

# 2021 SCSG GI SYMPOSIUM







# Updates from DDW 2021

## Inflammatory Bowel Diseases

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# Disclosures

No relevant conflicts of interest

# Outline

- To review the impact of nutrition support on post-surgical outcomes
- To recognize the effects of corticosteroids use in pregnancy
- To evaluate the prognostic value of calprotectin for ulcerative colitis
- To understand the role of the Mediterranean diet vs. Specific Carbohydrate Diet for Crohn's disease



# **Impact of Perioperative Nutritional Support in Patients Undergoing Major Inflammatory Bowel Disease Surgery: A Nationwide Analysis**



# Perioperative Nutrition

- Patients with IBD frequently require surgical intervention
- Protein-calorie malnutrition (PCM) is common among patients with IBD
- PCM is associated with adverse postoperative outcomes

## Study Aim

- To assess the impact of perioperative nutrition support on relevant postoperative outcomes and complications

# Methods

- Nationwide Readmissions Database (NRD) 2010-2017
- ICD diagnostic and procedure codes
- Postoperative outcomes
  - 30-day readmission
  - Infection, wound dehiscence
  - Pneumonia, UTI, DVT, CLABSI
  - Death
- Multivariable analyses adjusted for potential confounders

# Results

- 27665 patients with IBD and concomitant PCM who underwent major intestinal surgery
- 14017 received nutrition support
  - 475 EN alone
  - 13098 PN alone
  - 444 EN and PN
- 13648 controls did not receive nutrition support



# Results

	Odds Ratio	95% CI	<i>P</i>
30-day readmission	1.04	0.92 – 1.19	0.47
30-day mortality	0.72	0.59 – 0.89	<0.01
Overall infection	1.26	1.06 – 1.50	<0.01
Wound dehiscence	0.93	0.68 – 1.28	0.67
Pneumonia	1.04	0.90 – 1.22	0.58
Urinary tract infection	1.08	0.94 – 1.24	0.27
Deep vein thrombosis	1.39	1.14 – 1.70	<0.01
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# Strengths and Limitations

## Strengths

- Nationally representative cohort

## Limitations

- Observational study
- Inability to control for potential confounders that prompted us of nutrition support
- Lack of granular data on severity of PCM

# Conclusions

- Perioperative nutrition support in patients with IBD and PCM undergoing major intestinal surgery was associated with lower 30-day mortality
- Nutrition support was associated with increased infectious complications and DVT

## Clinical Practice Pearl

- We should be vigilant about patients' nutritional status prior to surgery and focus on nutrition optimization as needed



# **Exposure to Corticosteroids in Pregnancy is Associated with Adverse Perinatal Outcomes among Infants of Mothers with Inflammatory Bowel Disease**



# Pregnancy and IBD

- IBD flares complicate 30% of pregnancies
- Active IBD is associated with complications including pre-term birth, spontaneous abortion, and infant infection
- Exposure to biologics, thiopurines, and combination therapy during pregnancy is not associated with increased maternal or infant adverse events

# Pregnancy and IBD

- However, there remains safety concerns leading to increased rates of cessation/avoidance of maintenance therapies
- When IBD flares complicate pregnancy, corticosteroids are often needed
- The impact of corticosteroids on infant and maternal outcomes in mothers with IBD is not well understood

# Study Design

## Population

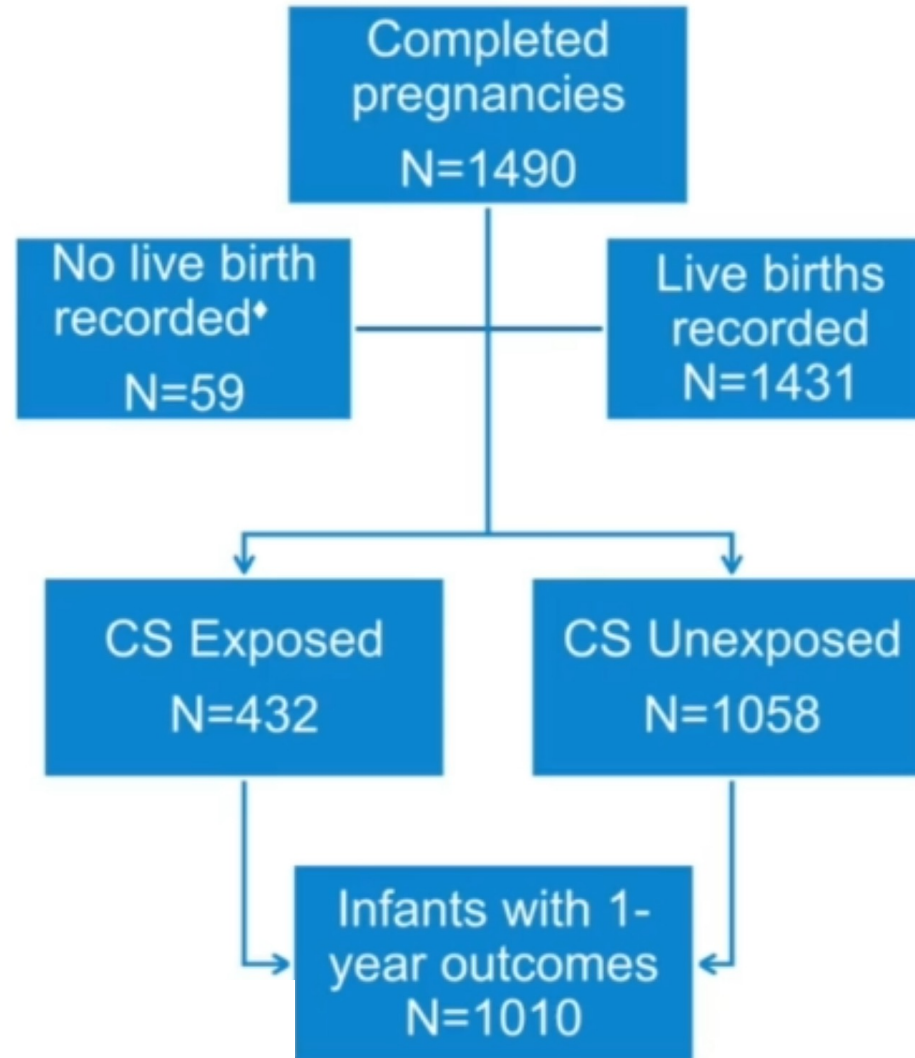
- **Pregnancy in Inflammatory Bowel Disease And Neonatal Outcomes (PIANO)**

## Outcomes

- Adverse pregnancy outcomes
  - SAB, preterm birth, IUGR, SGA, LBW, Cesarean section, NICU at birth
- Infant infections
- Developmental milestones
  - Communication, fine motor, gross motor, personal social, problem-solving
- Congenital malformations



# Enrollment



# Demographics

	Overall N = 1490	No Steroid N = 1058	Corticosteroid Use N = 432	<i>P</i>
Maternal age at birth (years)	32.0	32.2	31.4	0.002
Disease duration (years)	8.3	8.7	7.1	<0.001
Mean # pregnancies	2.1 (1.3)	2.0 (1.2)	2.2 (1.3)	0.007
Medication use, n (%)				0.26
No exposure	379 (25)	263 (25)	116 (27)	
Biologics	642 (43)	455 (43)	187 (43)	
Immunomodulator	242 (16)	184 (17)	58 (13)	
Combination therapy	227 (15)	156 (15)	71 (16)	
Smoking status, n (%)				0.03
Current	23 (2)	12 (1)	11 (3)	
Former	307 (22)	209 (21)	98 (25)	
Never	1055 (76)	769 (78)	286 (72)	

