

Can We Start Using Diet to Treat IBD?

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Chair, IOIBD

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Pharma Disclosures 2022

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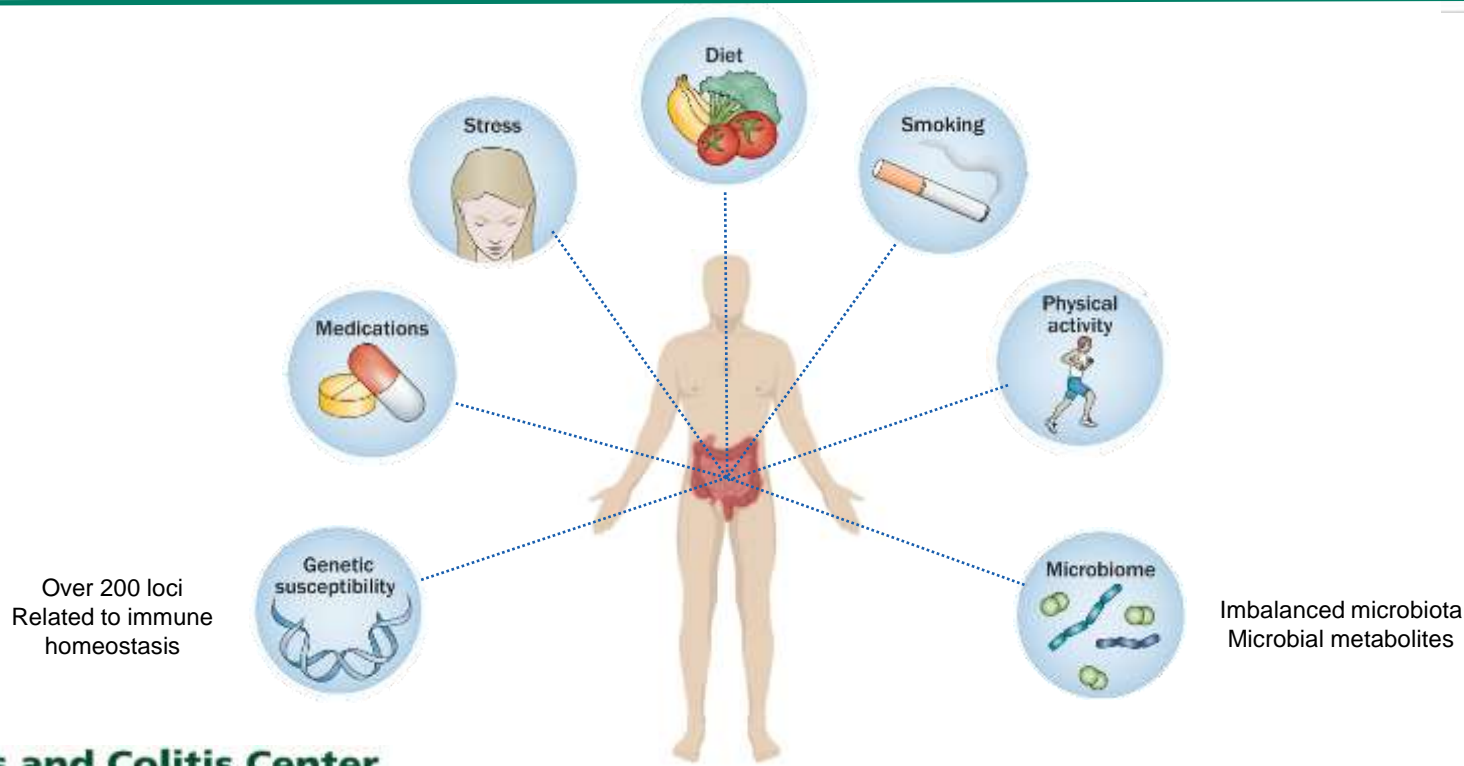
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IBD is multifactorial: host, microbial, environmental



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Ananthakrishnan, A. N. *et al*, *Nat. Rev. Gastroenterol. Hepatol.*, 2015

What is there to discuss about diet?

- Does diet cause IBD?
- Can diet worsen the symptoms of IBD?
- Can diet be used to “treat” IBD?
 - Is that mucosal healing?
 - Is it symptomatic improvement?
- Can diet be used to prevent IBD?

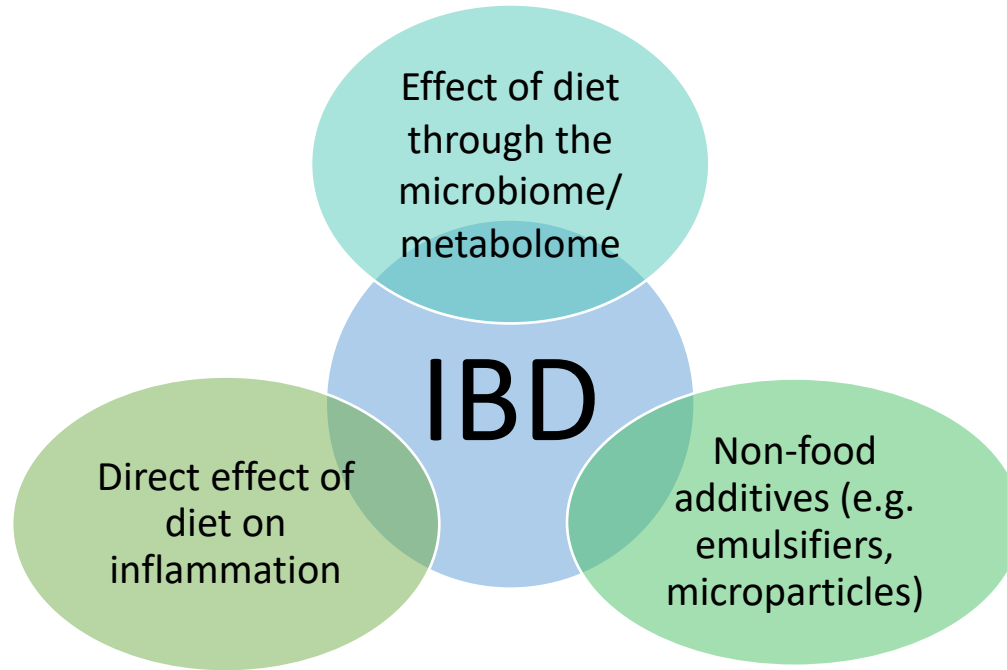
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Model of how diet can impact IBD



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Why suspect diet as a trigger of IBD?

