

Brain-Gut Care in IBD: an Integrative Approach

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Canada Future Directions in IBD



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Disclosures

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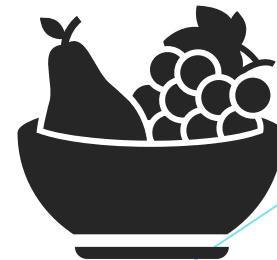
- ▶ Speaker - Abbvie, Janssen, Takeda, NovoNordisk,
- ▶ Grant - Takeda, Janssen, Amgen, Bausch, Pfizer
- ▶ LyfeMD shareholder

Dr. Lesley Graff

- ▶ Consultant -Roche Canada
- ▶ Investigator initiated grant funding Takeda Canada, Pfizer Canada

Objectives

- a) Examine psychological, physical and dietary interventions as adjunct therapies for IBD management
- b) Discuss how to select and engage patients in these approaches, including CBT, mindfulness, yoga, exercise and diet, to appropriately enhance outcomes



Treatment Goals in IBD

IBD Clinic Goals

- ▶ improving symptoms
- ▶ reducing inflammation
- ▶ promoting mucosal healing for lasting disease remission

Patient Goals

- ▶ **improving quality of life**
- ▶ improving symptoms/ensuring pain control
- ▶ normal endoscopy
- ▶ information needs when active disease: stress/coping and work disability

Self Management /Active Patient Engagement

- ▶ Effective disease self-management (incl medication adherence, self-care) improves disease outcomes¹
 - ▶ fewer symptoms, fewer hospitalizations, decreased need for medical treatment escalation
- ▶ Self-efficacy relates to resilience; predicts self management better than education/disease literacy²
- ▶ **Healthy lifestyle and IBD study**
 - ▶ 3 large cohorts (n~300,000); healthy lifestyle = adherence to 3 -5 of moderate physical activity, Mediterranean diet, BMI 18-24.9, no smoking, modest alcohol
 - ▶ **Significant reduction in all cause mortality for adults with IBD (CD or UC)³**
hazard ratio [HR], 0.29; 95% CI, 0.16-0.52; ptrend<.0001)

¹Saibil et al 2008; ²Plevinsky et al 2016; ³Lo et al 2021

Patient

- ▶ 32 y.o. male with moderately active ileo-colonic CD
 - ▶ presents with **6 weeks of increasing RLQ pain, bloating, frequent BMs (5-6 loose, daily) and urgency**
- ▶ Diagnosed 2013
 - ▶ Treated with prednisone and 5-ASA (Severe insomnia)
 - ▶ Induced and maintained with **Adalimumab (since 2014); dose escalation 2018**
 - ▶ Ileo-Colonic Resection 2019 (stricture); Entyvio induction and maintenance
- ▶ Mild unintentional weight loss, 3-5 pounds over past 6 weeks, current weight 72 kg, BMI 26.5 kg/m²
- ▶ **Harvey Bradshaw Index - 9; CRP - 10; FCP - 300 ug/g**
- ▶ Recent colonoscopy (2-weeks ago)
 - ▶ Ascending colon numerous aphthous ulceration with **2 medium sized ulcers** in the cecum, mild erythema
 - ▶ **2 Moderate ulcers in the TI + mild erythema**
 - ▶ No strictures

Patient (continued)

- ▶ Struggled with **insomnia** and **fatigue** for several years (worst when previously taking prednisone)
- ▶ Reports new symptoms of **decreased mood, energy, and increased anxiety**
- ▶ Missing days from work (stress, mood)
- ▶ Social History:
 - ▶ Married with 2-year old child
 - ▶ Working full time; wife has full time job
 - ▶ Expecting second child shortly
 - ▶ Lives in Fort McMurray, AB
- ▶ Diet History:
 - ▶ Frequent meals outside the home (fast food)
 - ▶ Mild weight loss (not overtly malnourished)
 - ▶ No dietary restrictions / interventions

Questions

- ▶ What outcomes are important to your IBD patient? What is he/she able and willing to do ?
- ▶ In addition to standard medical management (biologic switch), is there a role for behavioral interventions?
 - ▶ Is this patient a candidate for psychological intervention?
 - ▶ Is this patient an appropriate candidate for dietary intervention/ how would you select/know?
- ▶ What behavioral approaches can be introduced in the clinic setting?
- ▶ What tools can assist your patient with self management, self efficacy?

Optimizing Patient Outcomes: PSYCHOLOGICAL INTERVENTIONS



When do you think about Psychological Therapies in IBD?

- A) When my IBD patient has IBS overlap
- B) When my patient reports distress
- C) When screening for depression or anxiety is positive
- D) When the clinic nurse identifies coping as a concern
- E) When my patient identifies fatigue, sleep or chronic pain issues

COGNITIVE BEHAVIORAL THERAPY and IBD



- 70% with IBD report stress as influencing disease course¹
- 85% with IBD report effective stress coping has positive impact on disease symptoms¹
- MH comorbidities in IBD= greater disease activity/worse complications²
- CBT in IBD; multiple RCTs and systematic reviews
 - strong evidence for improved psychological outcomes and QoL in IBD³
 - direct disease impact? reduces inflammatory markers^{4,5}
- CBT - changes thinking and behavior to enhance adaptive response, increase psychological flexibility, strengthen resilience, calm ANS
- Common ‘active ingredients’ in CBT for IBD⁶:
 - self monitoring, shifting perspective, flexible problem solving, paced exposure to anxiety triggers, relaxation training

COGNITIVE BEHAVIORAL THERAPY and IBD



Examples:

Cognitive flexibility/perspective shifting

Recognize and challenge “what If” thinking

Under stress, we often overestimate how bad situation could be; underestimate how well we will be able to cope

Focus on what can be controlled

What can you do vs what you can't do

Coach patient on self-compassion

With disease flare, may need to relax standards at home, may not be as efficient at work; ok to adjust



