Diet in Inflammatory Bowel Diseases: Food for Thought?

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UPMC | CHILDREN'S HOSPITAL OF PITTSBURGH

Disclosures

The speaker has no disclosures to report

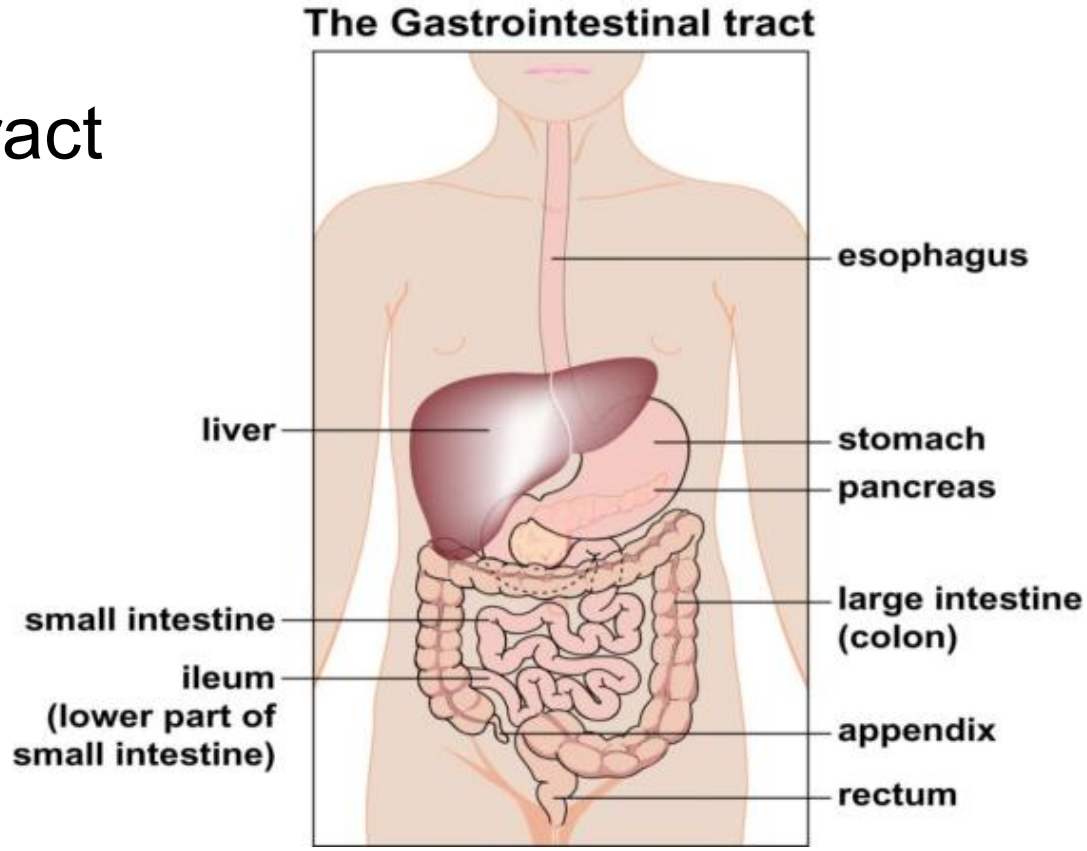
(*Disclaimer: I am an overprotective and adoring 1st time puppy owner. I also admit that my puppy follows a CDED – like diet: no emulsifiers or processed grains for Lexie!)