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Epidemiologic evidence supports diet playing a role in IBD risk

- Prospective cohorts have demonstrated an association between various dietary components and risk of CD or UC

	Crohn's Disease	Ulcerative Colitis
Increases Risk	Low Vitamin D Increased animal protein Inflammatory Diet Ultra-Processed Foods	Trans-saturated fats Increased animal protein High sugary and soft drinks
Decreases Risk	Potassium Zinc High Fiber (fruits ,vegetables) Fish Mediterranean Diet	n3 PUFA(long Chain)

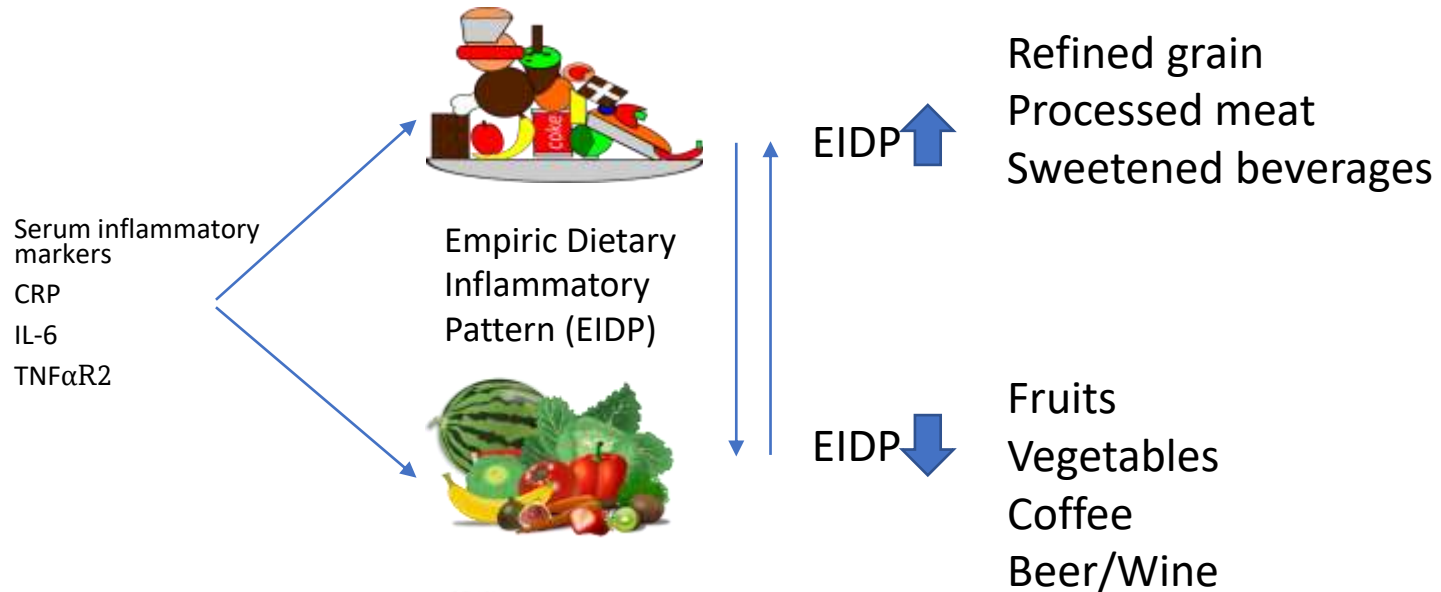
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Hou JK et al. Am J Gastroenterol. 2011;106(4):563-573
Chassaing B et al. Nature. 2015;519(7541):92-96

Dietary Patterns – Inflammatory Diet



- CD: $HR_{Q4 \text{ vs } Q1} = 1.51$, 95% CI 1.10-2.07, $P_{\text{trend}} = 0.01$
- Shift from a low to high inflammatory potential of diet increased risk of CD: HR 2.05; 95% CI 1.10-3.79

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Lo CH, Lochhead P, Khalili H, et al. Dietary Inflammatory Potential and Risk of Crohn's Disease and Ulcerative Colitis. *Gastroenterology*. 2020;159(3):873-883.e1. doi:10.1053/j.gastro.2020.05.011

Dietary Patterns – Mediterranean Diet

- Swedish cohorts:

- Adherence to Mediterranean style diet assessed at baseline in 1997 (mMED questionnaire)
- Through 2017, 164 new CD and 395 new UC cases

mMED score	0-2	3-4	5	6-8
CD	1	0.69 (0.48-0.99)	0.78 (0.49-1.24)	0.42 (0.22-0.80)
UC	1	1.35 (1.04-1.76)	1.37 (0.99-1.90)	1.08 (0.74-1.58)

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Khalili H, Håkansson N, Chan SS, et al. Adherence to a Mediterranean diet is associated with a lower risk of later-onset Crohn's disease: results from two large prospective cohort studies. Gut 2020;69:1637-1644

Role of Food Processing



Added Sugar, Salt , Fats, Preservatives and Emulsifiers
Loses Nutrient Content

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Ultra-processed foods

Ultra-processed foods

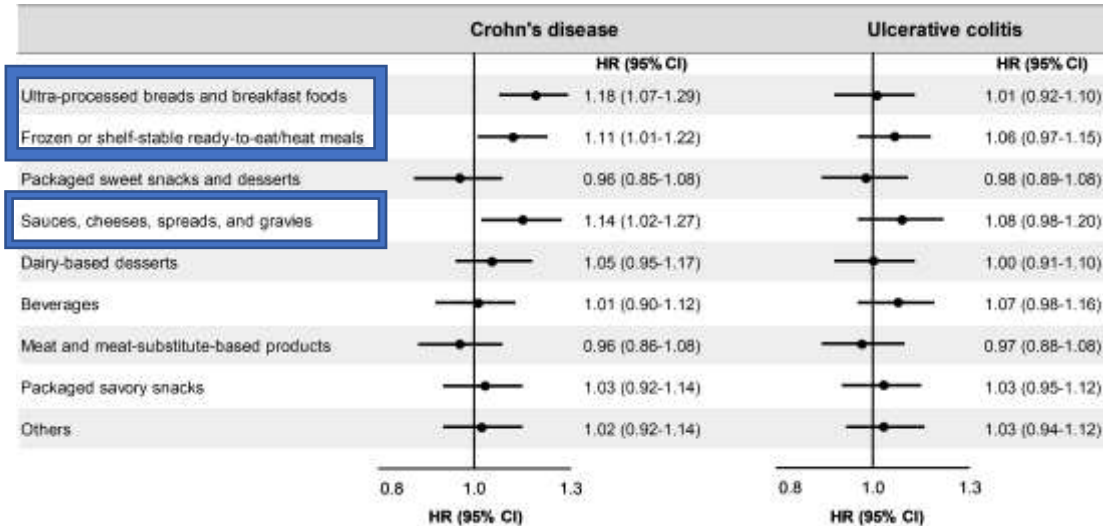


245, 112 participants

5,468,444 person-years of follow-up

Crohn's disease
(CD) (n=369)

Ulcerative colitis
(UC) (n=488)



Increased risk of CD: Q4 vs Q1: HR, 1.70, 95% CI, 1.23-2.35, $P_{\text{trend}} = 0.0008$

