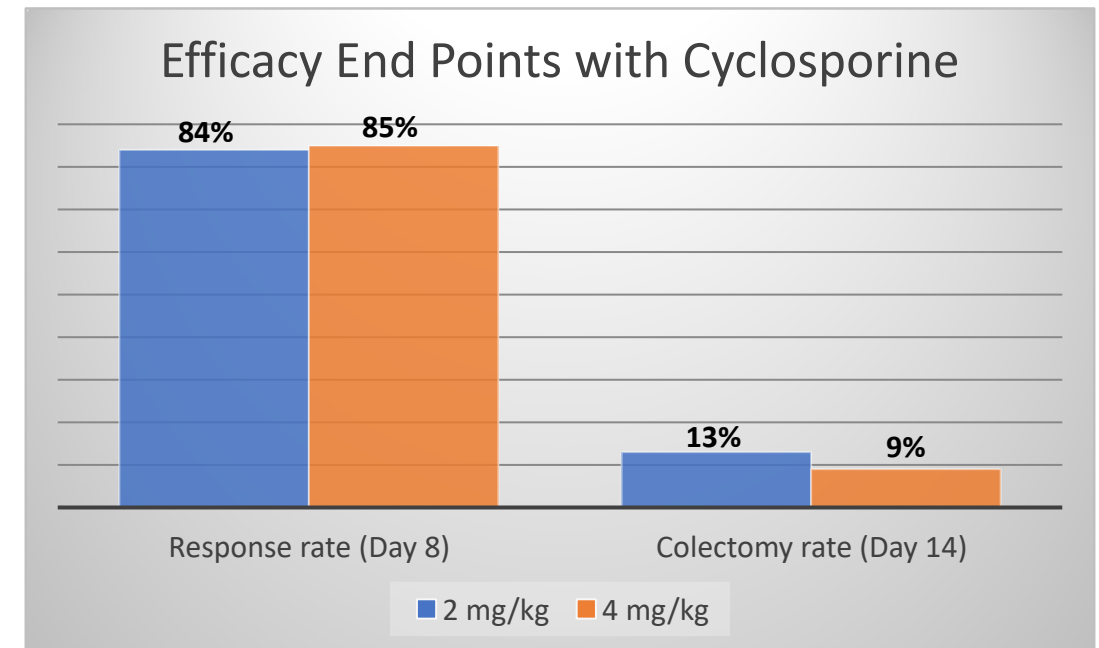
Rescue therapies

# **ASUC: A Practical Approach**

# Cyclosporine Rescue: Landmark Trial in ASUC



- Landmark 1994 NEJM trial established IV cyclosporine efficacy
- Similar efficacy at 2 mg/kg vs 4 mg/kg → Day 8 response ~85%
- Higher toxicity (HTN, nephrotoxicity) with 4 mg/kg

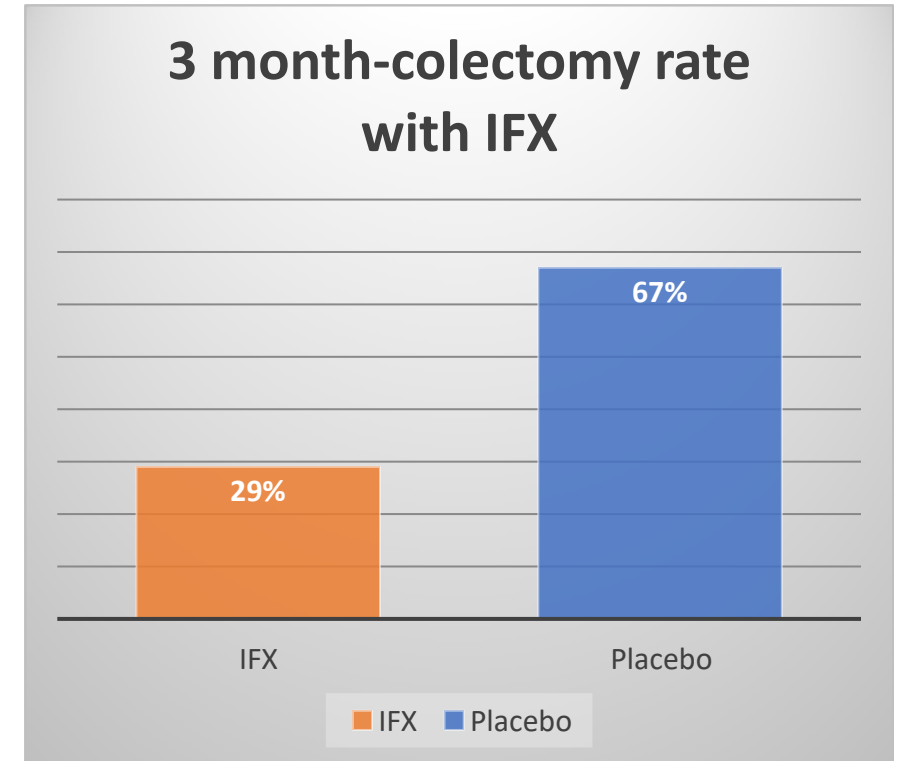


☞ Cyclosporine is effective for steroid-refractory ASUC, but lower-dose (2 mg/kg) is equally effective with fewer side effects