Behavioral

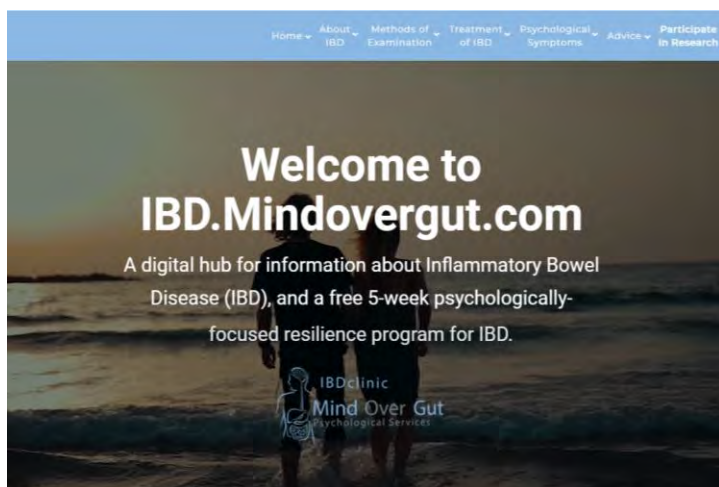
- self monitoring - symptoms, activities
- Challenge avoidance - what not doing b/c IBD; reclaim
- Pacing activities



Patient Tools

CBT-based self-management programs

▶ IBD specific:



▶ IBD Stress Kit developed with patients; significant improvements in pilot; RCT underway



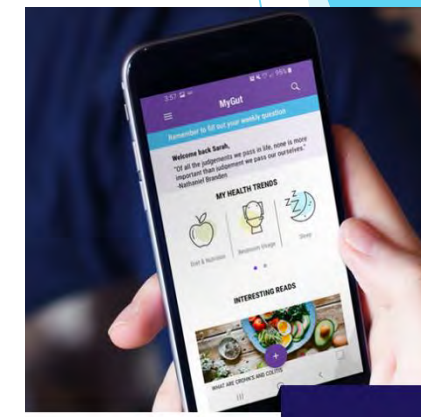
▶ General

Mindshift CBT (Anxiety Canada)

IBD Apps - self monitoring/learning (free)

▶ MyGut

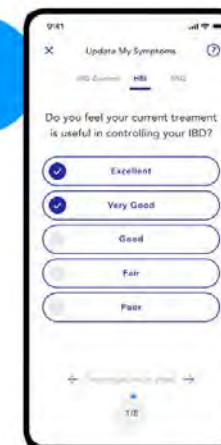
Crohns Colitis Canada
McMaster U



▶ MyIBDCare

Crohns Colitis UK
NHS approved

Track signs of a flare and intervene before relapse



Build positive habits through expert-led courses



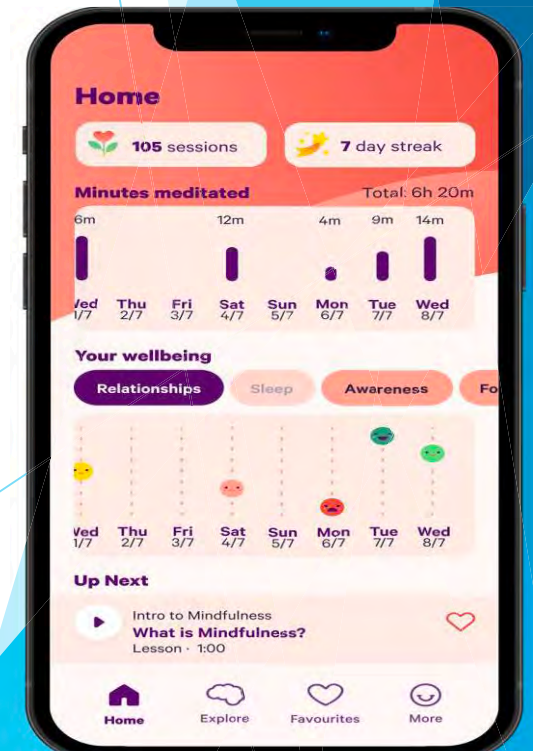
MINDFULNESS and IBD



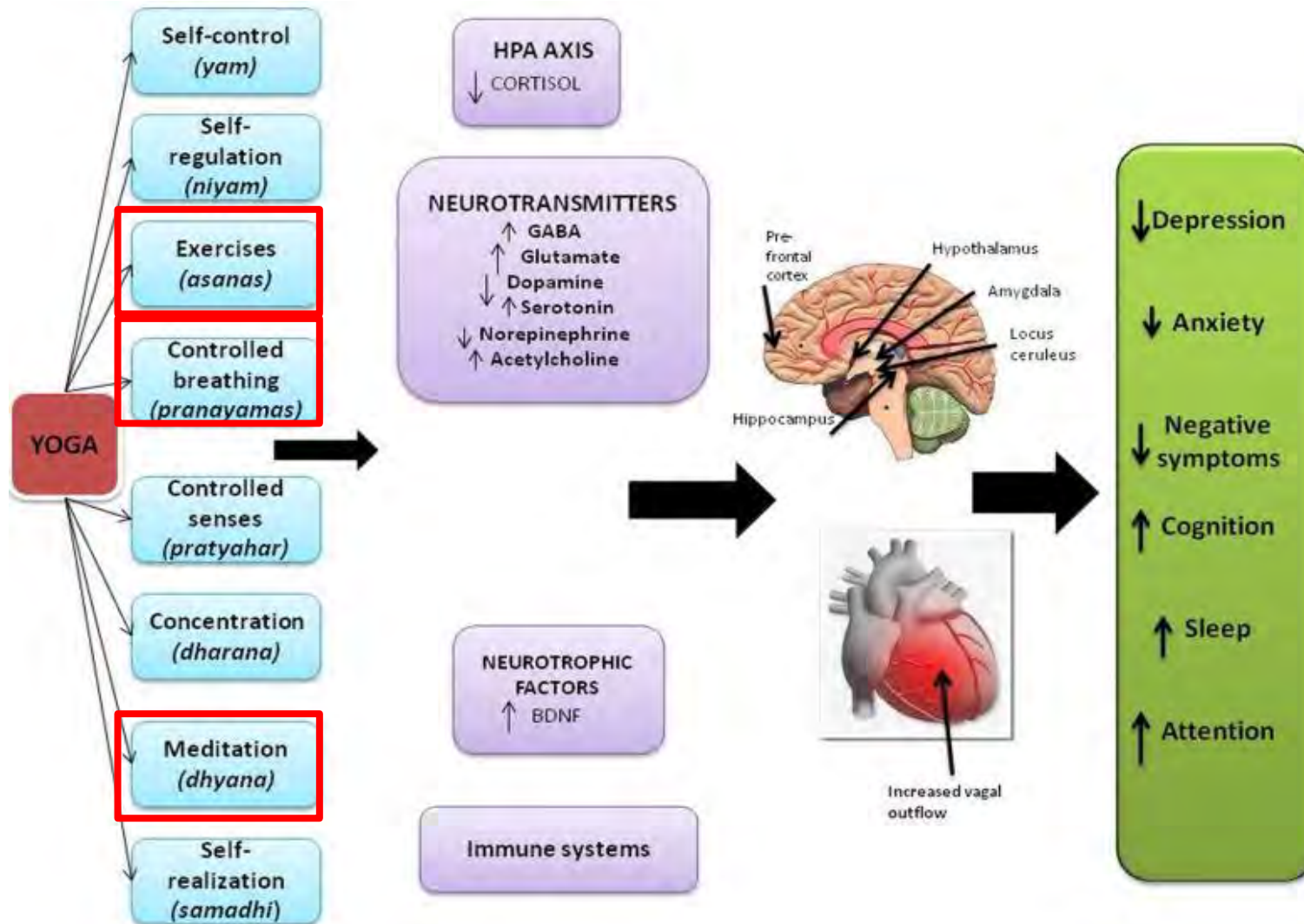
- train mind to focus in present in non-reactionary way
- use meditation, relaxation, and awareness exercises
- Mindfulness therapy in IBD
 - significant improvement in psychological outcomes and QoL¹
 - mechanism may be through ANS and/or immune system
 - direct disease impact? improved inflammatory biomarkers 6 m post trtmt²