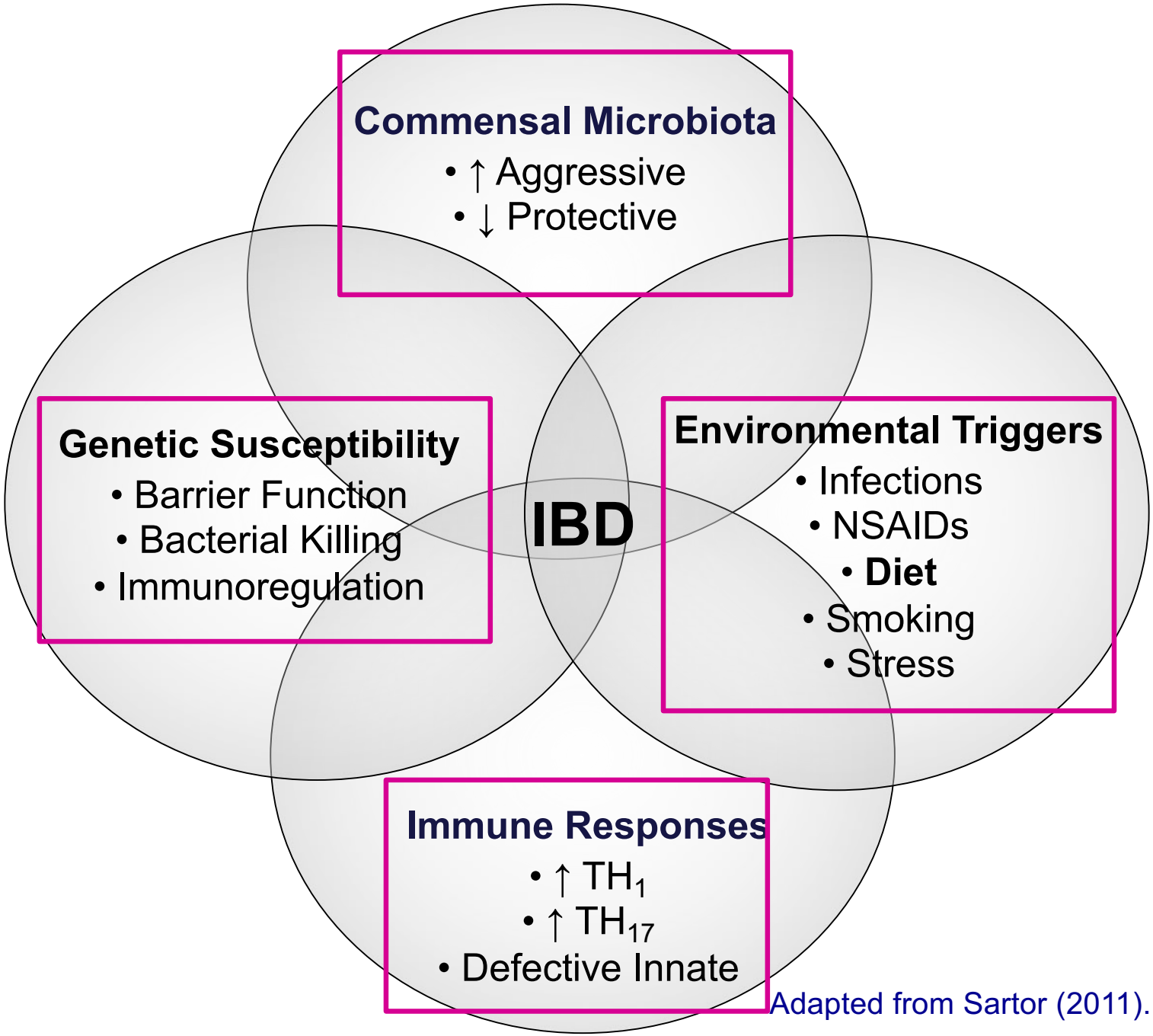
Objectives

- Impact of diet on inflammatory bowel diseases (IBD)
- Review the efficacy of nutritional therapies in IBD
  - Enteral therapy in Crohn's disease
  - Specific defined diets which have been utilized in IBD