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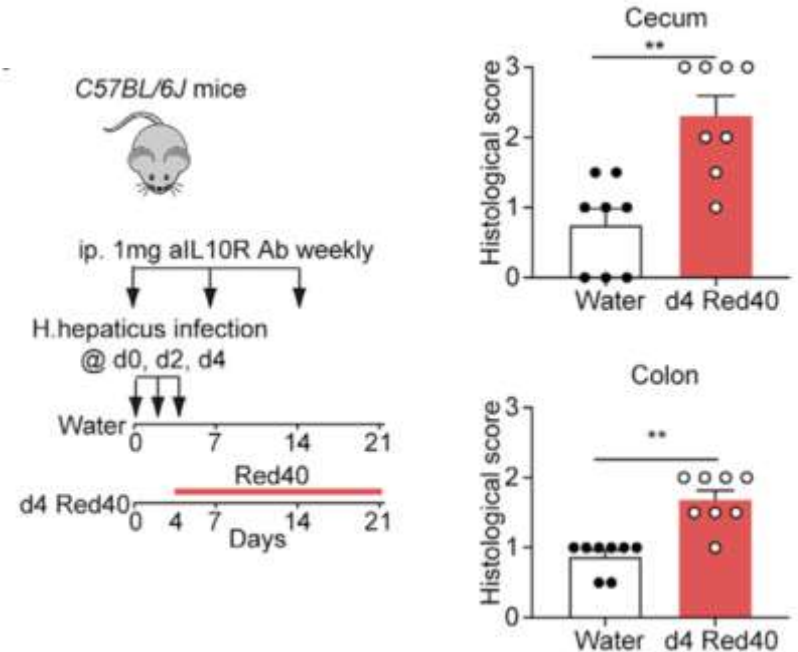
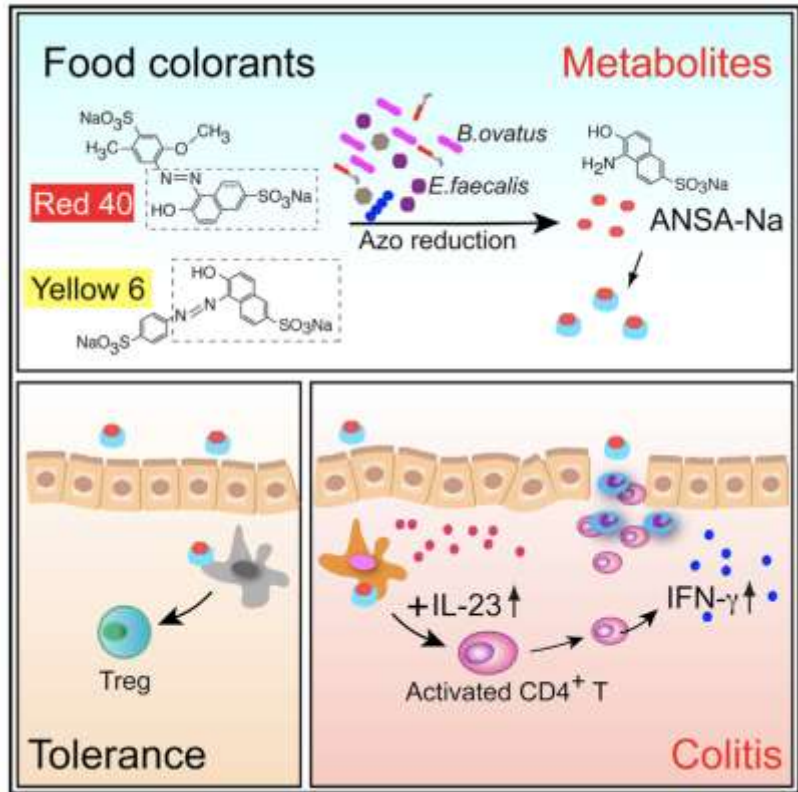
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Lo CH, et al. Ultra-processed Foods and Risk of Crohn's Disease and Ulcerative Colitis: A Prospective Cohort Study. Clin Gastroenterol Hepatol. 2021 Aug 28:S1542-3565(21)00911-3

Food colorants metabolized by commensal bacteria promote colitis in mice with dysregulated expression of interleukin-23



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Can diet worsen the symptoms of IBD?

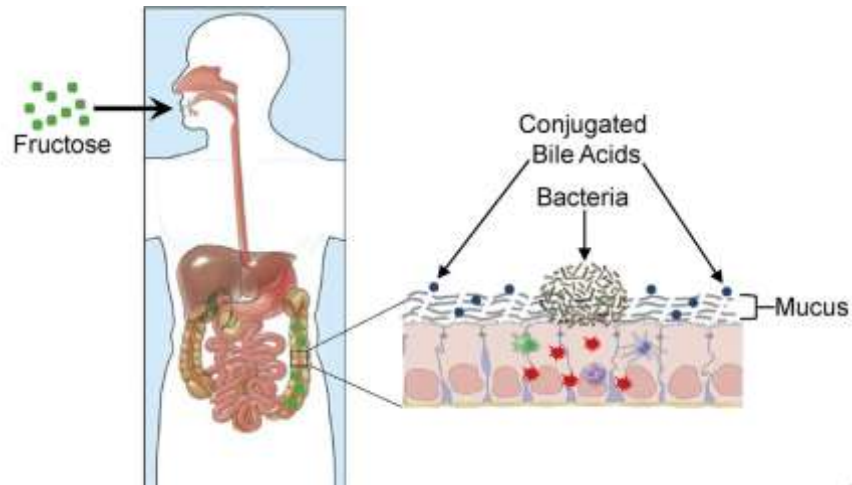
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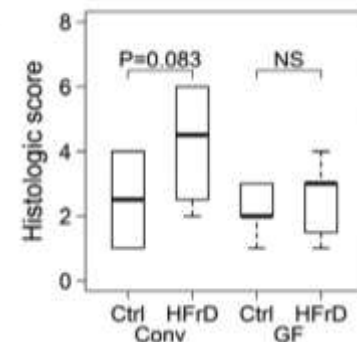
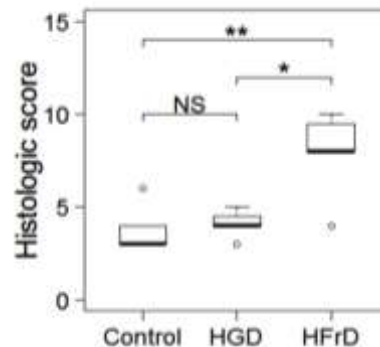


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Excess dietary fructose has a pro-colitic effect by altering microbiota and metabolites



Reducing or eliminating bacteria attenuated HFrD-mediated worsening of DSS-induced colitis.



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Can diet be used to “treat” IBD?

Is that mucosal healing?

Is it symptomatic improvement?

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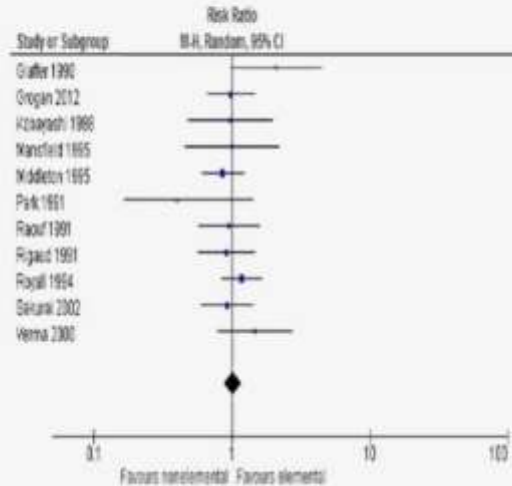
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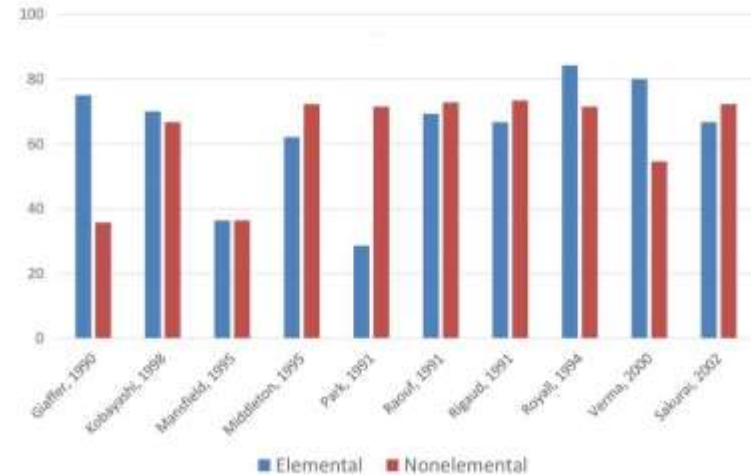
Elemental vs Non-elemental Formula