- Patient tools : meditation (free) apps
 - UCLA Mindful (UCLA Health)
 - Smiling Mind (Australia - children/adults)

¹Ewais et al 2019; ²Gonzalez-Moret et al 2020



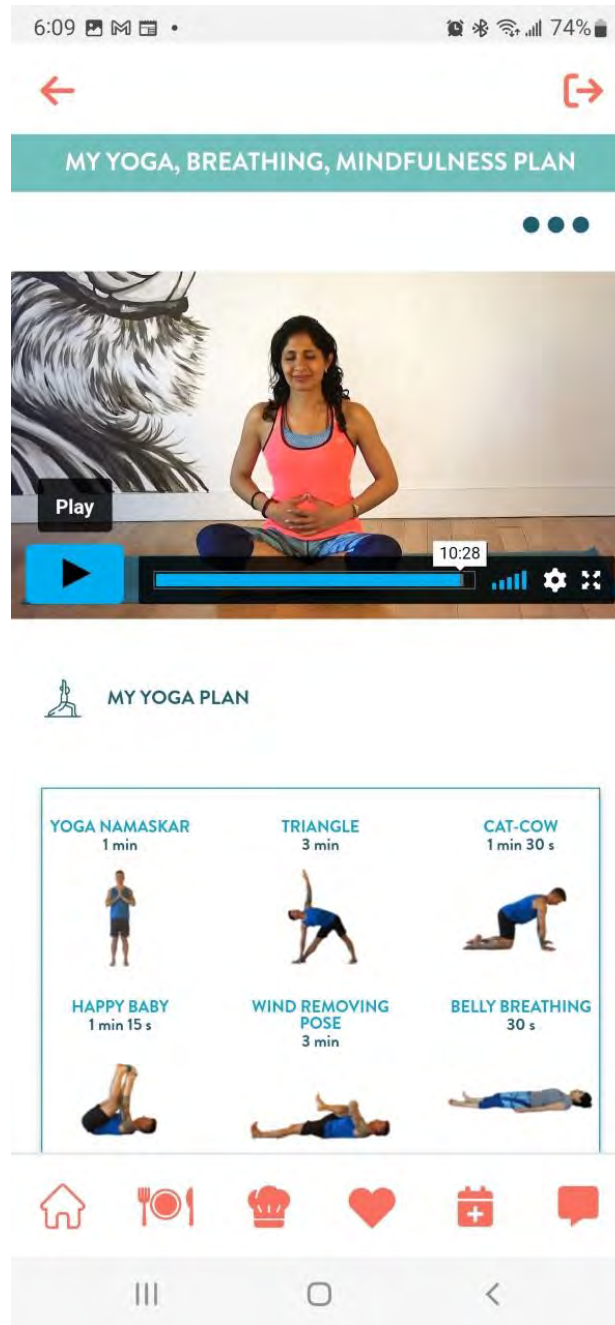
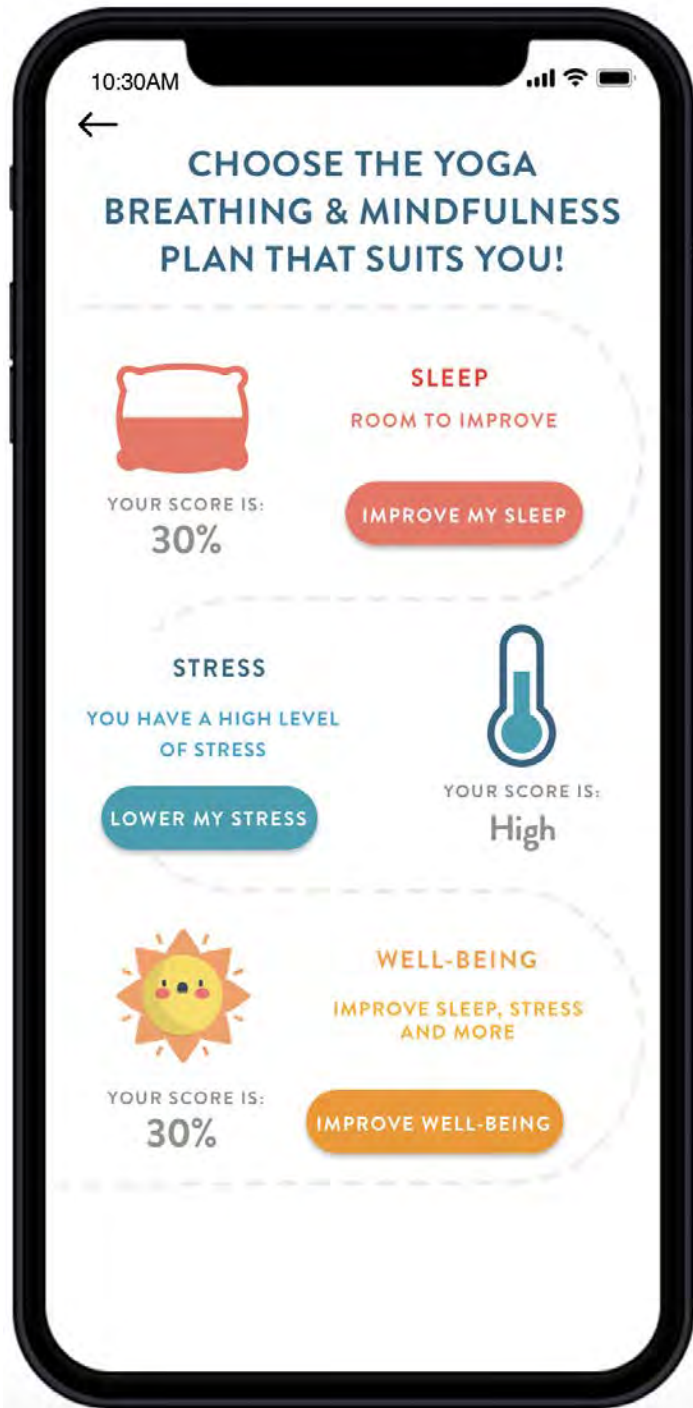
Yoga Breathing Mindfulness Interventions