- Future directions

Inflammatory Bowel Diseases: IBD

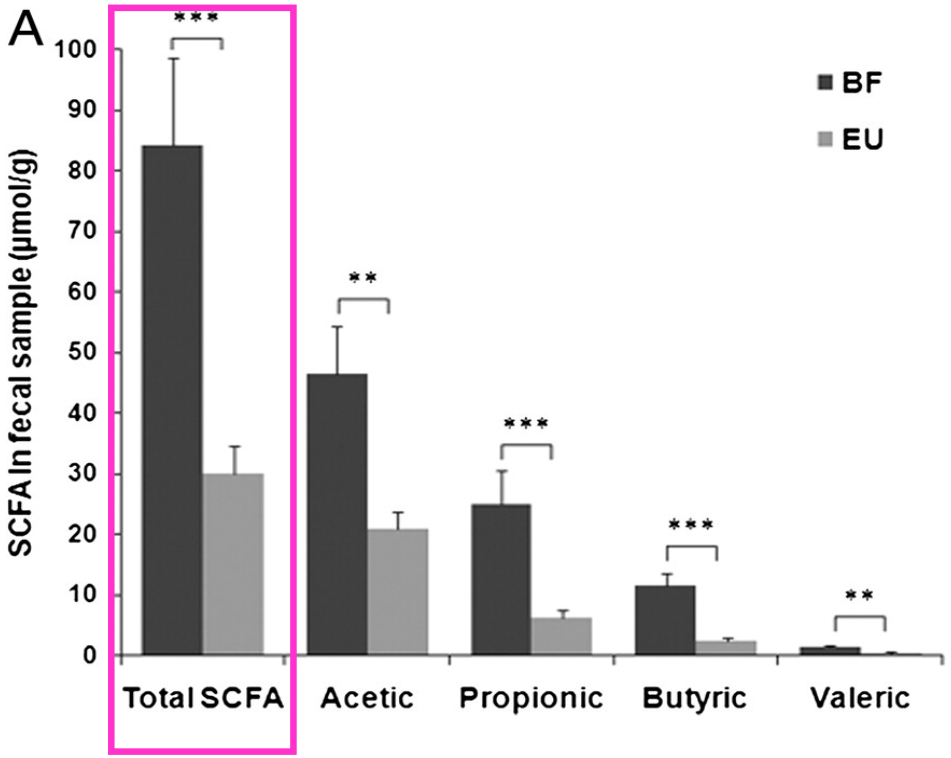
- Chronic inflammatory diseases involving GI tract
- Abdominal pain
- Bloody stools
- Diarrhea
- Weight loss
- Growth problems
- Fatigue
- Fevers of unknown origin (FUO)