# Pregnancy Related Complications

	Overall IBD N = 432	CD N = 240	UC N = 192
Spont Abort (gestation $\leq$ 140 days)	1.28 (0.52-2.65)	0.81 (0.25-2.58)	1.88 (0.65-5.38)
Spont Abort (all gestation ages)	1.28 (0.53-2.59)	0.75 (0.24-2.39)	1.86 (0.68-5.07)
Preterm birth (<37 weeks)	1.79 (1.18-2.73)	2.33 (1.39-3.92)	1.19 (0.57-2.51)
Small for gestational age	1.10 (0.01 -2.07)	0.90 (0.41-2.00)	4.29 (1.51-12.45)
Low birth weight (<2500 g)	1.76 (1.97-2.88)	1.38 (0.72-2.66)	2.78 (1.21-3.40)
Intrauterine growth restriction	1.57 (0.69-3.59)	1.00 (0.67-5.33)	0.87 (0.20-3.78)
Cesarean section	1.02 (0.78-1.32)	1.49 (1.05-2.00)	0.67 (0.42-1.06)
NICU at birth	1.51 (1.02-2.30)	2.06 (1.26-2.35)	0.93 (0.44-1.97)
Congenital malformations	1.22 (0.80-1.87)	1.28 (0.75-2.20)	1.17 (0.58-2.36)
Any of the above	1.00 (0.77-1.31)	1.08 (0.75-1.55)	1.04 (0.69-1.56)



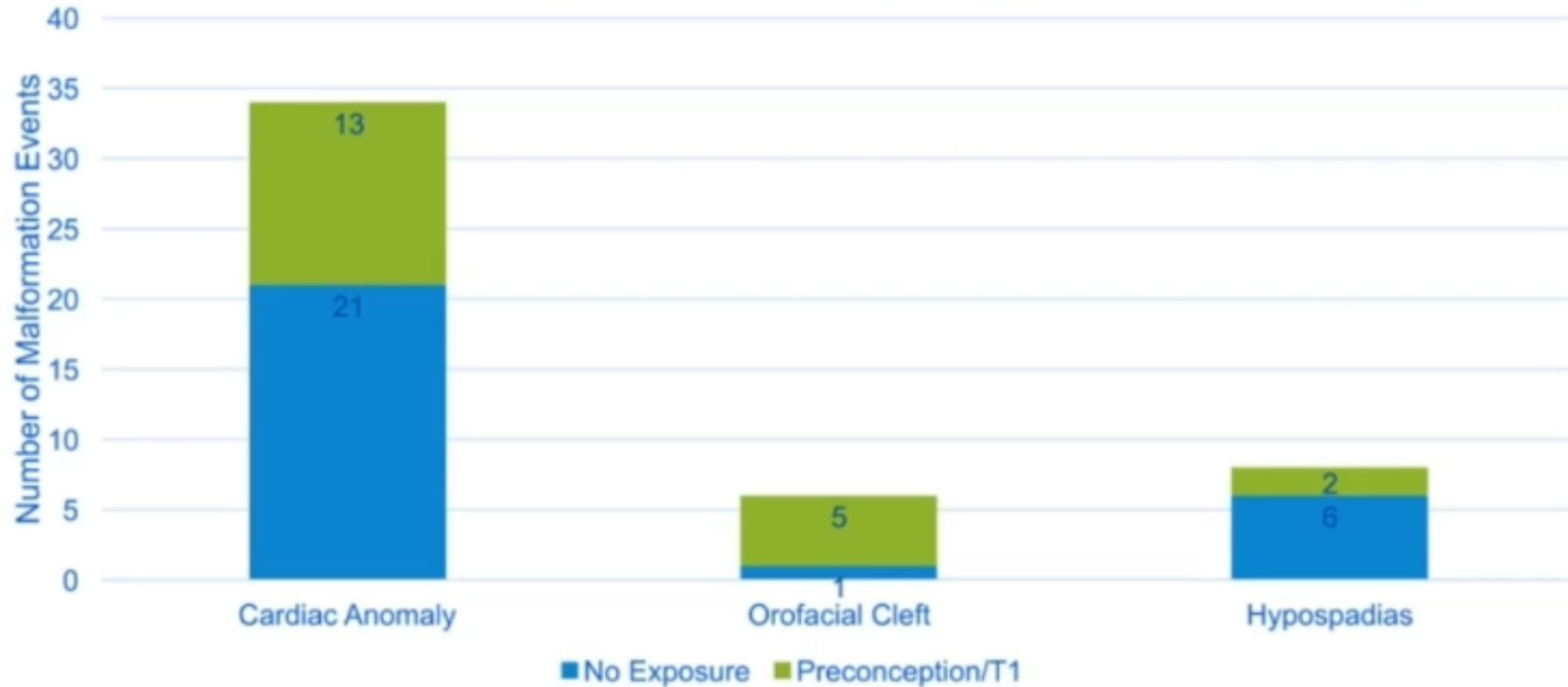
# Infant Infections in the First Year

	Any Steroids N = 409	<i>P</i>
Newborn		
Serious infection	1.4 (0.7-3.1)	0.37
First 12 months		
Serious infection	1.0 (0.6-1.7)	0.90
Non-serious infection	1.1 (0.9-1.4)	0.40
Any infection	1.1 (0.9-1.4)	0.52

# Infant Infections in the First Year

	Comm	Fine Motor	Gross Motor	Per Soc	Prob Solv
12 months	=	=	=	↓	=
24 months	=	=	=	=	=
36 months	=	=	=	↓	=
48 months	=	=	=	=	=

# Congenital Malformations



Congenital Malformation	Total (%)	No Exposure	Pre-conception/T1	T2/T3	P Value
Any Congenital Malformation	126 (9%)	86 (9%)	37 (11%)	0 (0%)	0.04

# Strengths and Limitations

## Strengths

- Large, multicenter, prospective cohort design
- Long-term follow-up

## Limitations

- Self-reported participant responses
- Corticosteroid exposure not controlled for active disease
- Lack of detailed data regarding individual steroid medication dosing and duration
- Multivariable models did not completely adjust for confounders