Results (IBS)

	Treatment (n=38)				Control (n=41)				Difference in difference	Difference in difference
	Baseline	Week 8	Δ_{change}	<i>p</i> -value ^a	Baseline	Week 8	Δ_{change}	<i>p</i> -value ^b	Δ_{change}	<i>p</i> -value ^c
IBS Symptoms	255.2 (90.7)	200.5 (103.9)	-54.7	0.028*	236.1 (82.6)	213.5 (98.5)	-22.6	0.277	-32.1	0.149
Quality of Life	87.6 (21.9)	75.9 (22.1)	-11.6	0.047*	83.6 (26.9)	78.3 (28.0)	-5.3	0.399	-6.3	0.030*
Depression	7.5 (3.6)	7.0 (4.0)	-0.5	0.069	6.9 (3.8)	7.1 (4.6)	0.2	0.828	-0.7	0.056
Anxiety	5.9 (3.5)	5.9 (3.7)	0.06	0.199	5.6 (4.6)	6.1 (5.6)	0.5	0.703	-0.4	0.112
Fatigue	38.1 (11.4)	30.7 (18.0)	-7.3	0.045*	36.2 (17.4)	32.9 (19.6)	-3.3	0.433	-4.0	0.035*
Somatic symptoms	12.8 (3.1)	10.9 (3.6)	-1.9	0.116	12.8 (3.7)	11.9 (4.1)	-0.9	0.292	-1.0	0.077
Stress	6.6 (2.3)	4.3 (3.6)	-2.3	0.074	6.7 (2.6)	6.2 (3.4)	-0.5	0.472	-1.8	0.040*
COVID-19 stress	20.2 (17.1)	11.7 (10.9)	-8.4	0.005**	22.2 (12.9)	16.1 (12.6)	-6.2	0.037*	0.3	0.142
Self-compassion	17.18 (5.66)	18.89 (4.89)	1.7	0.297	17.68 (5.4)	19.14 (6.06)	1.5	0.270	-2.3	0.219

Note: All baseline and week 8 are presented as means (standard deviation). **p*<0.05; ***p*<0.01. ^a This *p*-value tests the change from baseline to week 8 in the treatment group. ^b This *p*-value tests the change from baseline to week 8 in the control group. ^c This *p*-value tests the difference between groups.



www.lyfemd.com

- Developed at the University of Calgary
- No cost for any patient with IBD in Canada
- 1200 people using the app





When/how introduce mind body approach¹

- impaired QoL?
- elevated distress including clinically significant depression, anxiety or high stress?
- Poor sleep quality or fatigue?
- Review rationale/benefit and explore
 - What is the patient interested in/what resonates?
 - Willing to implement behavioral changes and commit to practice?
- EXAMPLE - YOGA
 - Is yoga accessible - time, location, and cost?
 - DOSING: 5 days weekly for 6 weeks -(postures, breathing exercises, meditation); frequent multimodal practice associated with the greatest benefit

Optimizing Patient Outcomes: PHYSICAL INTERVENTIONS



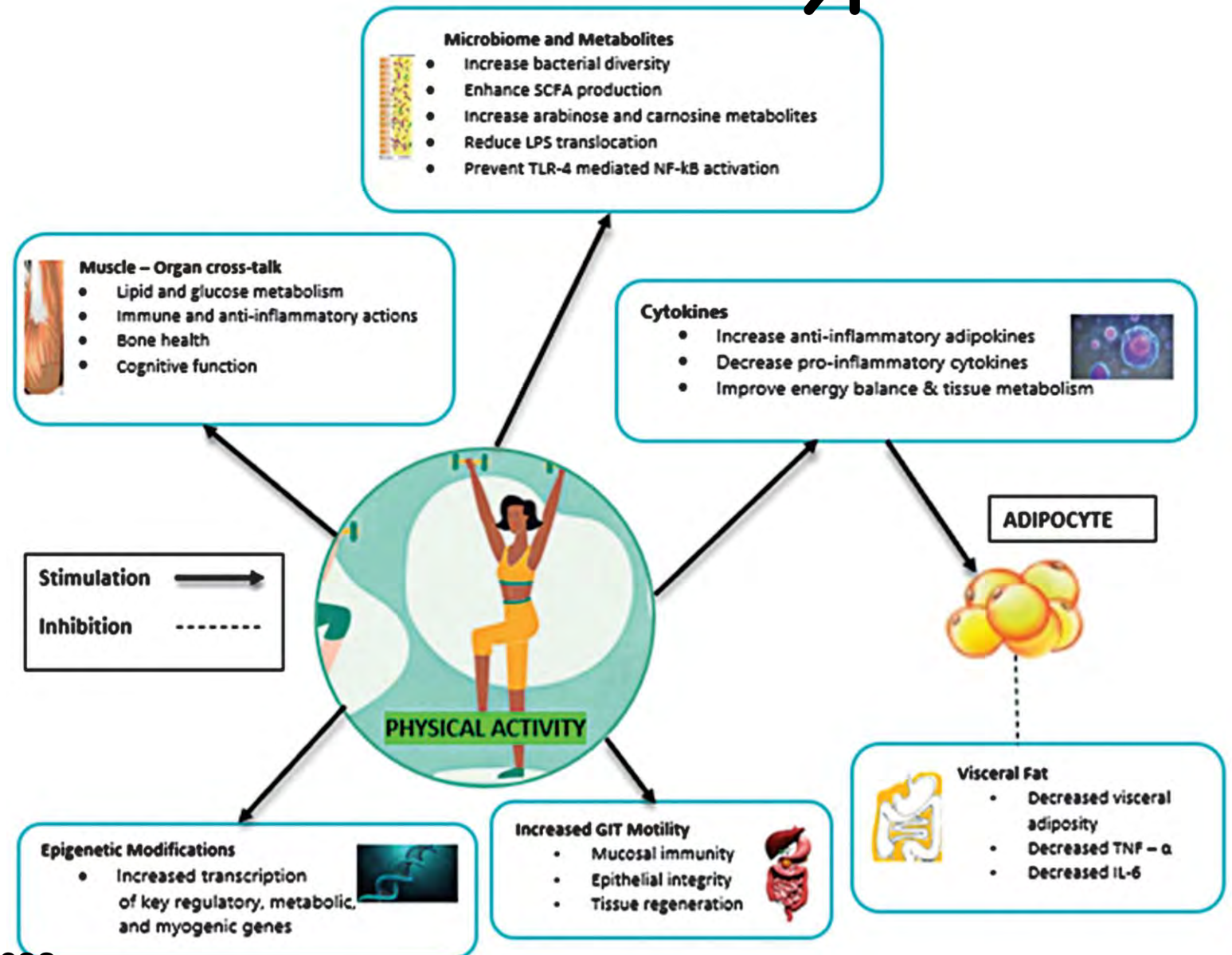
When do you raise physical activity with your IBD patient?