Remission Rates Nonelemental vs Elemental



Elemental vs. Nonelemental

Response to Dietary Therapy



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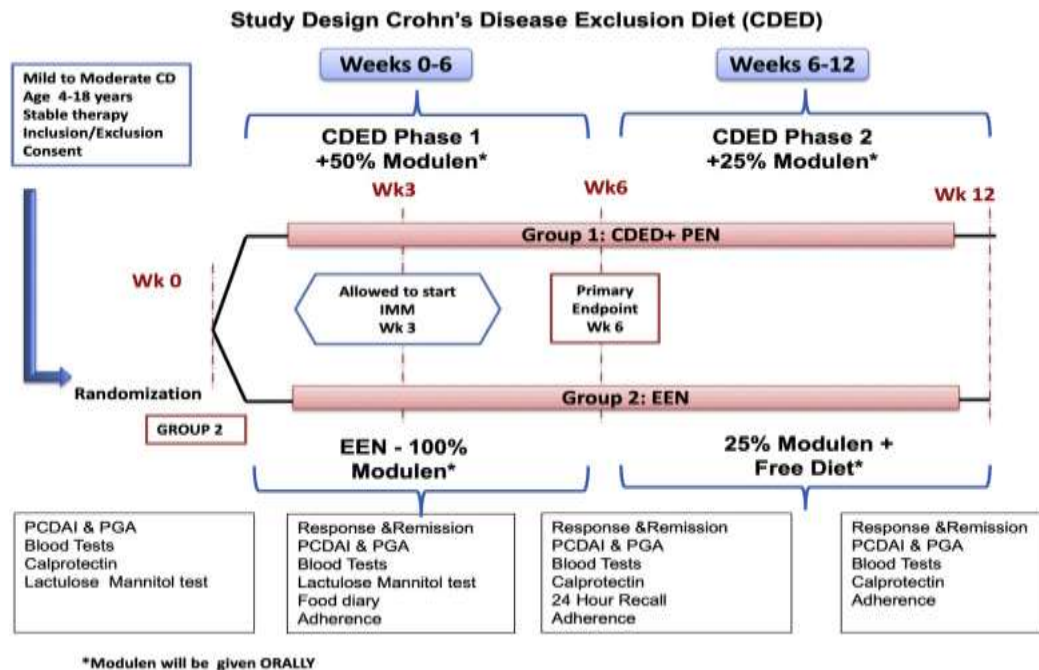
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Zachos M, Tondeur M, Griffiths AM. Enteral nutritional therapy for induction of remission in Crohn's disease. Cochrane Database of Systematic Reviews 2007, Issue 1

CD Exclusion diet (CDED) Plus PEN – Study Design



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Levine A, et al. Gastroenterology. 2019

Aug;157(2):440-450.

CDED – Dietary Instructions

- Disallowed foods items
 - Dairy
 - animal fat
 - Wheat
 - Emulsifiers
 - artificial sweeteners
 - several other food items
- Mandatory food items to be consumed daily – soluble fiber, apple pectin, and resistant starch
 - Eggs
 - Fresh chicken breast
 - Banana
 - Apple
 - Potato (must be cooked and refrigerated prior to consumption – increases resistant starch content)

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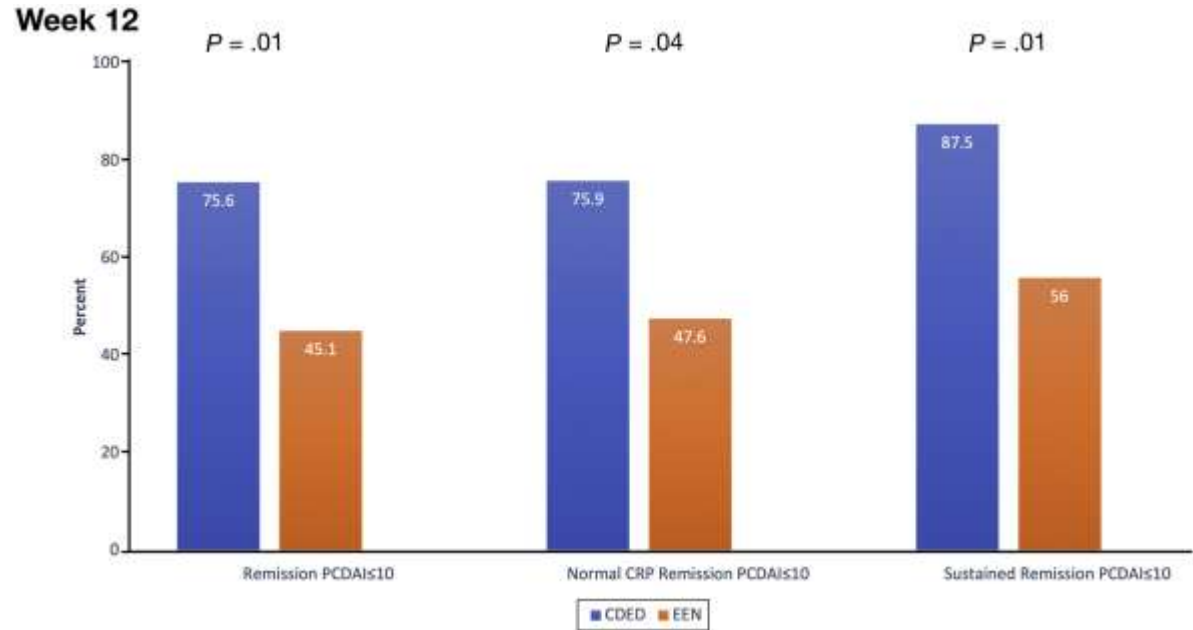
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CDED Plus PEN – Results

- Sustained remission in **87.5%** of CDED+PEN participants vs **56%** in EEN participants at week 12



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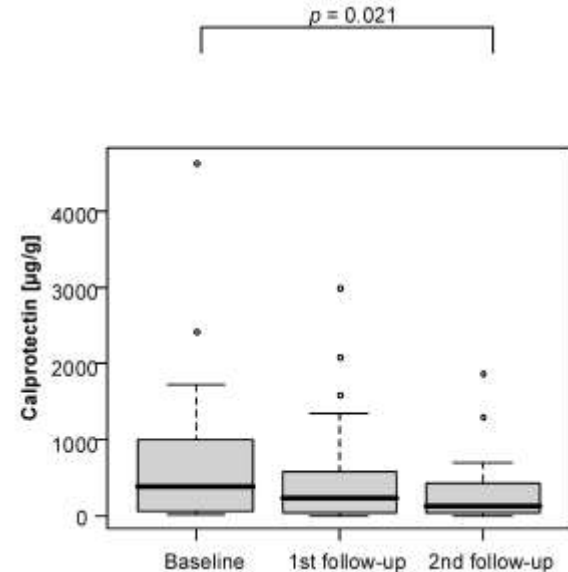
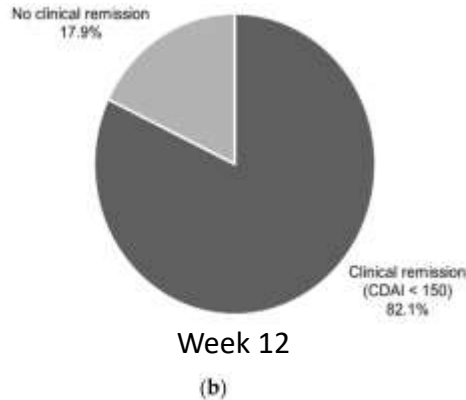
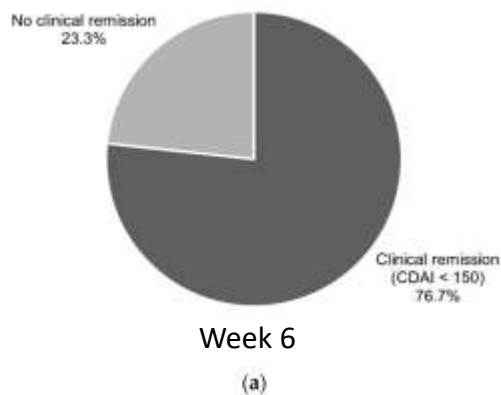
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Crohn's Disease Exclusion Diet (CDED) in Adults

Open label single arm trial in 32 adults



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Szczubetek M, et al. Effectiveness of Crohn's Disease Exclusion Diet for Induction of Remission in Crohn's Disease Adult Patients. *Nutrients*. 2021; 13(11):4112

Can we mimic exclusive enteral nutrition?