# Infliximab Rescue: Reducing Colectomy in ASUC

- RCT showed infliximab reduced colectomy vs placebo at 3 months
- Safe and effective as rescue therapy in steroid-refractory ASUC
- Long-term colectomy-free survival: 71% at 3 months, 53% at 5 years

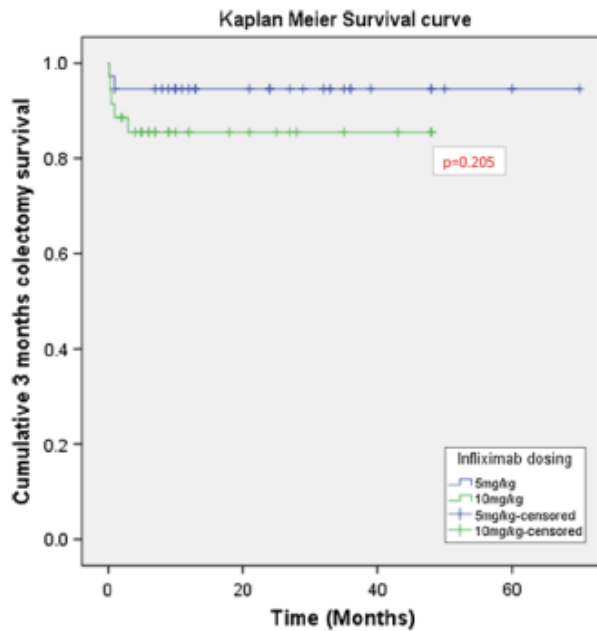
| 3 months | 12 months | 3 years | 5 years |
|----------|-----------|---------|---------|
| 71%      | 64%       | 59%     | 53%     |



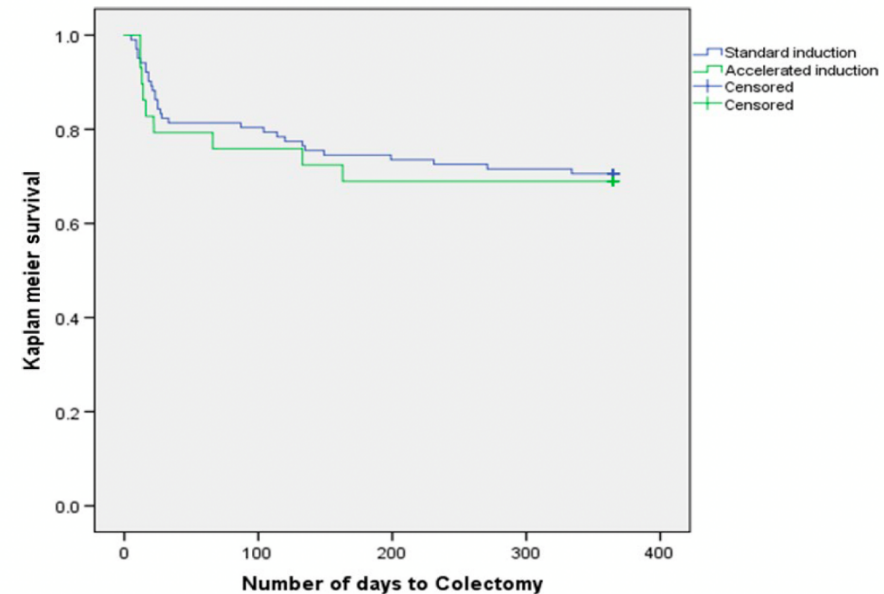
☞ **Infliximab is a proven rescue option for ASUC, significantly reducing colectomy rates and maintaining long-term survival**