- A. Never
- B. Depends on BMI /weight changes
- C. When the patient asks
- D. When the IBD is in remission

PHYSICAL ACTIVITY and IBD



- Moderate physical activity improved QOL, sleep quality, GI symptoms, fatigue in IBD¹
- Contributes to maintenance of clinical remission, improved mental health in IBD²
- IBD obstacles: joint pain, fatigue, bowel urgency, comorbid depression¹



¹Davis & Crane 2022; ²Raman et al 2022

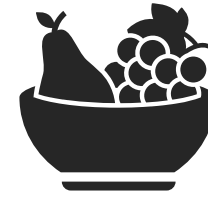
PHYSICAL ACTIVITY and IBD



- Regular moderate intensity exercise seen to yield best benefit
 - walking, running most common activities studied¹
- Mechanisms may be through gut microbiome, anti-inflammatory effects, reduction in visceral fat mass²
 - Improved mucosal healing in animal colitis³
- High intensity, strenuous exercise can *exacerbate a pro-inflammatory response*³
- Study limitations: mostly remission/mild IBD; short study duration
- No evidence-based guidelines yet for PA and IBD patients⁴
 - Review with patient what feasible for regular engagement; moderate intensity

¹Davis & Crane 2022; ²Raman et al 2022; ³Bilsky et al 2016; ⁴Torres et al ECC guidelines

Optimizing Patient Outcomes: DIET INTERVENTIONS



When do you think about dietary interventions in IBD treatment?

- A) Malnutrition management
- B) Induction of Remission
- C) Maintenance of Remission
- D) Micronutrient Deficiencies
- E) Symptom Management
- F) Only when my patient asks about it

How do you implement dietary interventions in your clinic?

- A. Refer to the Registered Dietitian
- B. I refer to websites (no access to an IBD RD)
- C. I provide printed clinic materials (no access to an IBD RD)
- D. I discuss diet and nutrition in the clinic

Could adjuvant nutrition therapy be helpful in this patient's care?

- A. Yes, with partial enteral nutrition using ONS
- B. Yes, with Mediterranean diet to manage symptoms and inflammation
- C. Yes, with EEN
- D. Yes, with low FODMAP diet
- E. No, the data are not robust enough
- F. I don't know