EEN beneficial in pediatric IBD

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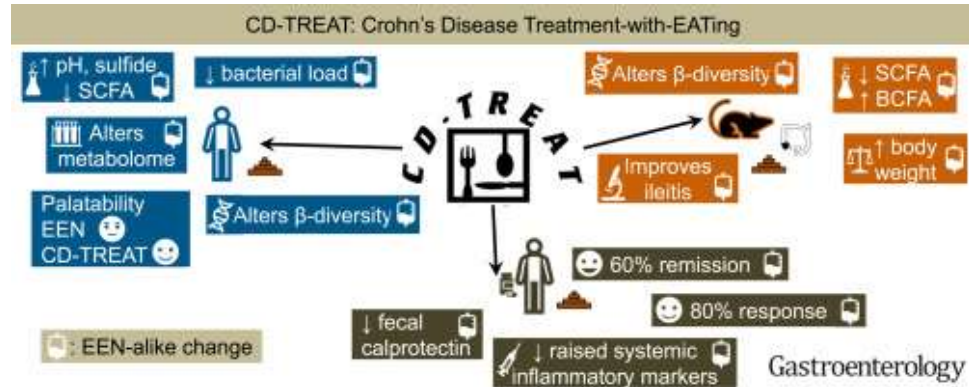
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Crohn's Disease Treatment-with-eating (CD – TREAT)

- ✓ Goal – to mimic EEN by exclusion of certain dietary components (ex: gluten, lactose, and alcohol) while matching macro and micronutrients using ordinary food

Example: matching components of enteral formula and food – maltodextrin replaced by food high in starch and low in fiber

- ✓ Composition of CD-TREAT based on Modulen IBD (most popular enteral formula in Europe)



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CD – TREAT

- Study compared CD-TREAT diet to EEN
 - Total of 25 healthy participants, results found similar changes in the microbiome between CD-TREAT and EEN in randomized controlled trial
 - Five children with Crohn's disease
 - Improved disease activity index score
 - Rate of remission was 60% after 8 weeks of CD-TREAT

Table S1: A day's menu of CD-TREAT diet for a boy with CD, 15 y, 48 kg and 170cm.

Breakfast:
1 multivitamin tablet
Full fat milk (360ml)
Rice breakfast cereals (45g)
Apple juice (360ml)
Morning snack:
Pineapple juice (360ml)
1 peeled apple
Lunch:
1 sandwich with white bread (2 slices), cheddar (45g) and cream cheese (45g), lettuce (20g) and peeled cucumber (20g)
1 bowl chicken and rice soup
Afternoon snack:
1 rice pudding
Dinner:
1 portion grilled salmon (180g) with mashed potatoes (260g) and cheese sauce
All dairy products were lactose free; all cereal-based products were gluten free

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IBD go-to Diets: Low FODMAP Diet

- FODMAPS are poorly absorbed carbohydrates that are fermentable by gut bacteria
- May cause colonic gas and excess water retention in the intestinal lumen → abdominal pain, bloating, diarrhea, gas, constipation
- Includes all foods devoid of FODMAPS
- Excludes foods containing FODMAPS:
 - Fructo-oligosaccharides (wheat, onions, legumes)
 - Lactose (milk, ice cream)
 - Fructose (apples, honey)
 - Galactans (legumes)
 - Sorbitol (stone fruits, artificial sweetener)

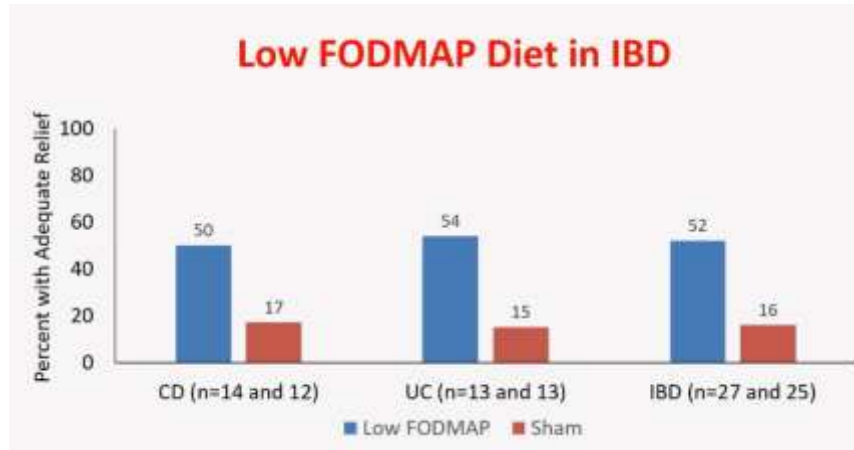
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Low FODMAP Diet in IBD



- ✓ No significant difference after 4 weeks on change in irritable bowel syndrome severity scores,
- ✓ significant improvements in specific gut symptom scores and the numbers reporting adequate symptom relief.
- ✓ The low FODMAP diet reduced fecal abundance of microbes believed to regulate the immune response, compared with the control diet, but had no significant effect on markers of inflammation.

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COX, GASTROENTEROLY AGA CLINICAL—ALIMENTARY TRACT | [VOLUME 158, ISSUE 1](#), P176-188.E7, JANUARY 01, 2020