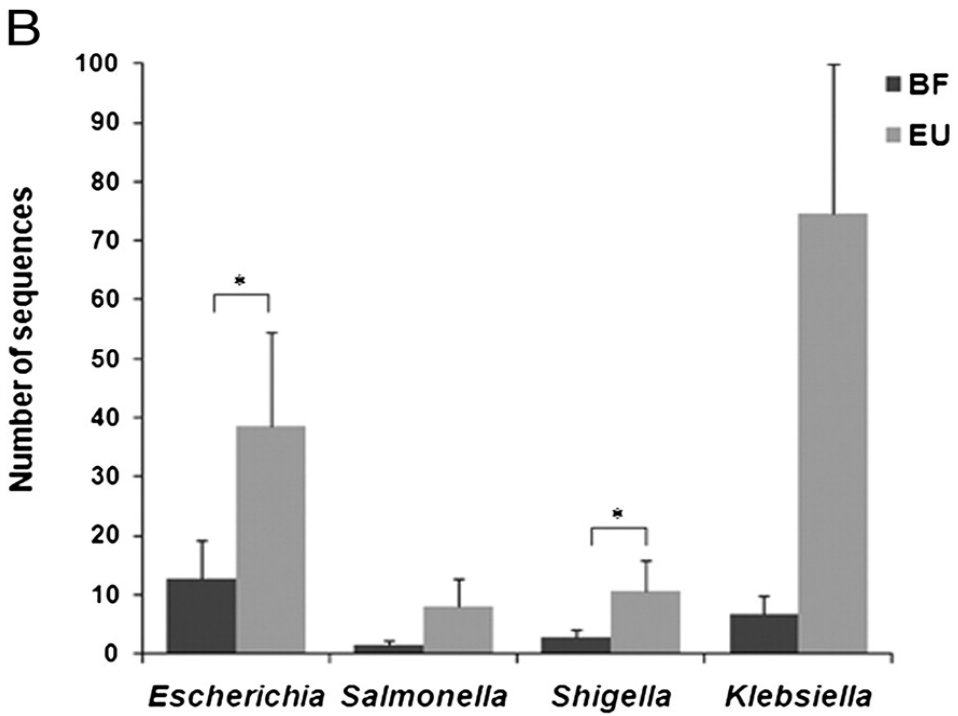




Adapted from Sartor (2011). *Mucosal Imm*

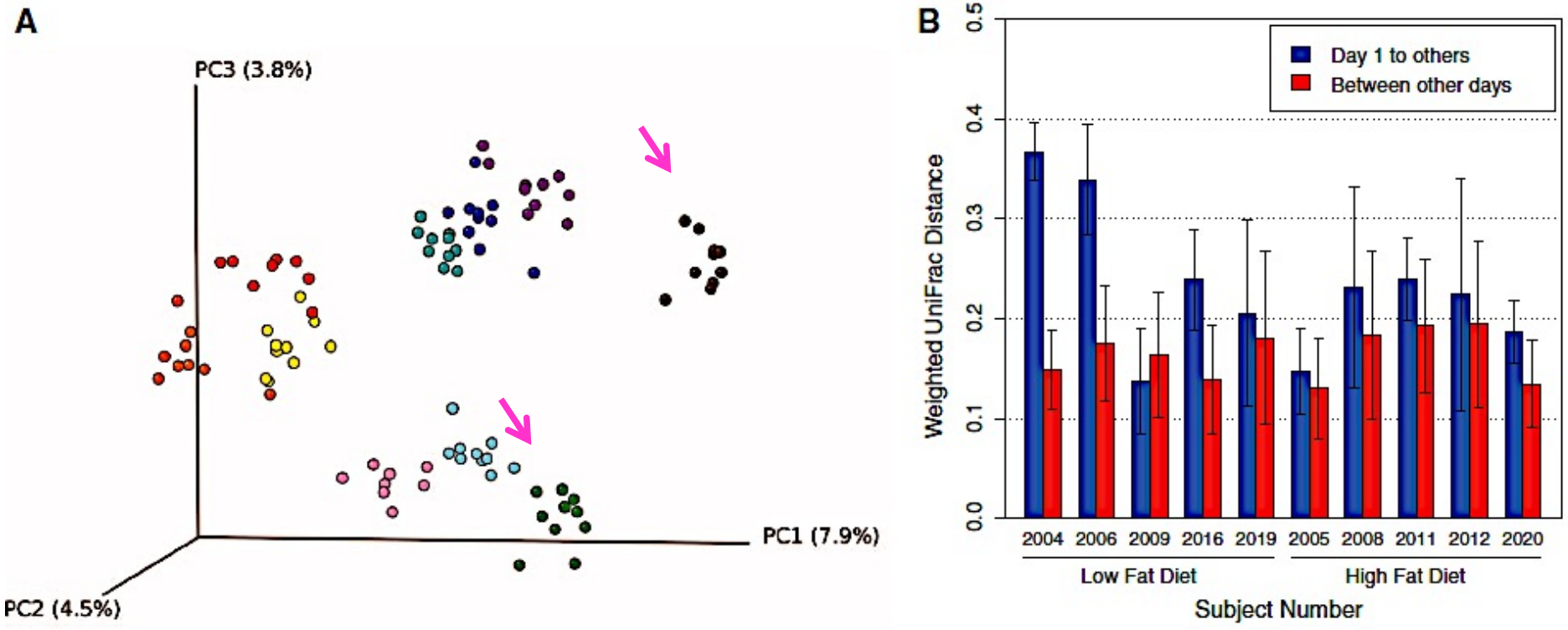
SCFA-Producing Bacteria Suppress Potentially Pathogenic Intestinal Bacteria