# Does Higher or Faster IFX Induction Improve Outcomes in ASUC?

High-dose infliximab rescue therapy

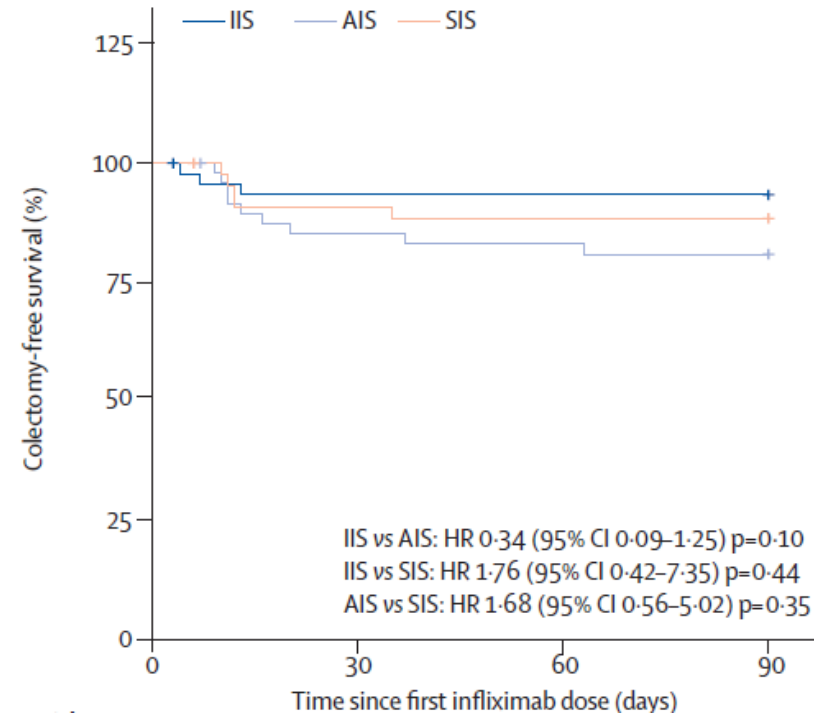
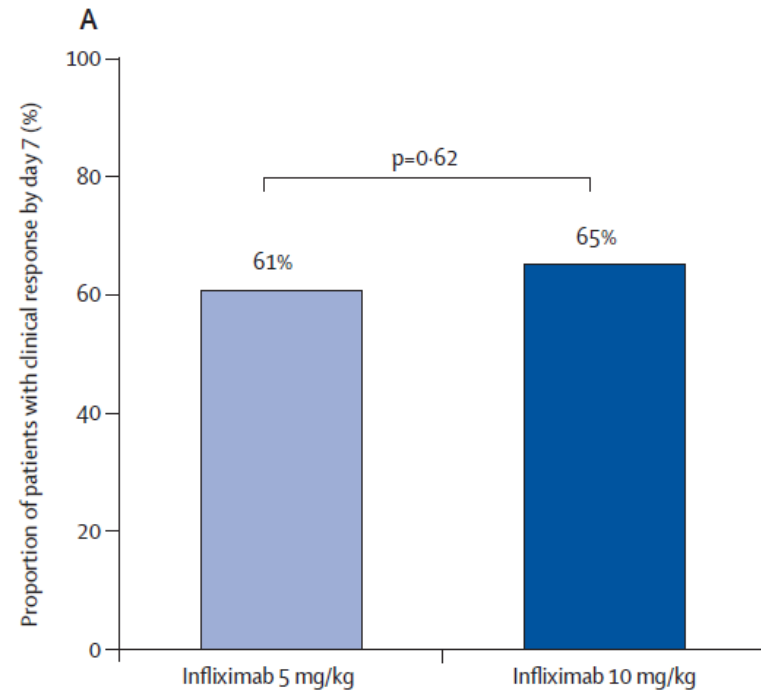


Accelerated induction IFX regimen



☞ Neither high-dose (10 mg/kg) nor accelerated IFX induction has shown clear benefit over standard dosing. More evidence is needed

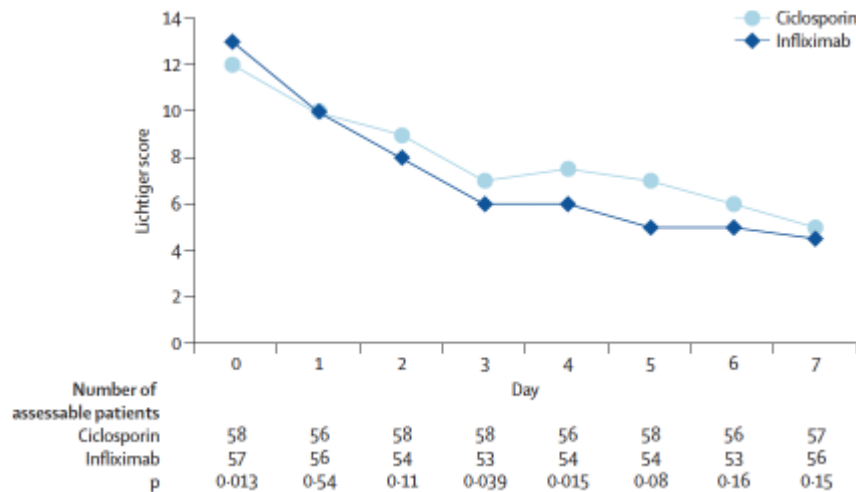
# PREDICT UC: Standard vs Intensified IFX Induction