Results from recent diet intervention studies

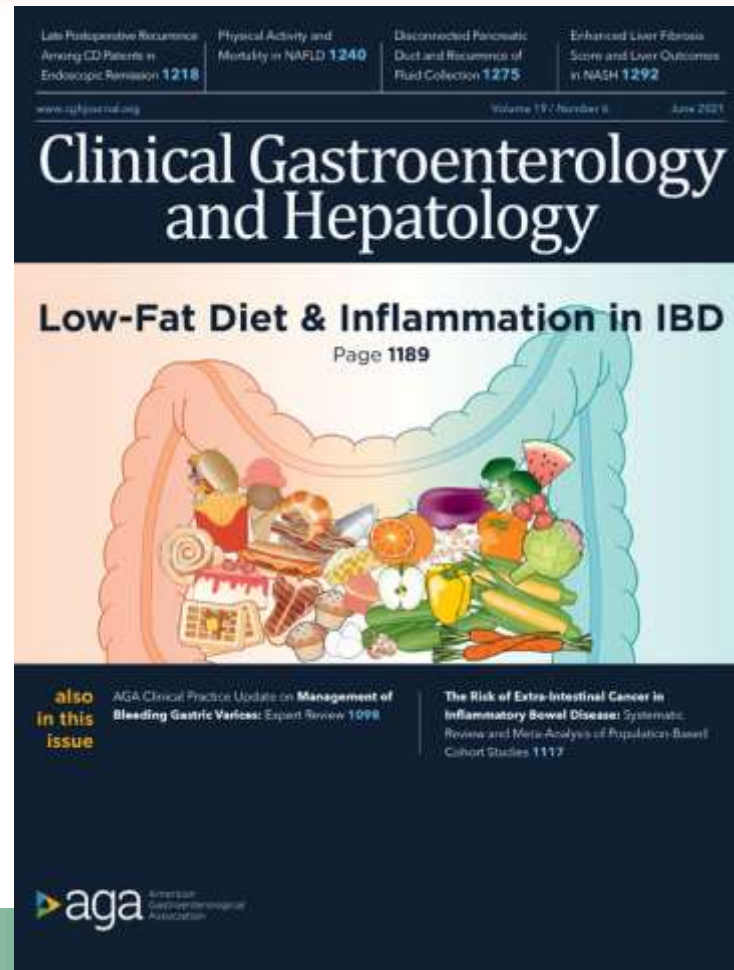
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We made the cover!



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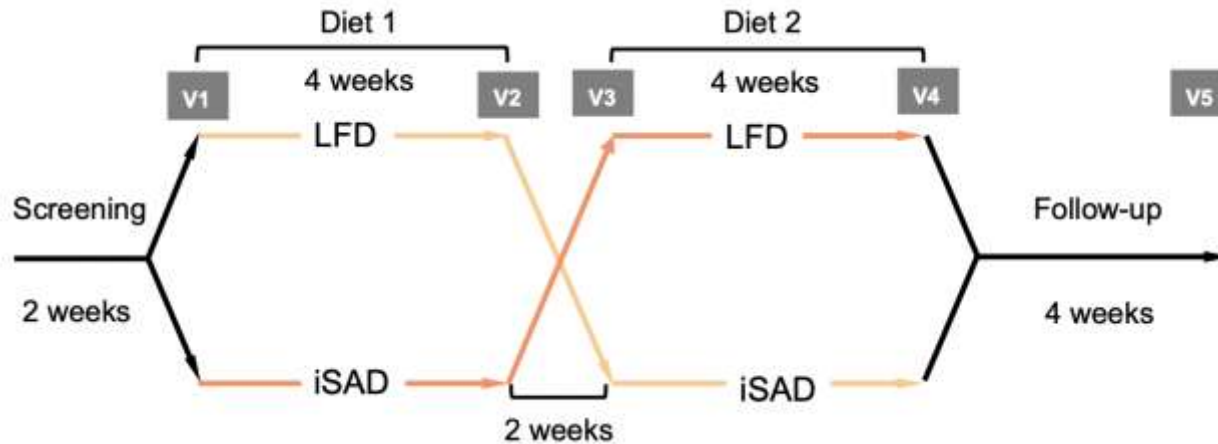
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High fat versus low fat/high fiber diet in UC patients in remission

Pilot study completed: 18 patients



- LFD: 10% of calories from fat, 1-5% saturated fat, and 5-9% MUFA and PUFA. High fiber
- Idealized SAD: 35-40% of calories from fat, 10-11% of saturated fat, 25-29% MUFA and PUFA

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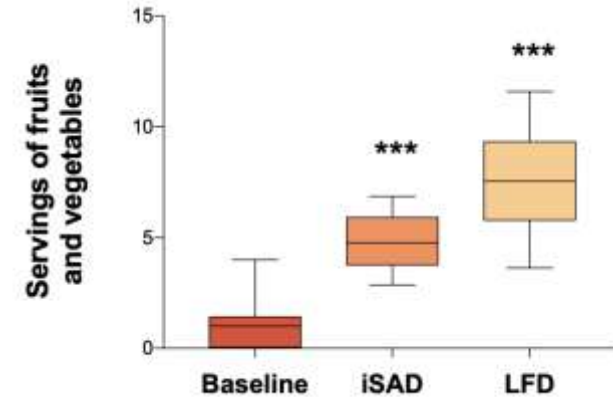
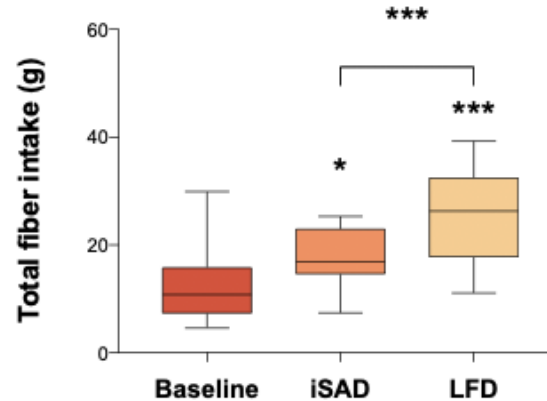
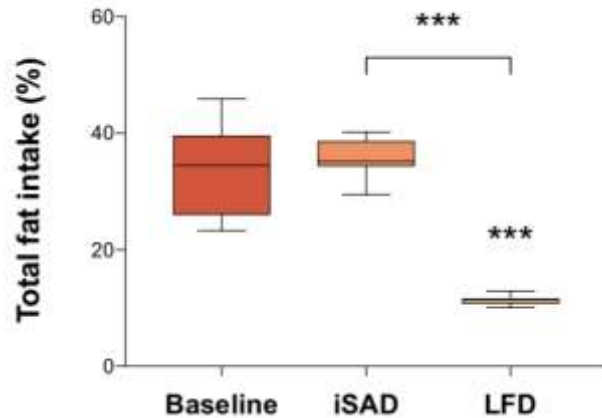
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Fritsch et. al CGH 2020

Fat intake at baseline is high in UC patients



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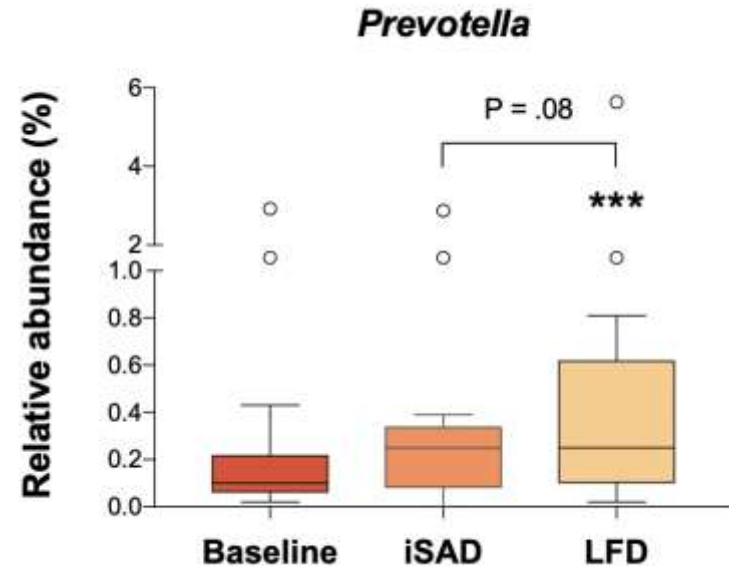
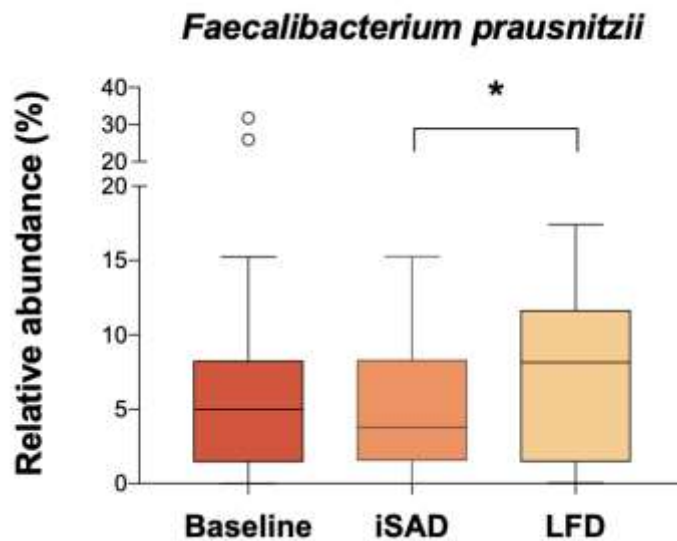
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Fritsch et. al *CGH* 2020