Therapeutic Diets

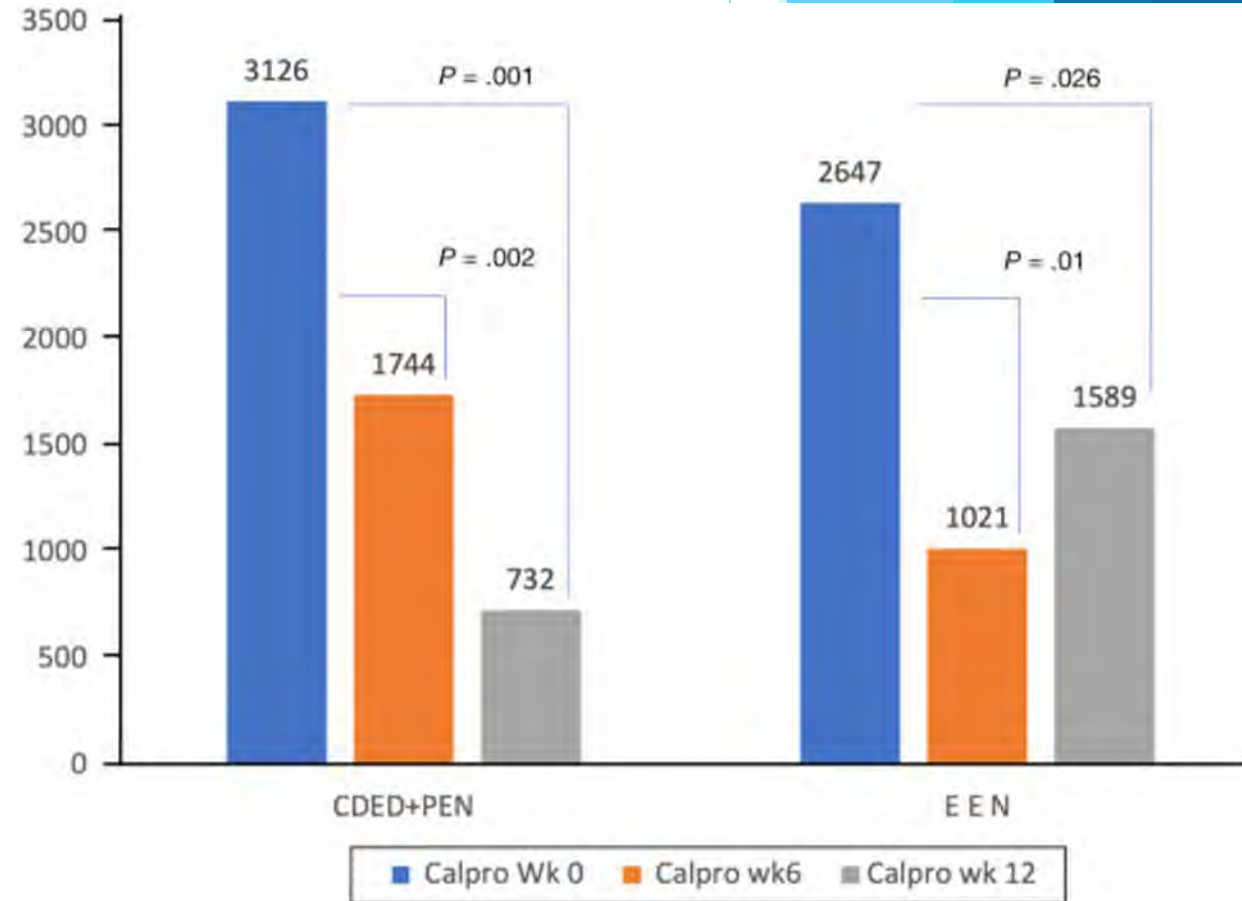
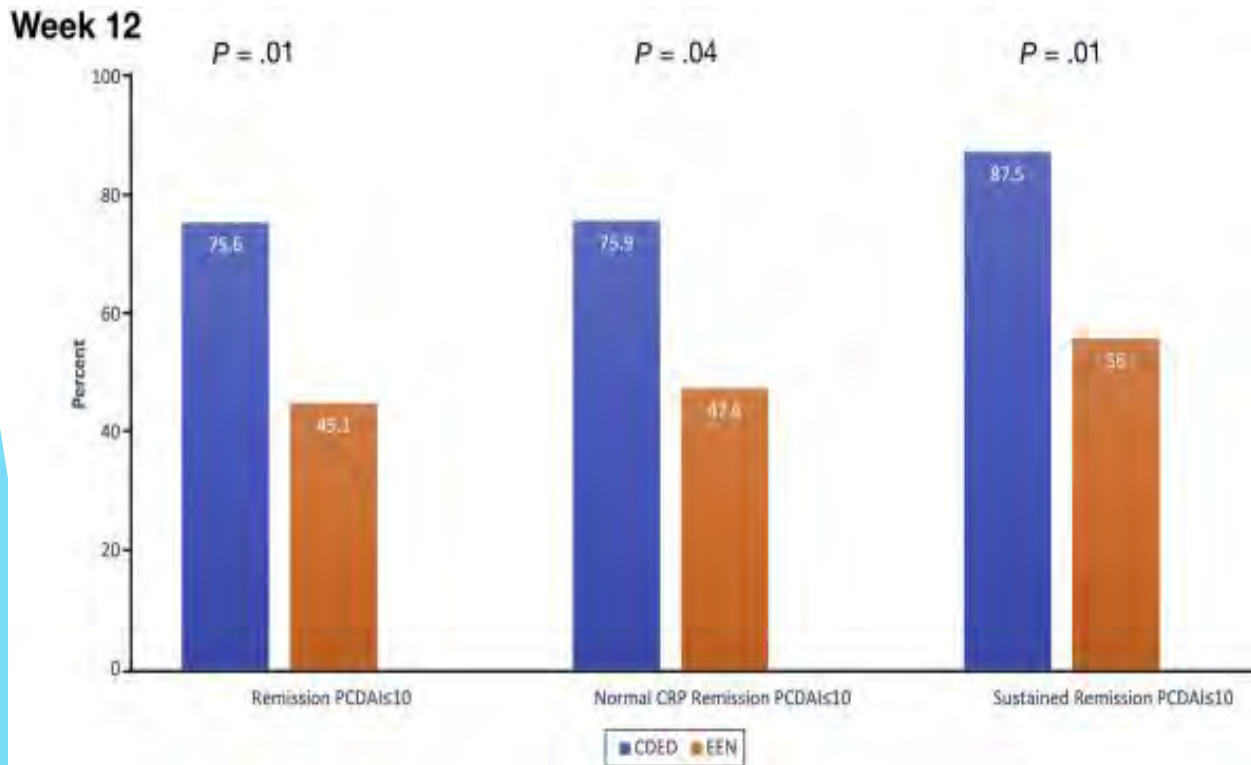
- Specific Carbohydrate Diet
- Modified Specific Carbohydrate diet
- IBD AID
- Autoimmune Protocol diet
- CDED Induction
- CDED Maintenance
- Mediterranean Diet
- IBD Food Pyramid