# Conclusions

## Clinical Practice Pearls

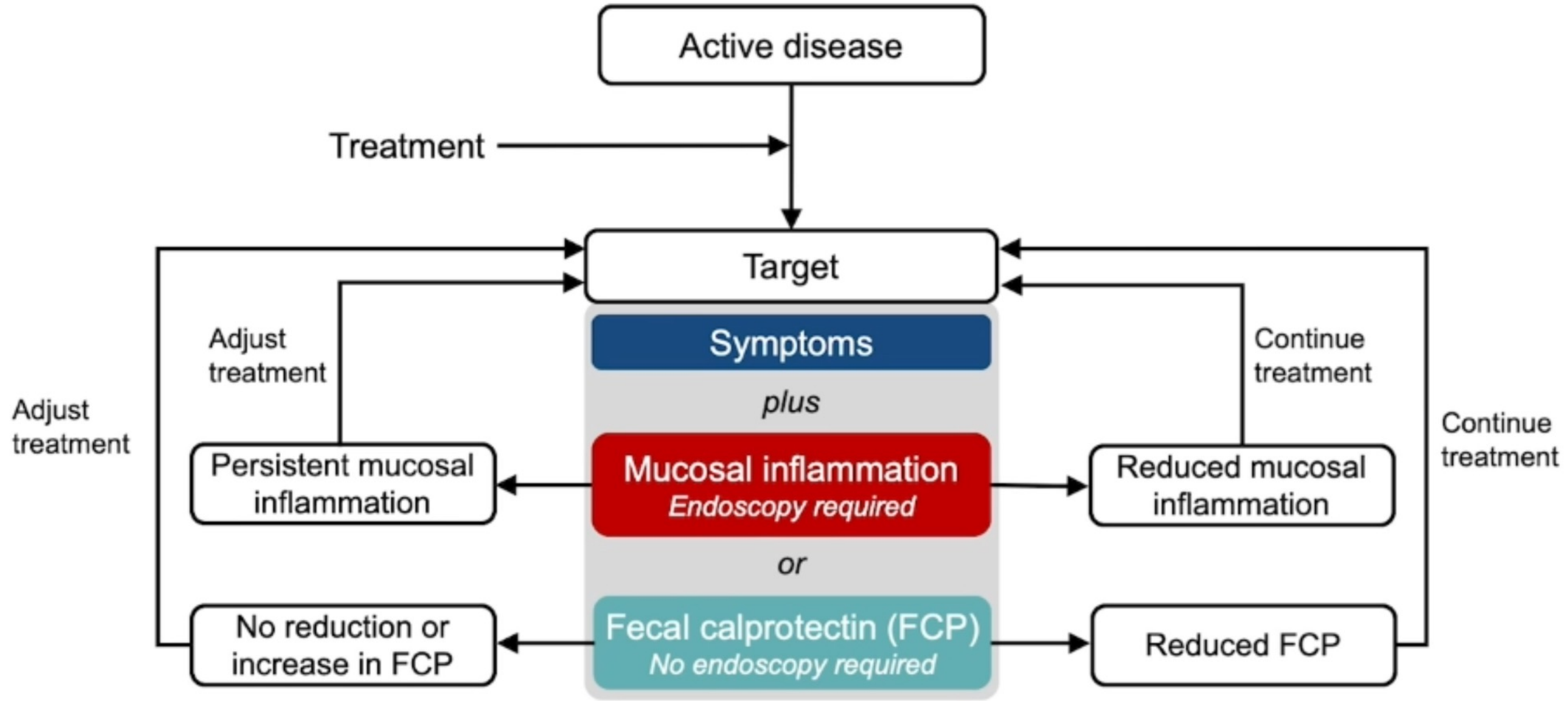
- Women with IBD should be in stable remission on appropriate IBD therapy prior to attempting conception
- In pregnant women with IBD, the need for corticosteroids during pregnancy is associated with increased adverse events for both mother and child





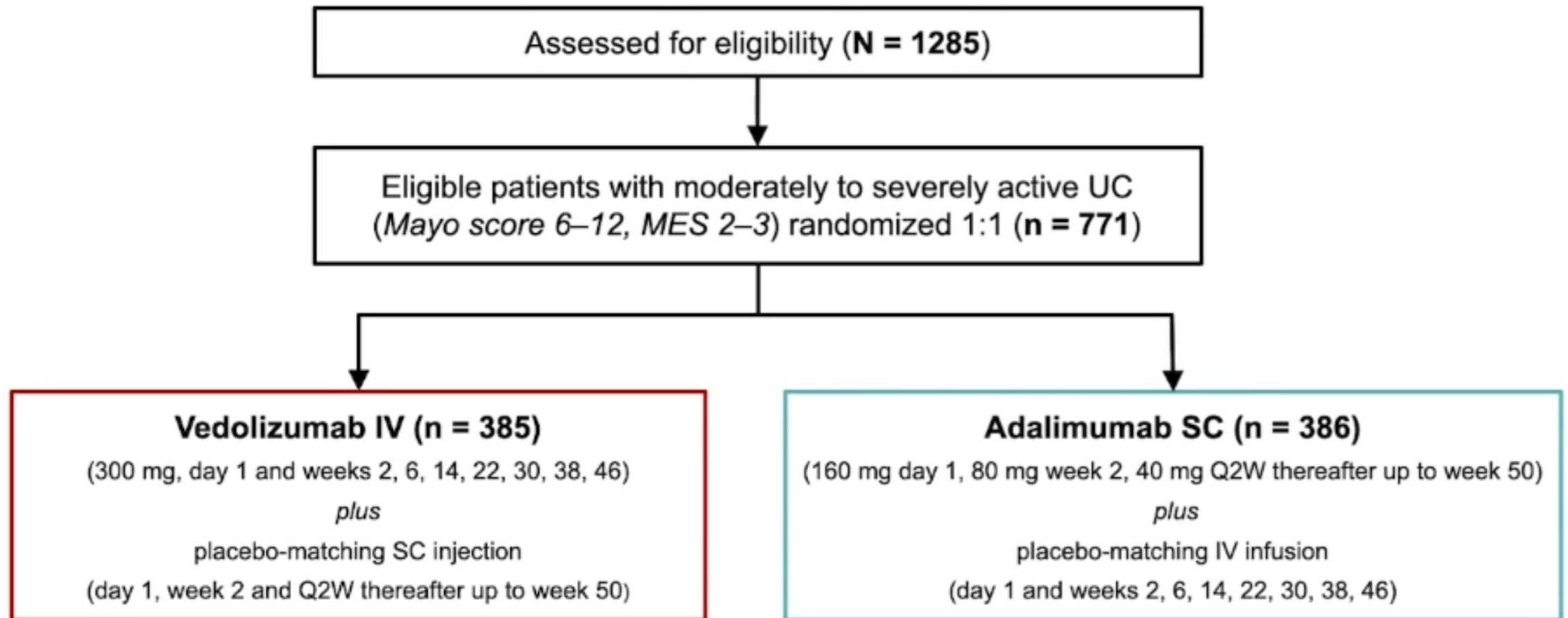
# **Prognostic Value of Fecal Calprotectin in Patients with Biologic-treated Ulcerative Colitis**

# Treat-to-Target Paradigm



# Post-hoc Analysis of VARSITY Trial

**VARSITY is a phase 3b randomized, double-blind, double-dummy, multicenter, active-controlled study**



# Outcomes

- Analyses explored the relationship between FCP concentration and outcomes after treatment initiation
  - Cross sectional at week 14
  - Prognostic at weeks 14 and 52

Outcomes	Definition
Symptomatic remission	Mayo rectal bleeding subscore of 0 and a stool frequency subscore $\leq 1$
Clinical remission	Complete Mayo score $\leq 2$ and no individual subscore $> 1$
Endoscopic improvement	Mayo endoscopic subscore (MES) $\leq 1$
Endoscopic remission	MES 0
Histologic remission	Robarts histopathology index (RHI) $< 3$ or Geboes grade $< 2$
Mucosal healing	Endoscopic improvement and histology remission with RHI and Geboes grades analyzed separately

Characteristic	Patients, n	
Age, years, mean (SD)	40.7 (13.6)	771
Sex, male, n (%)	450 (58.4)	771
White, n (%)	686 (89.0)	771
Body weight, kg, mean (SD)	73.1 (17.7)	769
Current smoker, n (%)	42 (5.4)	771
Duration of disease, years, mean (SD)	6.8 (6.7)	768
Mayo Clinic score, mean (SD)	8.7 (1.6)	764
Partial Mayo Clinic score, mean (SD)	6.1 (1.4)	765
<b>Fecal calprotectin, µg/g, median (min–max)</b>	<b>1441 (10–87,938)</b>	<b>673</b>
Concomitant medications for ulcerative colitis, n (%)		
Corticosteroid only	196 (25.4)	771
Immunomodulator only	118 (15.3)	771
Corticosteroid and immunomodulator	83 (10.8)	771
Prior anti-TNF therapy, n (%)	161 (20.9)	771