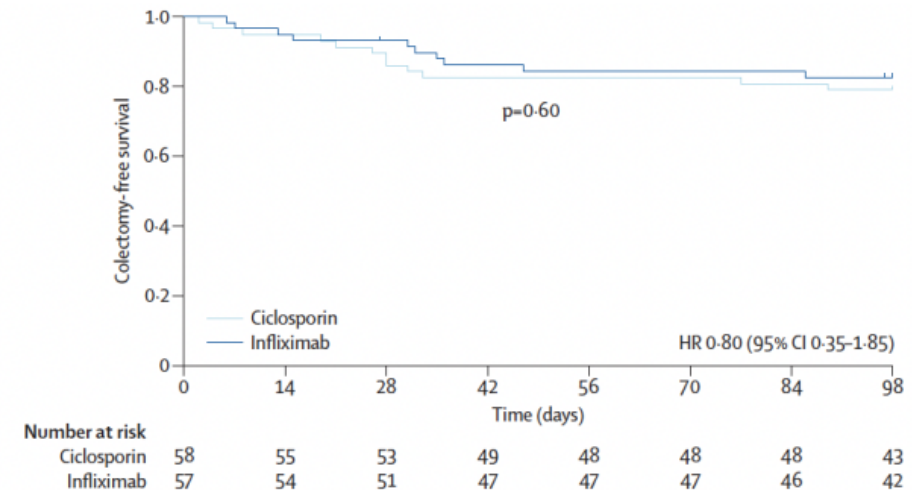
👉 Potential higher response signal in high-risk subgroup: **low albumin (<25 g/L) and high CRP (≥50 mg/L)**

# CYSIF Trial: Cyclosporine vs Infliximab in Steroid-Refractory ASUC

Clinical response at day 7



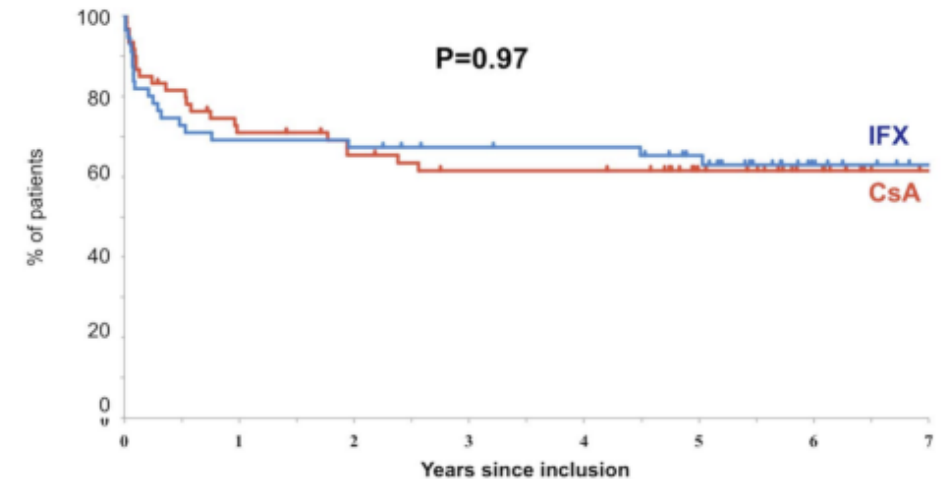
Colectomy-free survival



- No significant difference in short-term response at day 7
- No difference in colectomy-free survival

# CYSIF Long-Term Outcomes (5-Year Follow-up)

- 1-year colectomy-free survival: 71% (CsA) vs 69% (IFX)
- 5-year colectomy-free survival: 61% (CsA) vs 65% (IFX)
- No significant difference ( $P = 0.97$ )
- 💰 Costs
- 💉 Administration route
- 👤 Patient preference



# Two Roads to Rescue

*Choosing Between Infliximab and Cyclosporine*

## Infliximab

- One step rescue
- Less intensive monitoring
- More clinician familiarity



- Limited if prior anti- TNF exposure
- Rapid clearance in high CRP/ low albumin
- High cost

## Cyclosporine

- Rapid onset
- Low cost
- Useful when anti-TNF fails or contraindicated



- Intensive monitoring required
- Drug-drug interaction
- Difficult maintenance transition