Evidence-Based Nutritional Therapy

An Option For Every Patient



Crohn's Disease Exclusion Diet



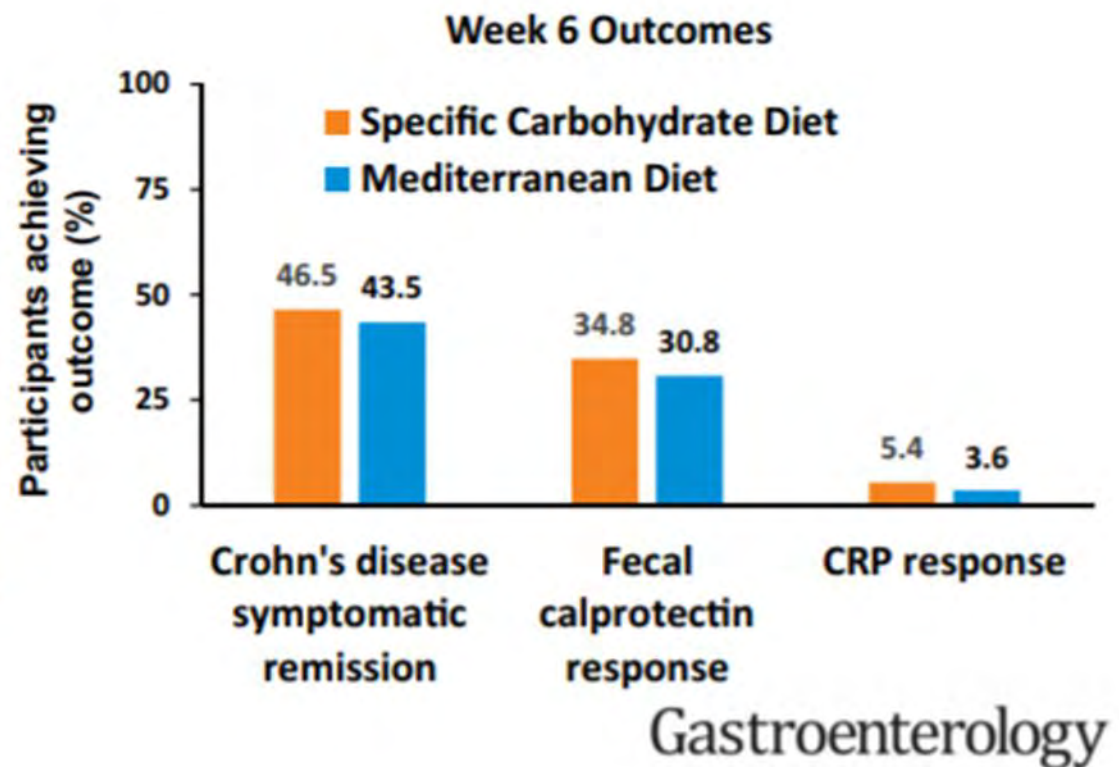
DINE-CD study: SCD vs Mediterranean Diet for mild-moderate CD



Specific Carbohydrate Diet



Mediterranean Diet



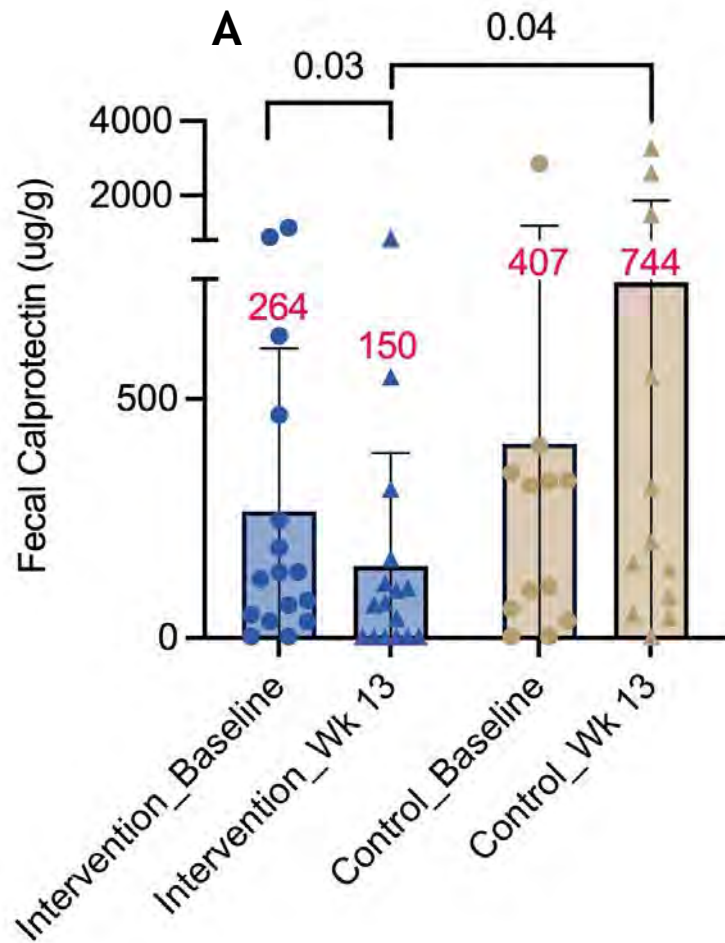
Crohn's Disease Therapeutic Diet Intervention (CD-TDI)



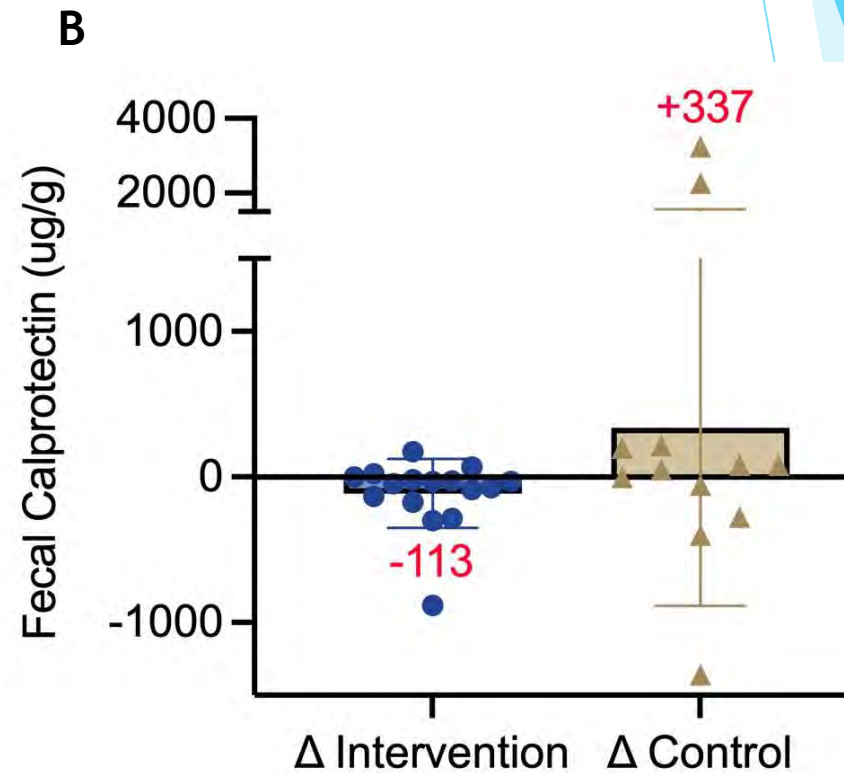
“a state of the art diet that incorporates evidenced-based dietary principles for management of IBD”

Figure 4. Recommended Food Pyramid for the IBD patient. Diagram suggesting the optimal intake and amount of dietary food groups for individuals with IBD based on combined results of recent dietary intervention trials.