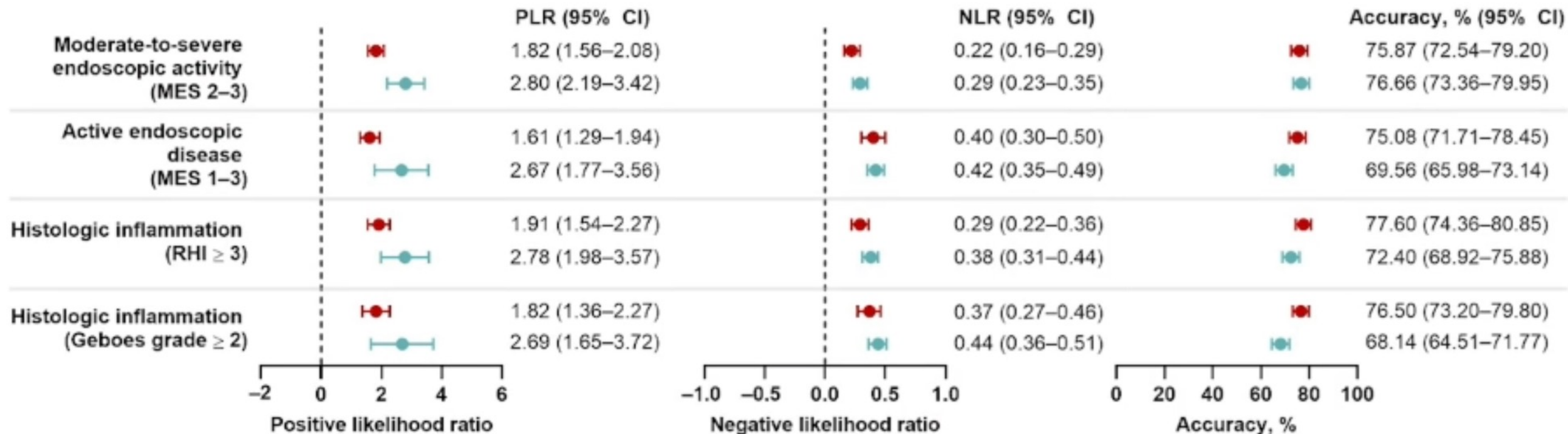


# FCP and Likelihood of UC Disease Activity at Week 14

N = 634

● FCP cut-off: > 100 µg/g, n = 475 (74.9%); ≤ 100 µg/g, n = 159 (25.1%)

● FCP cut-off: > 250 µg/g, n = 392 (61.8%); ≤ 250 µg/g, n = 242 (38.2%)



2, small (15%) increase in probability of disease; 5, moderate (30%) increase in probability of disease; 10, large (45%) increase in probability of disease.

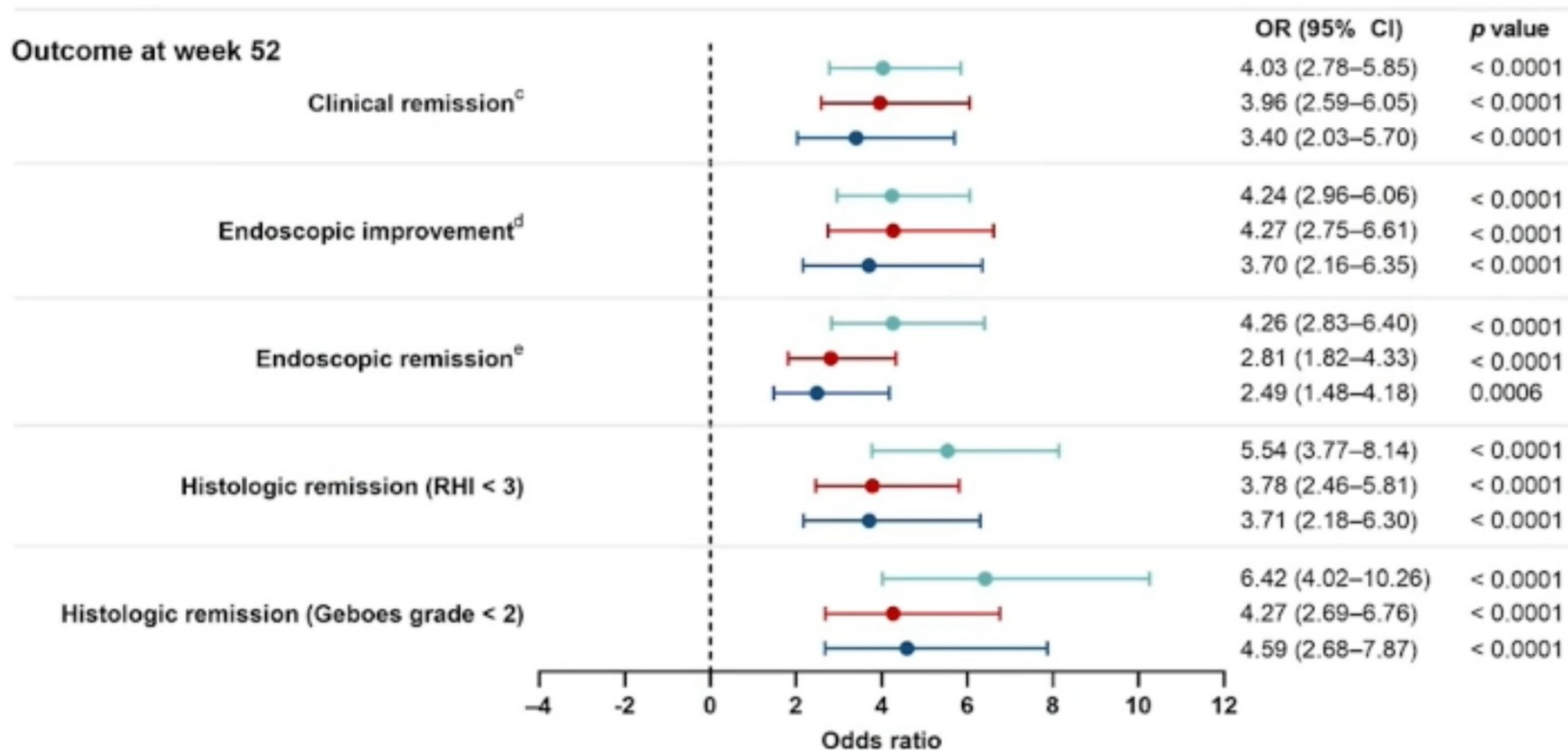
0.1, large (–45%) decrease in probability of disease; 0.2, moderate (–30%) decrease in probability of disease; 0.5, small (–15%) decrease in probability of disease