Species Level Changes with Important Implications to UC



Fritsch et. al CGH 2020

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

Scientific PI: James D. Lewis, MD, MSCE, University of Pennsylvania

Administrative PI: Angela Dobes, MPH, Crohn's & Colitis Foundation

Data Management Center Director: Robert Sandler, MD, MPH, University of North Carolina

Conducted by the Crohn's & Colitis Foundation Clinical Research Alliance

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Crohn's & Colitis Foundation

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Sherman award to Dr. Lewis

the **Crohn's and Colitis Center**



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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



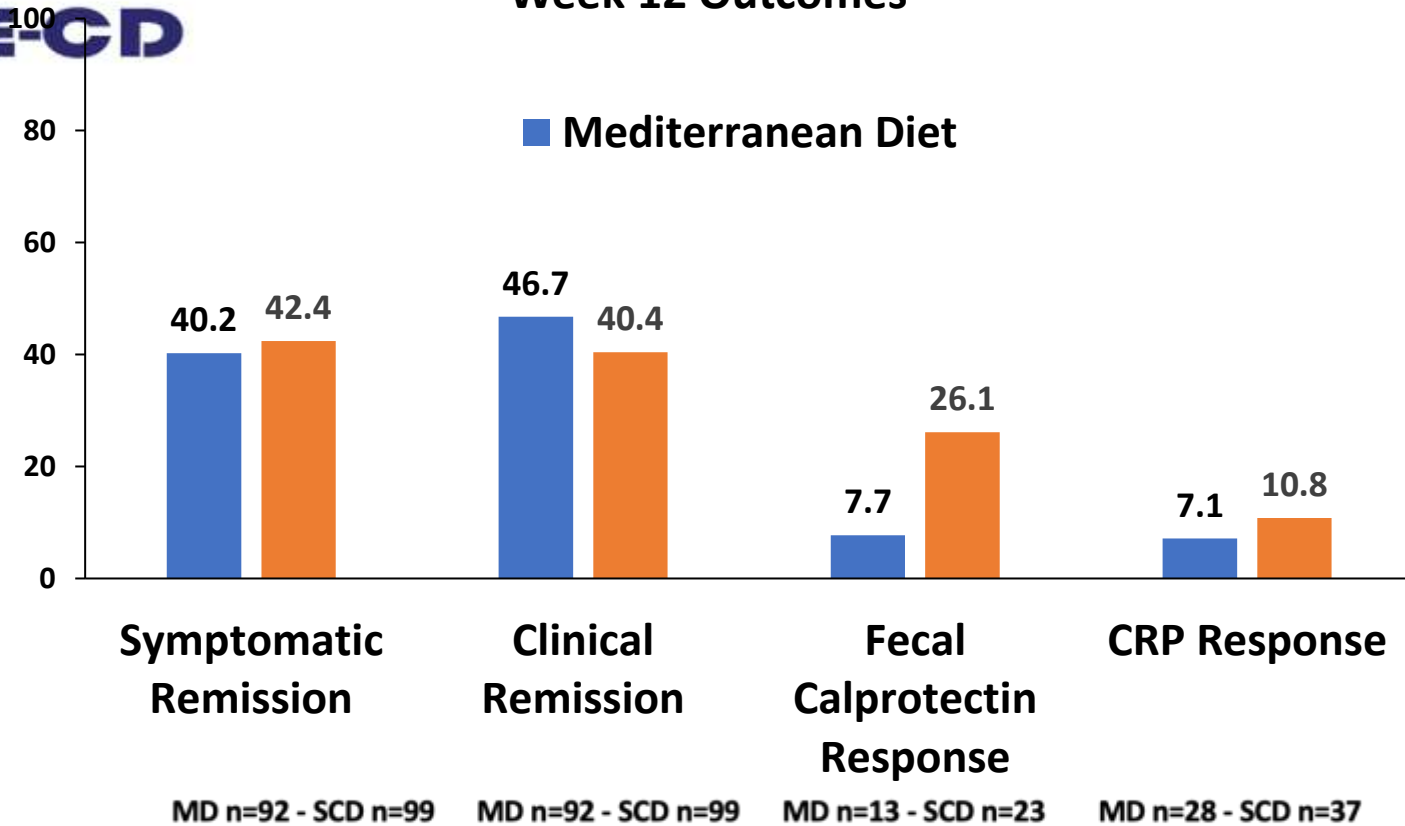
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Lewis JD et al. As presented at
Crohn's and Colitis Congress 2021

Week 12 Outcomes



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Conclusions from CD-DINE

- Both diets were well tolerated despite increased consumption of fruits and vegetables
- Symptomatic remission was common with both diets
 - Similar results with and without confirmed inflammation prior to randomization
- Neither diet was associated with normalization of CRP concentration

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Can we change people's diet behavior
long-term?

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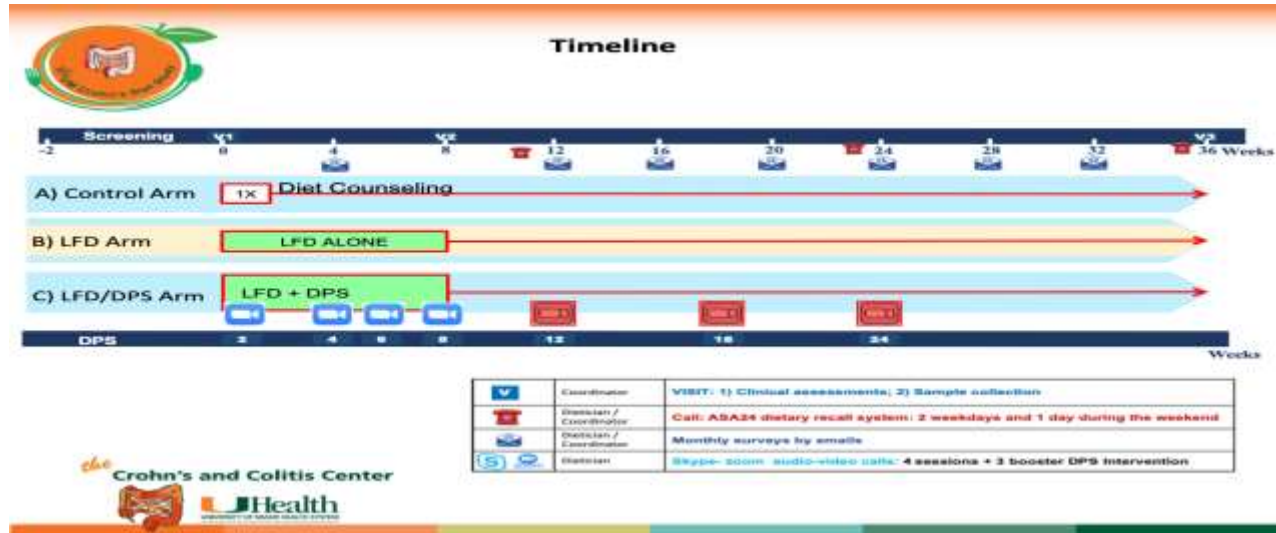
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A Holistic Diet Intervention For People With Crohn's Disease

- ✓ 3-arm study
- ✓ Test the effectiveness of a low fat, high fiber diet to reduce symptoms, inflammation, and improve quality of life in people with Crohn's disease.