TDI significantly decreases
mucosal inflammatory marker
FCP

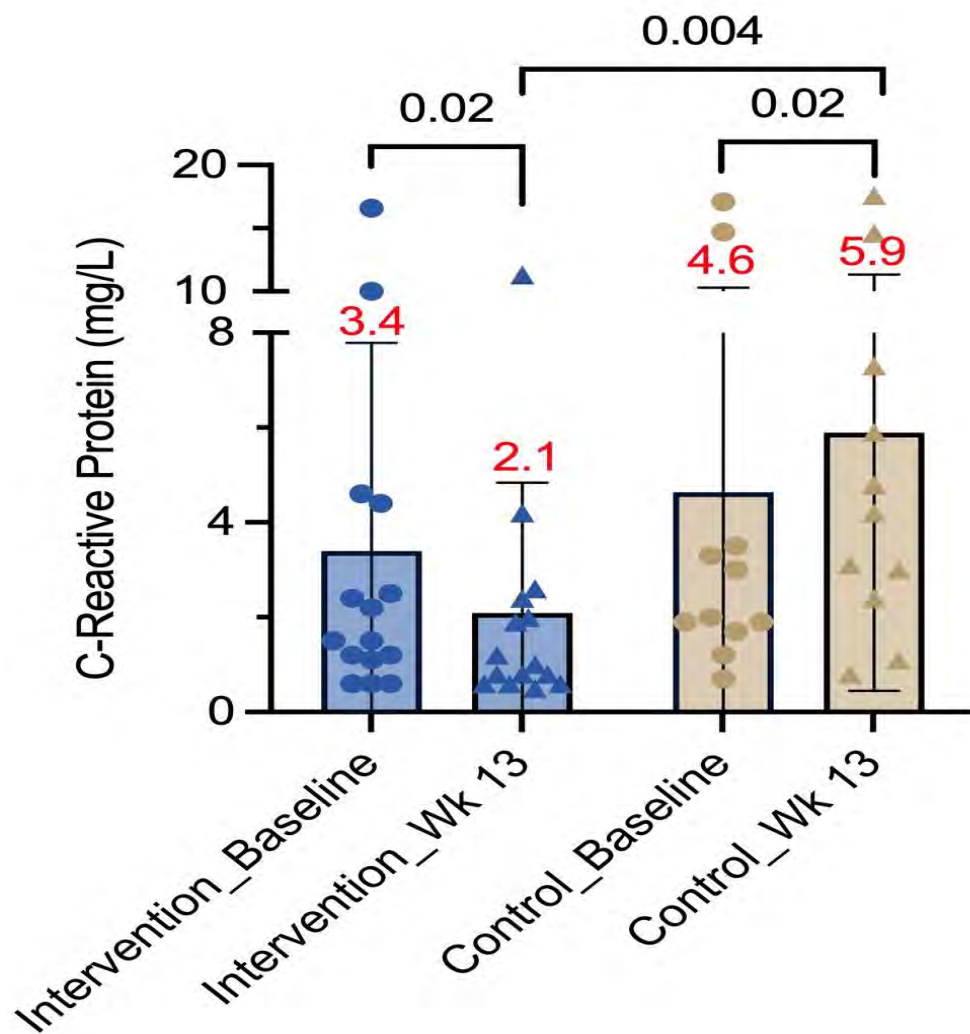


Magnitude of change in FCP
over 13 weeks



TDI significantly decreases CRP

A



Practical Implementation of Diet Intervention

Malnutrition - YES/NO
ARFID – Yes/NO

Define Disease Activity
YES

Clinical Symptoms
YES/NO

Patient Ready?
Current Medical Therapies?
Failed Therapies?
Diet Quality (MDS/HEI)
Support Available (RD, Coach)

Oral Therapeutic Diet
EEN

Monitoring (HBI, CRP, FCP,
Cross-Sectional Imaging, Endoscopy)

Define Disease Activity
NO

Clinical Symptoms
YES

IBS Overlap / Low FODMAPs
Mediterranean Diet

Define Disease Activity
NO

Clinical Symptoms
NO

Mediterranean Diet

Diet and Mental Health in UC

- **Cross-sectional sub-study of a RCT** designed to investigate the effects of a **dietary intervention on UC outcomes**
- Enrolled adults with UC, active or remission
- Baseline UC disease activity
 - partial mayo score, serum C-Reactive Protein (**CRP**), stool-calprotectin (**FCP**).
- Baseline mental health
 - Depression - Patient Health Questionnaire-8 (**PHQ-8**)
 - Anxiety -General Anxiety Disorder-7 (**GAD-7**)
- Diet
 - Healthy eating index (**HEI**) and Mediterranean Diet Score (**MDS**) calculated from 24-hour dietary recall questionnaire at enrollment.

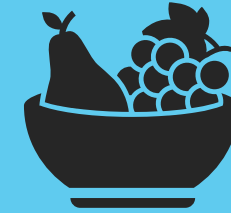
Diet and Mental Health in UC

- Participants
 - n=30; 53% males (16); mean age=38 years (SD 12.1)
 - BMI mean=26.2 kg/m² (SD 3.2)
- 43% (n=13) had active inflammation (fecal calprotectin > 250µg/g)
- Controlling for corticosteroid use, disease activity, BMI, age, sex:
 - **Severity of depression inversely correlated with diet (MDS)**
 $p = 0.03$, 95% CI: -0.26 to -0.01
 - **Severity of anxiety inversely correlated with diet (MDS)**
 $p = 0.02$, 95% CI: -0.34 to -0.03
 - No correlation between severity of depression or anxiety with HEI.

Back to the patient:

What would you recommend to this 32 yr old man with moderate ileo-colonic CD?

KEY TAKE AWAYS



- ▶ Mind-body approaches for IBD (CBT, mindfulness, exercise, therapeutic diets) have positive outcomes for aspects important to patients:
 - ▶ quality of life
 - ▶ extraintestinal manifestations such as anxiety, depression, stress
 - ▶ potential impact on disease directly over time
- ▶ Data limited for yoga/physical activity but evolving
- ▶ Introduce rationale and strategies in office, tailored to patient readiness and interests
- ▶ Direct to patient tools to support self-management
- ▶ Refer to professional: moderate-severe distress, mod-severe disease