# FCP at Week 14 Predicts Disease Activity at Week 52

## Outcome at week 14

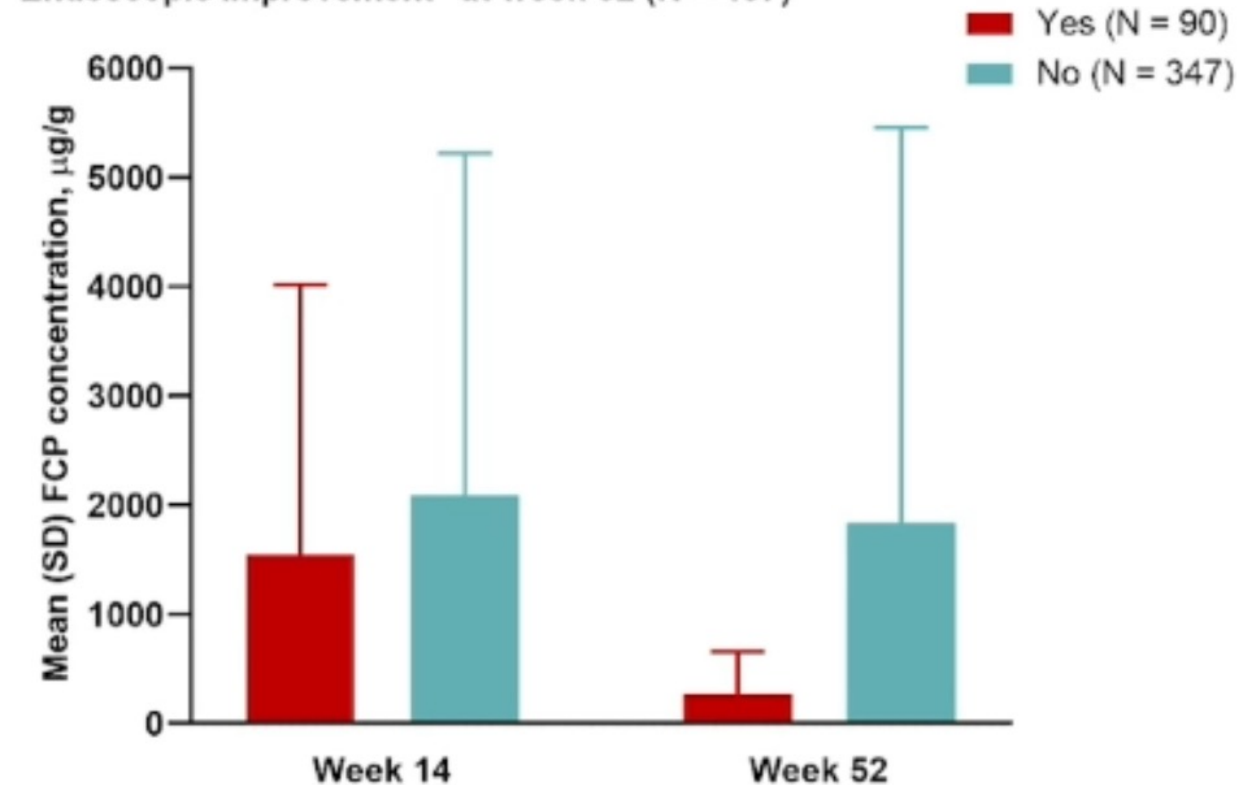
- FCP  $\leq 250$   $\mu\text{g/g}$  (N = 634)<sup>a</sup>
- Mucosal healing - histologic remission based on RHI and endoscopic improvement (n = 651)<sup>b</sup>
- Mucosal healing - histologic remission based on Geboes grade and endoscopic improvement (n = 656)<sup>b</sup>

## Outcome at week 52

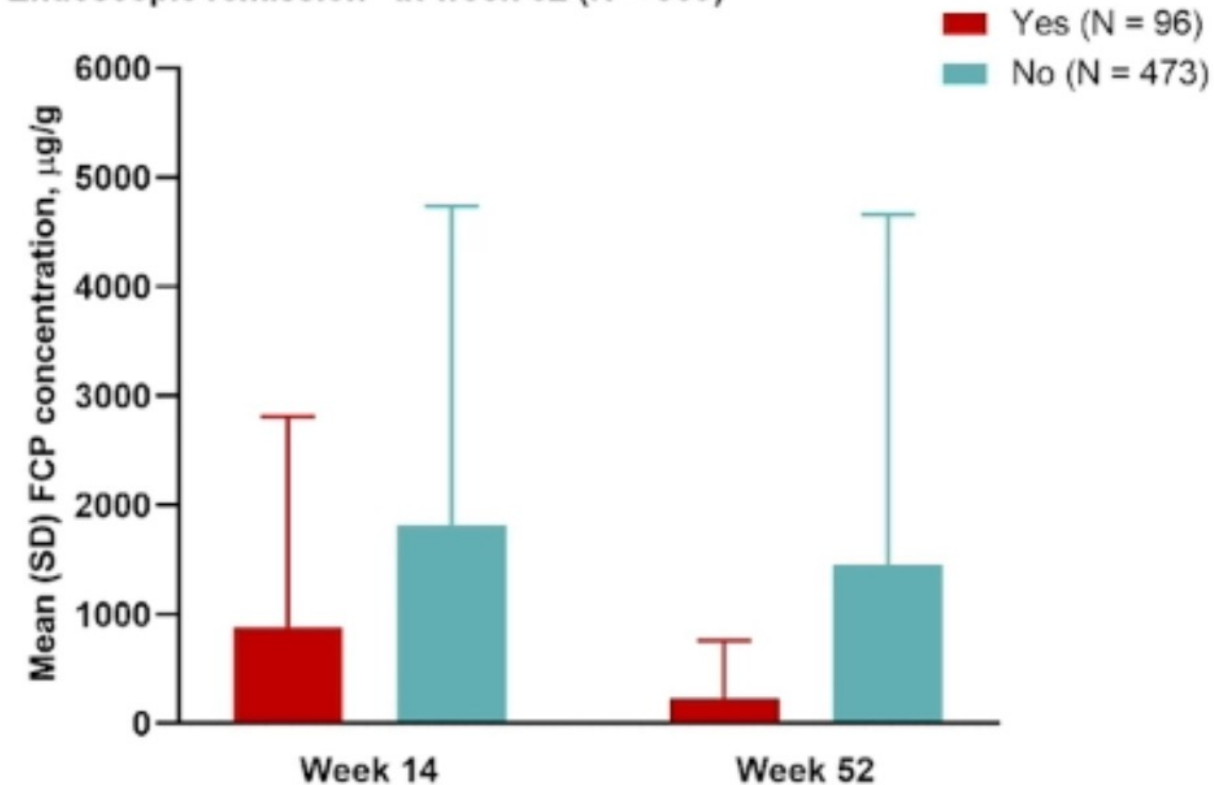


# Lower Week 14 FCP is Associated with Endoscopic Improvement at Week 52

Endoscopic improvement<sup>a</sup> at week 52 (N = 437)



Endoscopic remission<sup>b</sup> at week 52 (N = 569)



# Conclusions

- Fecal calprotectin at week 14 was modestly associated with disease activity at weeks 14 and 52

## Clinical Practice Pearls

- Integration of early FCP monitoring within treat-to-target algorithms should be considered



# **Diet to INducE Remission in Crohn's Disease Study: DINE-CD**





ask  
questions



🎯 Study Underway

👍 Great Fit for Partners

We should compare individuals who manage their disease with medication and those who manage their disease with popular diets in the IBD community, such as SCD

🍽️ Diet



📊 142 💬 16

# Mediterranean Diet's Associated Health Benefits

## General Population

- All cause mortality
- Cardiovascular disease
- Cancer

## Crohn's Disease

- Lower incidence of Crohn's disease
- Reduced symptoms and improved quality of life