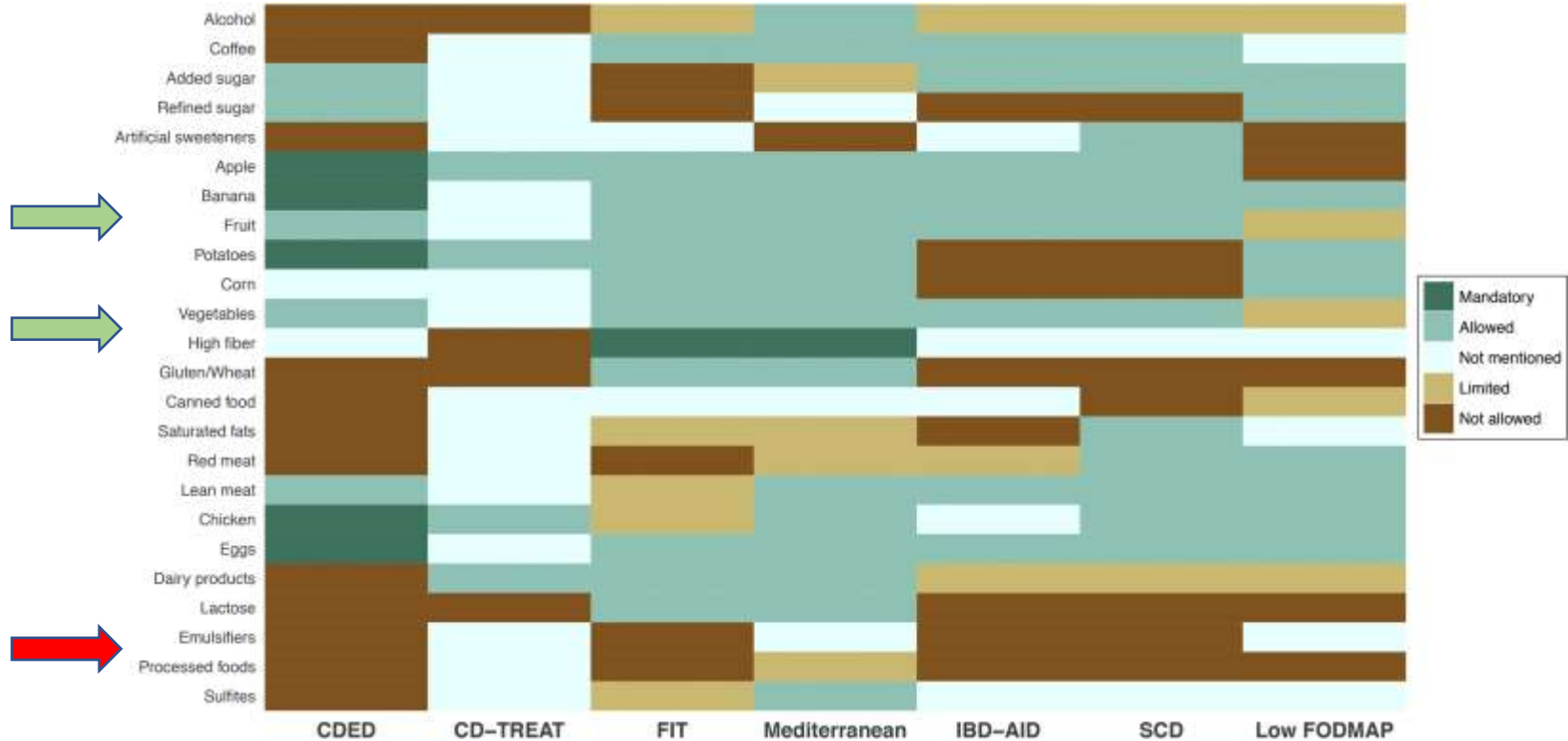
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Common Themes in Diets for IBD



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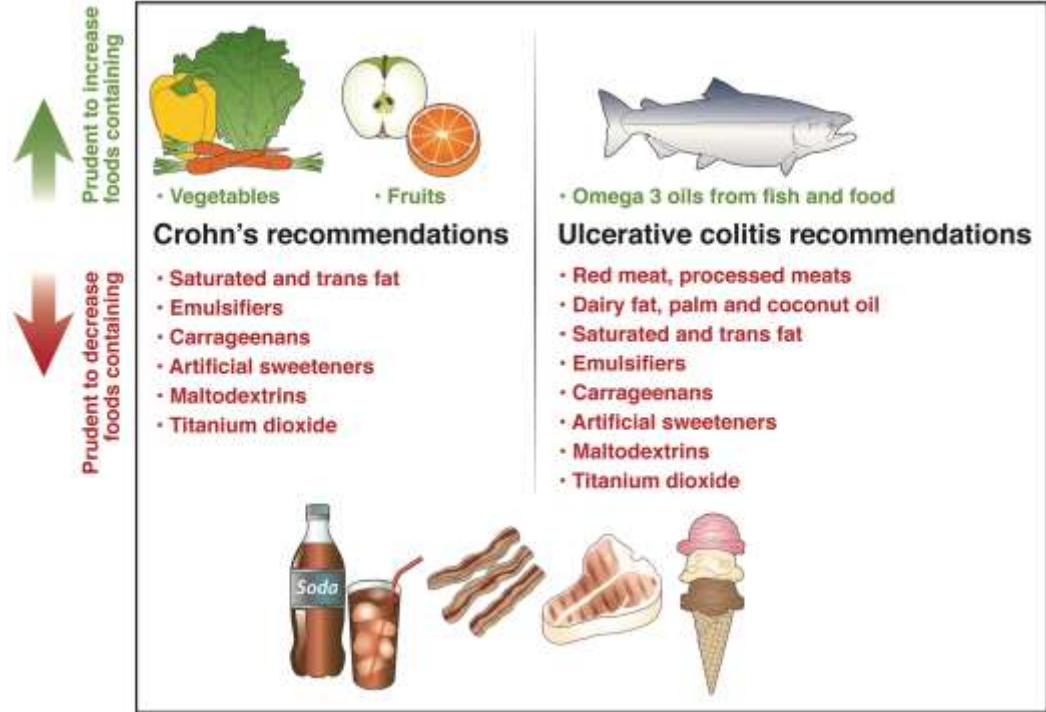
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IOIBD Practical Guidance for Patients

- **Whole Food diet as adjunct**

- Shop the outside aisle
- Fresh fruits and vegetables
- Fresh meats and fish
- Use olive oil as dominant fat
- Mixed nuts as an alternative snack to chips, cookies, etc



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Levine, A et al. Clin Gastroenterol Hepatol. 2020 May;18(6):1381-1392.

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