Choice depends on prior therapy, patient comorbidities, cost, and institutional experience



# JAK Inhibitors: Rapid Rescue in ASUC

Tofacitinib

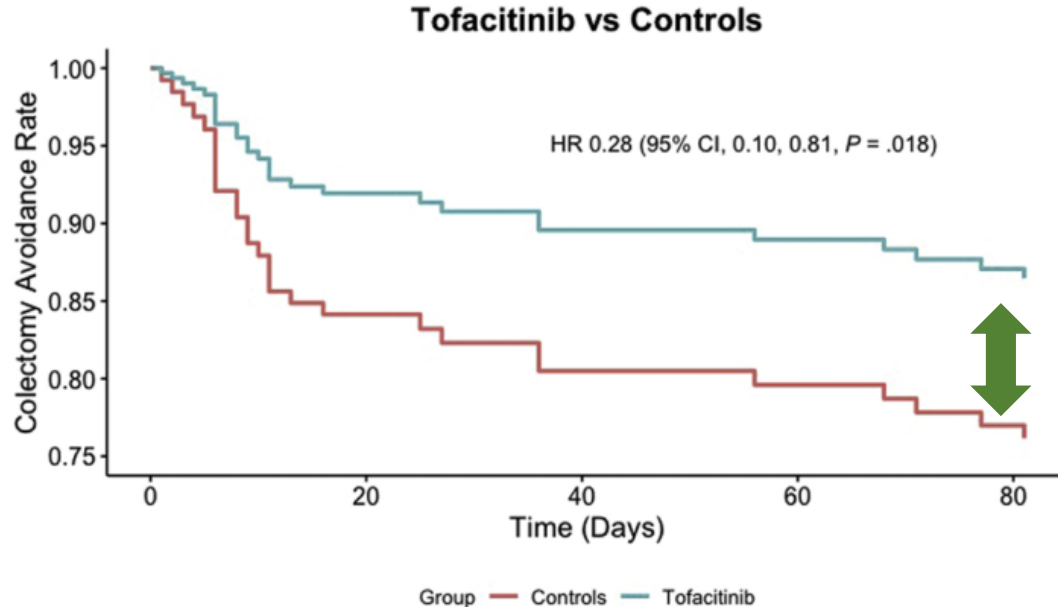
Upadacitinib

Fast onset of action

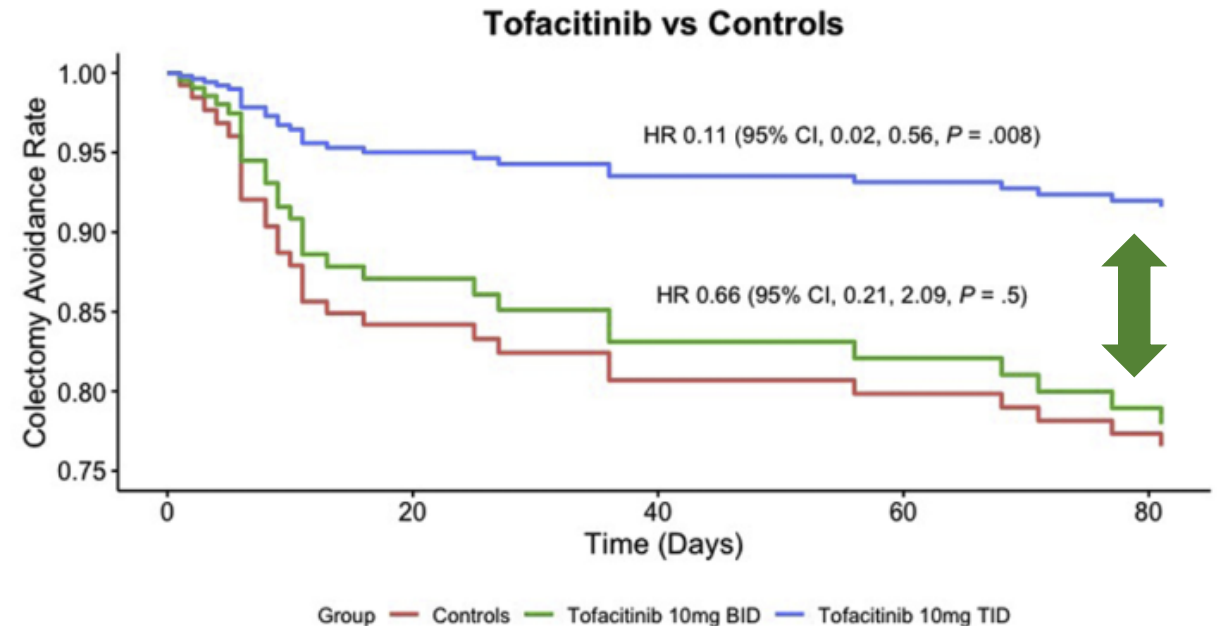
Cytokine Storm / Severe Inflammation

# Tofacitinib in ASUC: Reducing Colectomy Risk

Efficacy of Tofacitinib Induction in Biologic-Experienced ASUC Patients: A Retrospective Case-Control Study