# Study Design

## DINE-CD Study Diets



### Specific Carbohydrate Diet

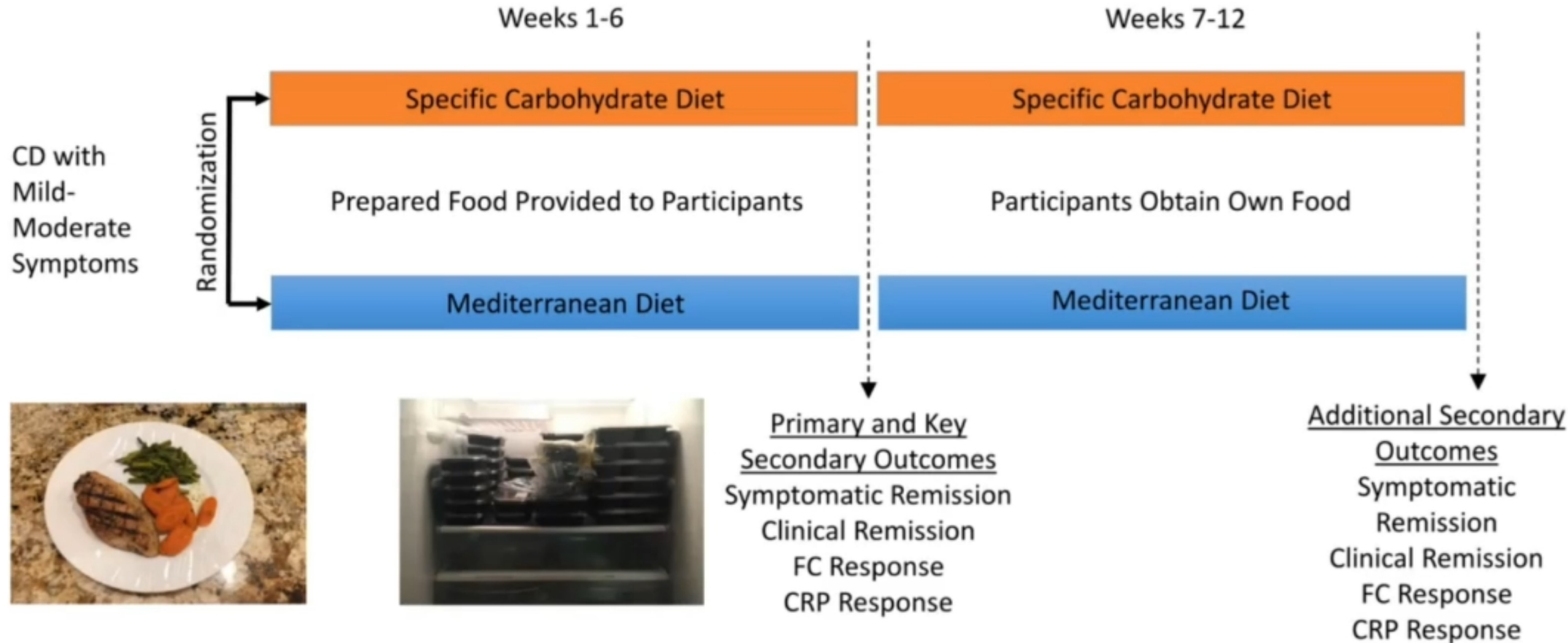
- High intake of
  - Unprocessed meats, poultry, fish, shellfish, eggs
  - Most vegetables (fresh, frozen, raw or cooked)
  - Most fruits and nuts
  - Some legumes
- Avoid
  - Grains
  - Dairy other than in some hard cheeses and homemade yogurt fermented for 24 hours
  - Sweeteners other than honey

### Mediterranean Diet

- High intake of
  - Olive oil
  - Fruits
  - Vegetables
  - Nuts
  - Cereals
- Moderate intake
  - Fish and poultry
  - Wine
- Limited intake
  - Red and processed meat
  - Sweets



# Study Design





# Outcomes

## Primary Outcome at 6 Weeks

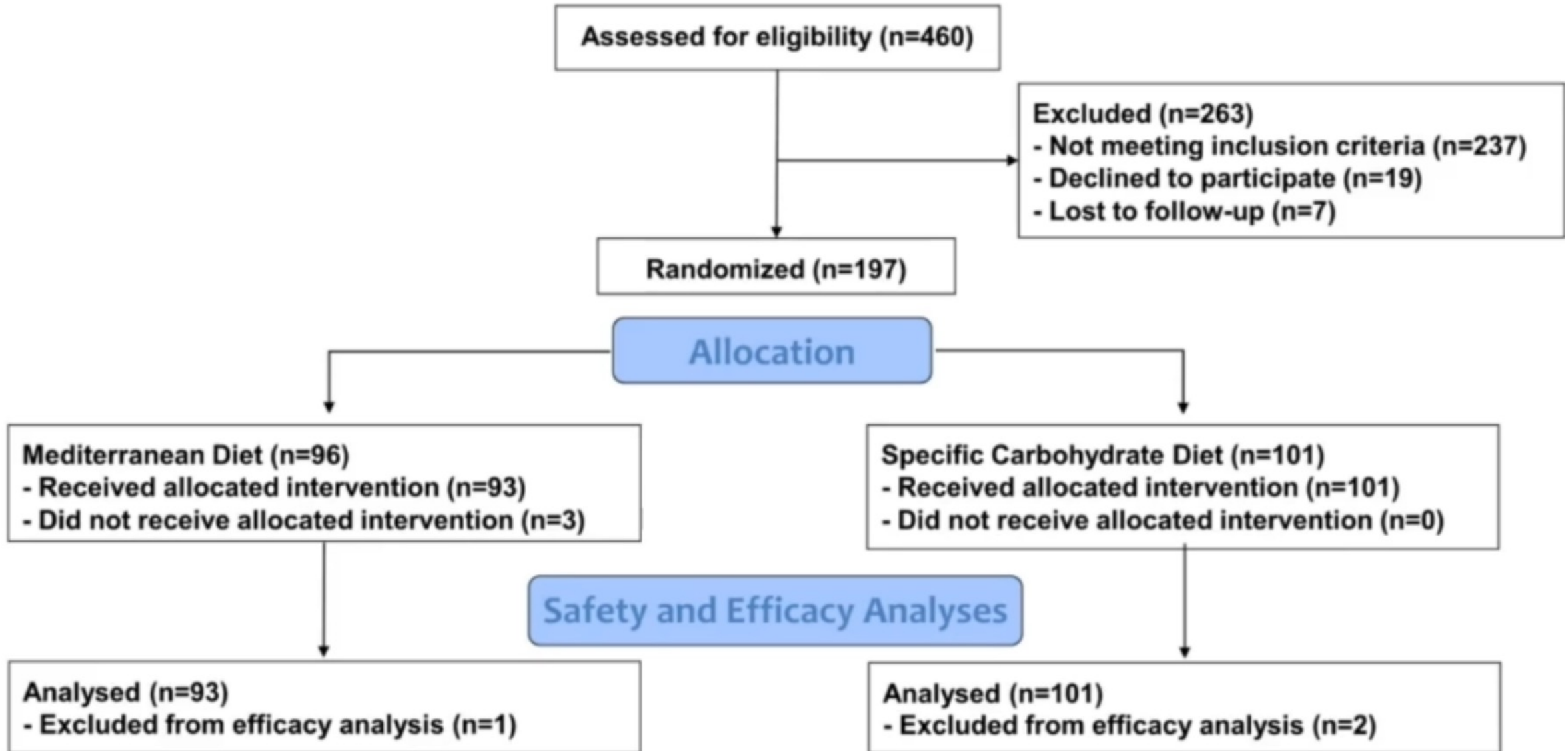
- Symptomatic remission (sCDAI < 150) in absence of initiation or increase of any CD medications

## Key Secondary Outcomes at 6 and 12 Weeks

- Clinical remission (CDAI < 150)
- Fecal calprotectin – reduction to <250 µg/g and >50% reduction from screening among those with screening FC >250 µg/g
- hsCRP – reduction to <5 mg/L and >50% reduction from screening among those with screening hsCRP >5 mg/L



# Randomization



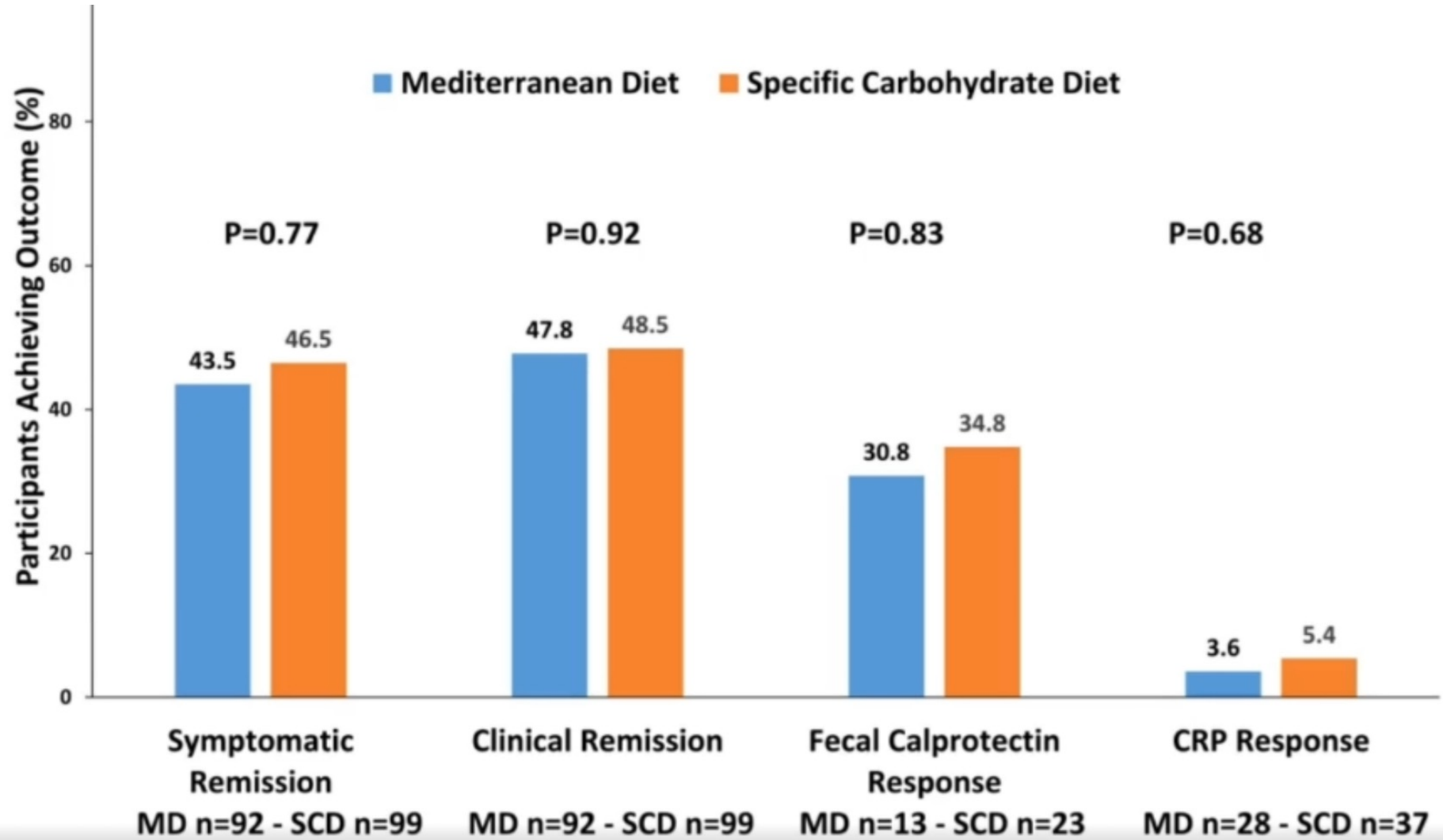
# Baseline Characteristics

Characteristic	Mediterranean Diet (N = 92)	Specific Carbohydrate Diet (N = 99)
Biologic therapy	55 (59.8)	53 (53.5)
Infliximab	10 (10.9)	12 (12.1)
Adalimumab	9 (9.8)	10 (10.1)
Certolizumab	3 (3.3)	2 (2.0)
Vedolizumab	11 (12.0)	7 (7.1)
Ustekinumab	22 (23.9)	22 (22.2)
Immunomodulators	11 (12.0)	11 (11.1)
Oral 5-ASA	6 (6.5)	15 (15.2)
Rectal 5-ASA	0 (0.0)	3 (3.0)
Oral corticosteroids	3 (3.3)	11 (11.1)
Rectal corticosteroids	1 (1.1)	2 (2.0)

# Baseline Characteristics

Characteristic	Mediterranean Diet (N = 92)	Specific Carbohydrate Diet (N = 99)
Evidence of ongoing inflammation	38 (41.8)	50 (52.1)
hsCRP > 5 mg/L	28 (30.4)	37 (37.4)
FC > 250 µg/g	13 (14.6)	23 (24.0)
Inflammation on colonoscopy		
Not performed	80 (87.0)	89 (89.9)
Yes	8 (8.7)	8 (8.1)
Probably	1 (1.1)	0 (0.0)
Probably not	1 (1.1)	1 (1.0)