Risk of Colectomy at 90 Days- Tofacitinib vs. control

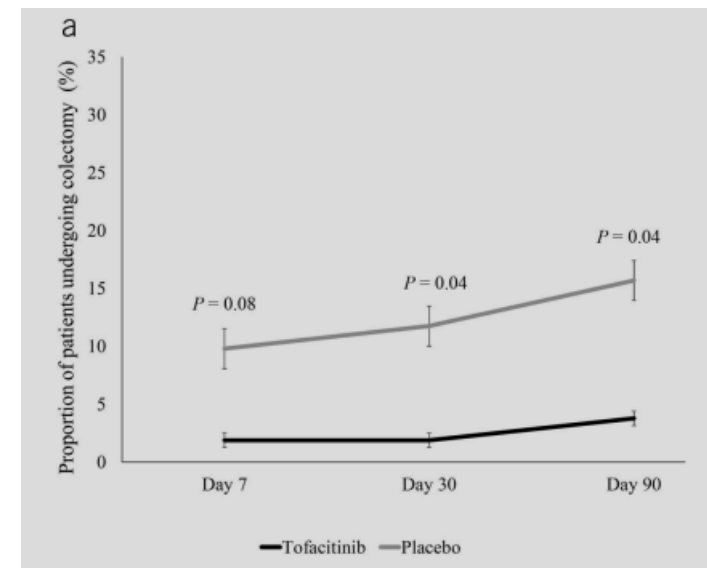
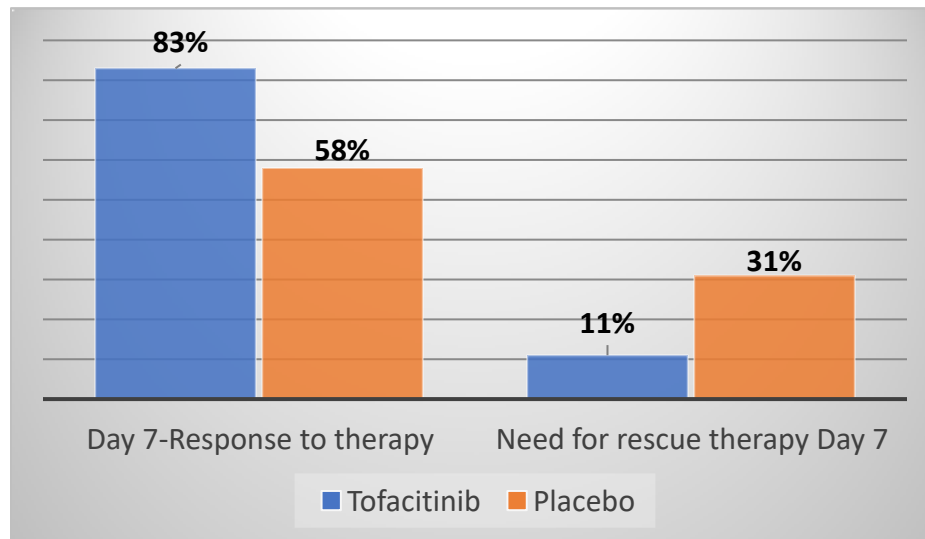