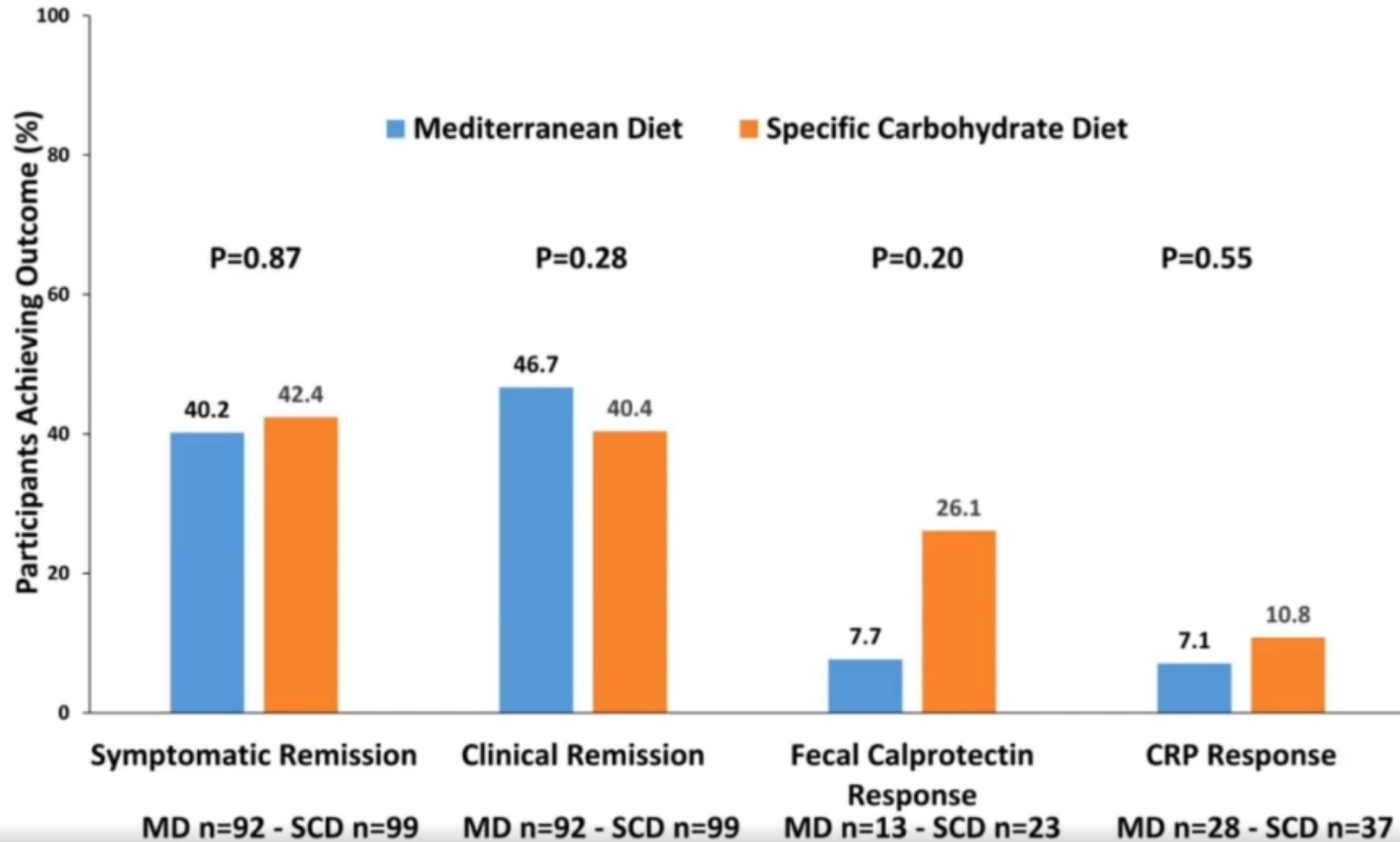
## Week 6 Outcomes



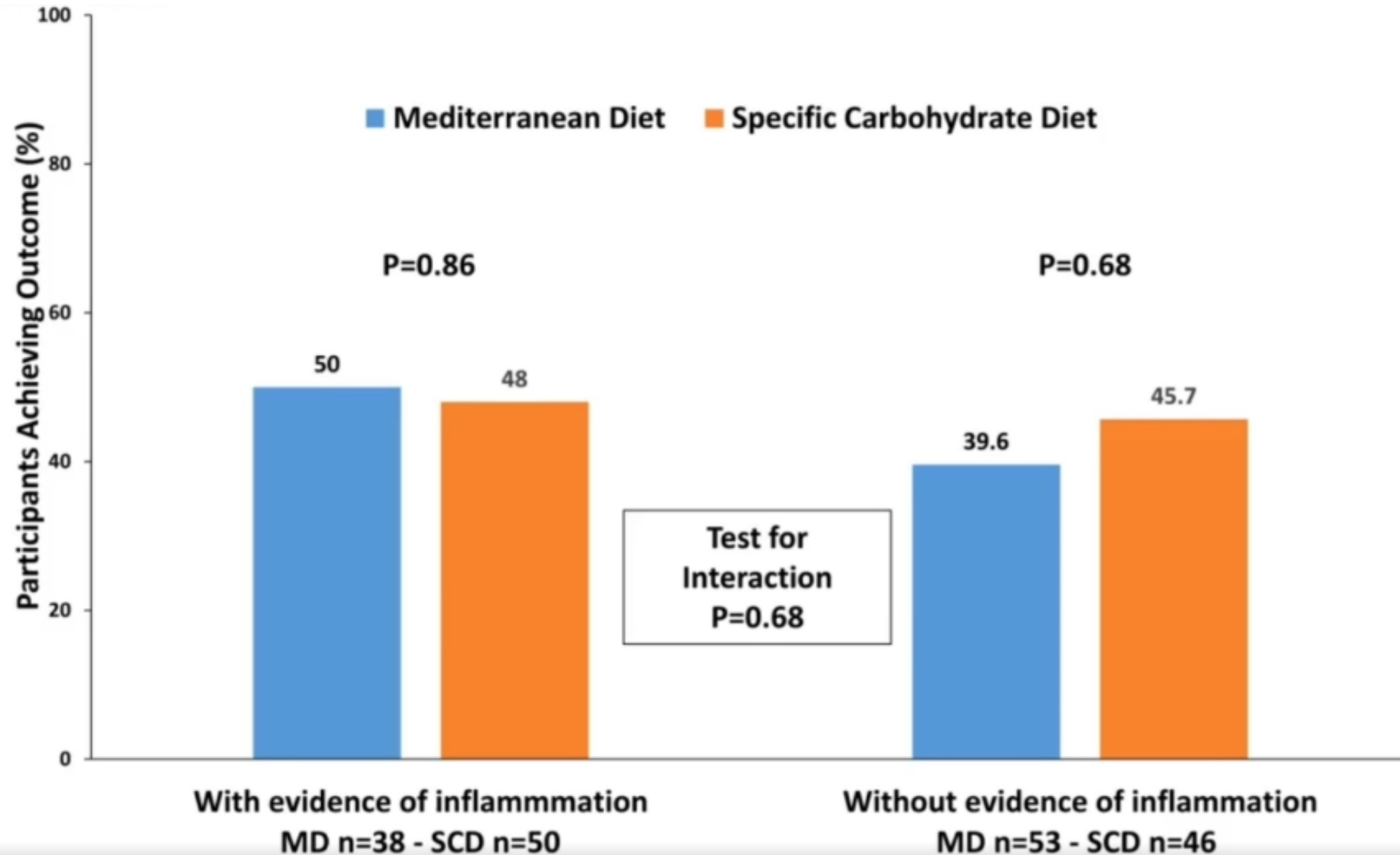
Outcome	MD		SCD		Change in MD vs. Change in SCD
	(change to week 6)	P value	(change to week 6)	P value	P value
sCDAI	-59.33 (64.53)	<.0001	-71.78 (75.94)	<.0001	0.23
CDAI	-55.54 (72.45)	<.0001	-67.47 (78.11)	<.0001	0.28
Short IBDQ	8.21 (10.66)	<.0001	8.85 (10.04)	<.0001	0.56
Fatigue	-5.24 (8.35)	<.0001	-5.37 (7.10)	<.0001	0.91
Pain interference	-5.10 (8.48)	<.0001	-5.73 (8.19)	<.0001	0.60
Sleep disturbance	-3.82 (7.87)	<.0001	-3.28 (7.76)	<.0001	0.63
Social isolation	-3.02 (7.56)	0.0002	-1.75 (7.21)	0.02	0.24



## Week 12 Outcomes



### Week 6 Remission Rates Stratified by Inflammation at Screening



# Limitations

- Both diets were “healthier” than the participant’s usual diet
- Generalizability
  - Provision of food
  - Mostly white females
- No endoscopic assessment of healing
- Primary outcome at 6 weeks
  - Based on patient recommendations
  - Similar results at 12 weeks

# Conclusions

- SCD was not superior to MD for achieving symptomatic remission
- Symptomatic remission was common with both diets
- Both diets were well tolerated despite increased consumption of fruits and vegetables
- Similar results with and without confirmed inflammation prior to randomization
- Normalization of CRP concentration was uncommon with both diets

## Clinical Practice Pearls

- Mediterranean diet and SCD can benefit symptoms and inflammation
- Their role may be more adjunctive than primary

# Presentation Summary

- Impact of perioperative nutrition support
- Effects of corticosteroids use in pregnancy
- Prognostic value of calprotectin
- DINE-CD: Mediterranean diet vs. SCD



A scenic coastal view featuring a rocky shoreline, palm trees on a hill, and a body of water under a clear sky. The image is overlaid with a semi-transparent green filter. The text "Thank You" is centered in white.

Thank You