Risk of Colectomy at 90 Days According to Tofacitinib Dosing

👉 **Rapid oral option in biologic-experienced steroid-refractory ASUC**

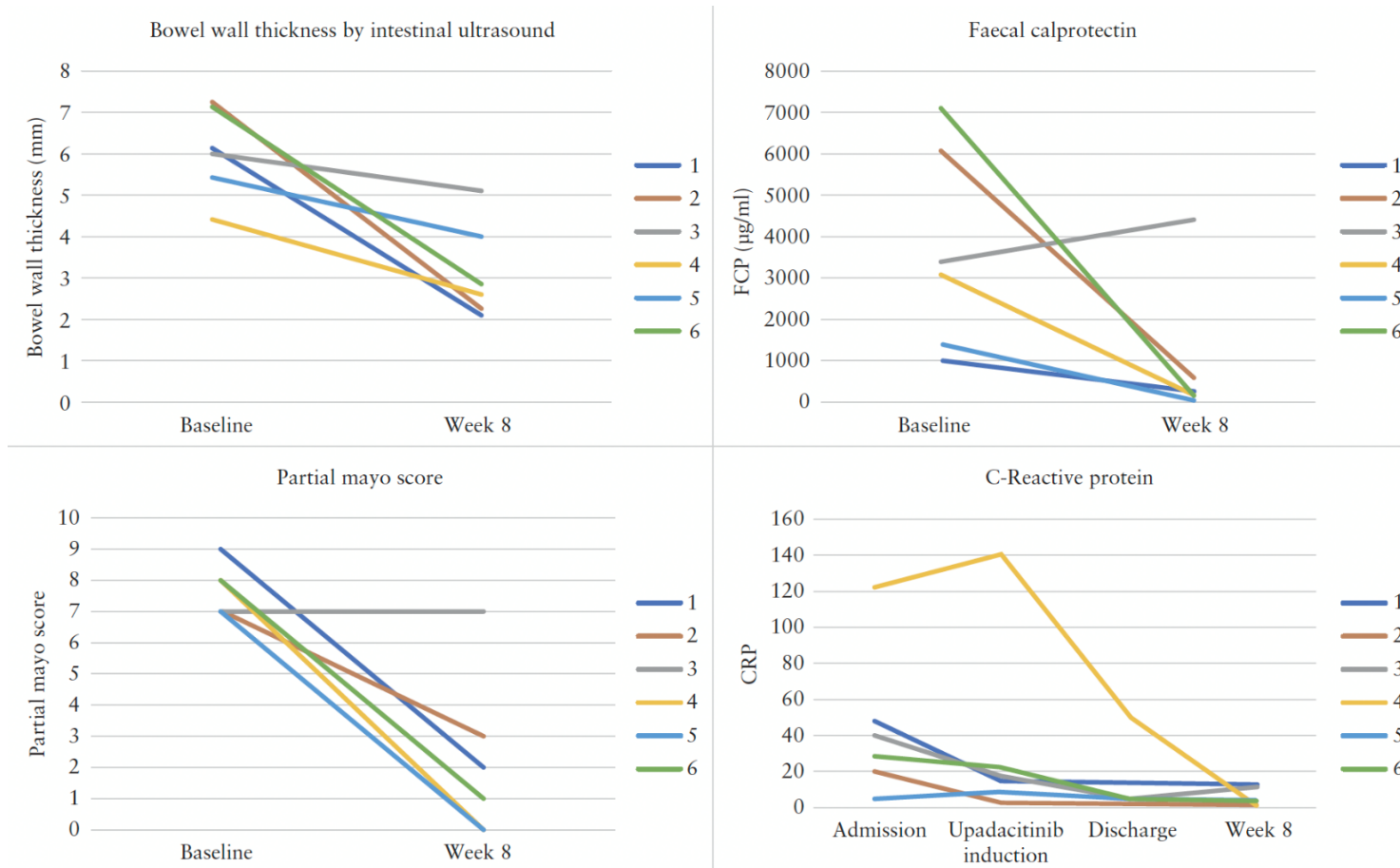
# TACOS RCT: Tofacitinib as Rescue Therapy in ASUC

Effectiveness of Tofacitinib in Acute Severe Ulcerative Colitis: Results from the TACOS Randomized Controlled Trial



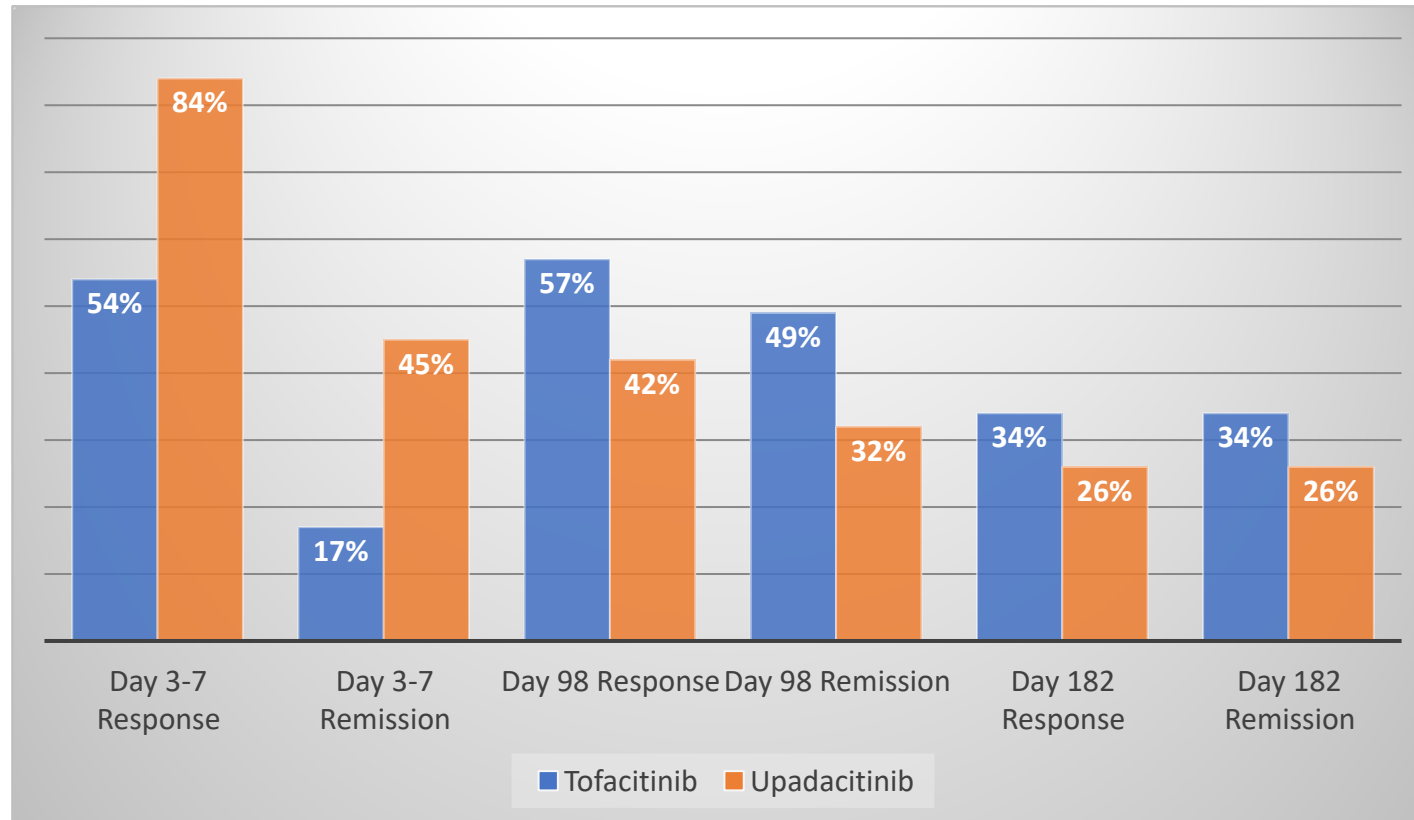
☞ Tofacitinib led to faster response, less need for rescue therapy, and reduced colectomy rates at 3 months

# Upadacitinib in ASUC



Outcomes of interest after 8 weeks of Upadacitinib 45 mg daily in ASUC

# Tofacitinib vs. Upadacitinib As Rescue Therapy



# Proposed Treat-to-Target Algorithm in ASUC

| Phase                             | Goal/Target                                    | Monitoring Tool                            | Action                                                                                                  |
|-----------------------------------|------------------------------------------------|--------------------------------------------|---------------------------------------------------------------------------------------------------------|
| <b>Admission (Day 0)</b>          | Confirm diagnosis, rule out infection          | Stool C. difficile, flexible sigmoidoscopy | Start IV steroids (e.g., methylprednisolone 60 mg/day)                                                  |
| <b>Day 3</b>                      | Evaluate clinical response                     | Oxford criteria: stool frequency + CRP     | ✓ Response: Continue IV steroids<br>✗ No response: Initiate rescue therapy (Infliximab or Cyclosporine) |
| <b>Day 5–7</b>                    | Reassess response to rescue therapy            | Clinical + CRP                             | ✓ Response: Transition to maintenance biologic<br>✗ No response: Surgery consult (colectomy)            |
| <b>Week 8–12 (Post-discharge)</b> | Achieve clinical remission                     | PROs (e.g., SCCAI), CRP, calprotectin      | Optimize/continue biologic; escalate if needed                                                          |
| <b>Month 3–6</b>                  | Mucosal healing (Mayo 0–1)                     | Sigmoidoscopy/colonoscopy                  | Continue T2T monitoring & de-escalate steroids completely                                               |
| <b>Ongoing</b>                    | Durable steroid-free remission, QoL, no flares | PROs, biomarkers, endoscopy as needed      | Adjust therapy as per STRIDE-II (step up/down)                                                          |

# Addressing Challenges in ASUC Management



# Conclusion: 5 pillars of ASUC care

**1.**

**Early and  
Accurate  
Diagnosis**

**2.**

**Optimizing  
Medical  
Therapy**

**3.**

**Managing  
Complications**

**4.**

**Nutrition  
Support**

**5.**

**Multidisciplinary  
Approach**

Thank you