De Filippo, *et al* (2010). *PNAS*

Dietary Impact on Microbiome Composition Within 24 Hours



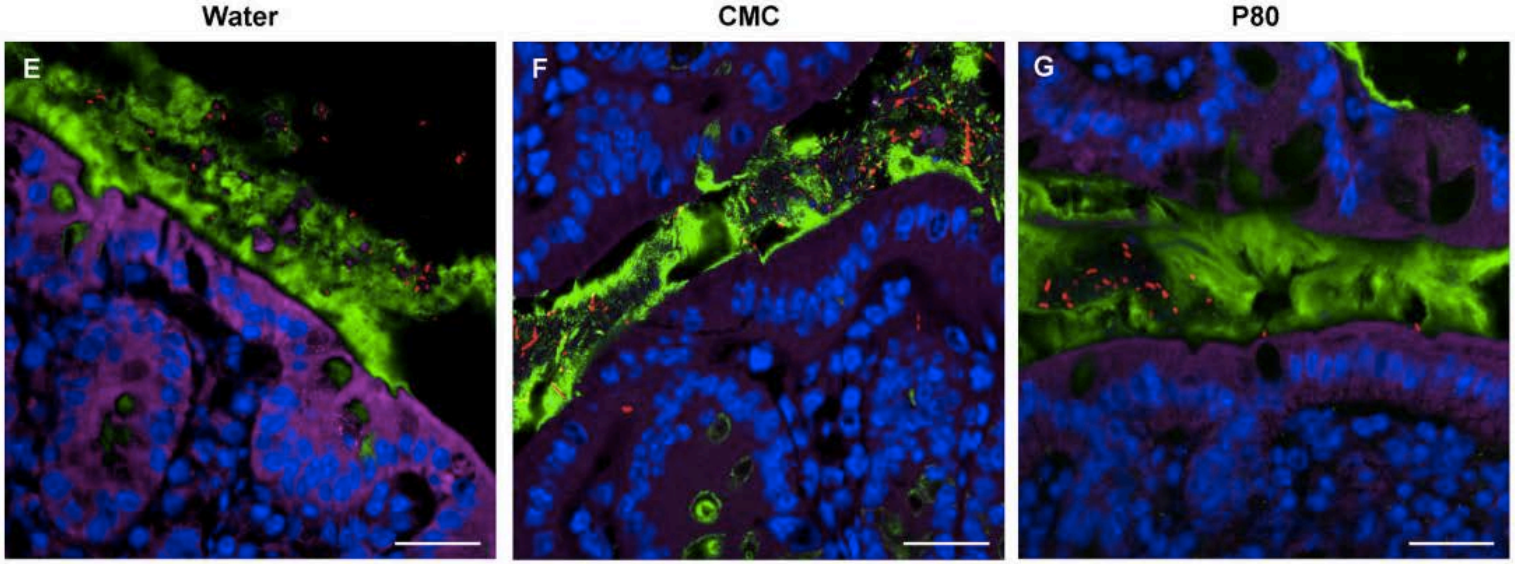
Wu, *et al.* (2011) *Science*

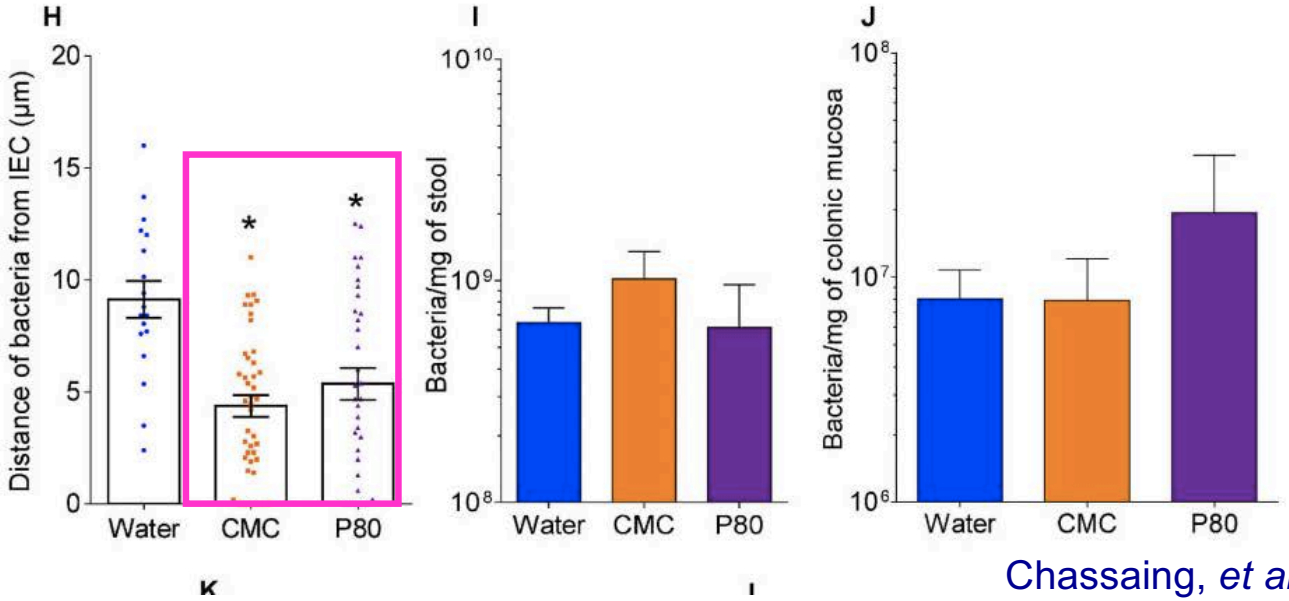
Impact of Diet and IBD Development

- Women in highest quartile of prudent diet score (fish, fruits/vegetables) during high school with 53% lower CD (but not UC) risk
  - Fish ($p = 0.01$) and fiber ($p = 0.06$)
- Risk of CD decrease by 13% for every 10 gram in fiber intake
- High fat diet: increased intestinal permeability (bile acid exposure; mast cell activation)
- Red/processed meat not associated with relapse in CD

1. Ananthakrishnan, *et al (*2015). *Inflamm Bowel Dis*
2. Liu, *et al* (2015). *Nut Research*
3. Devkota, *et al* (*2012). Nature*
4. Chassaing, *et al* (2015). *Nature*
5. Albenberg, *et al.* (2019). *Gastroenterology*

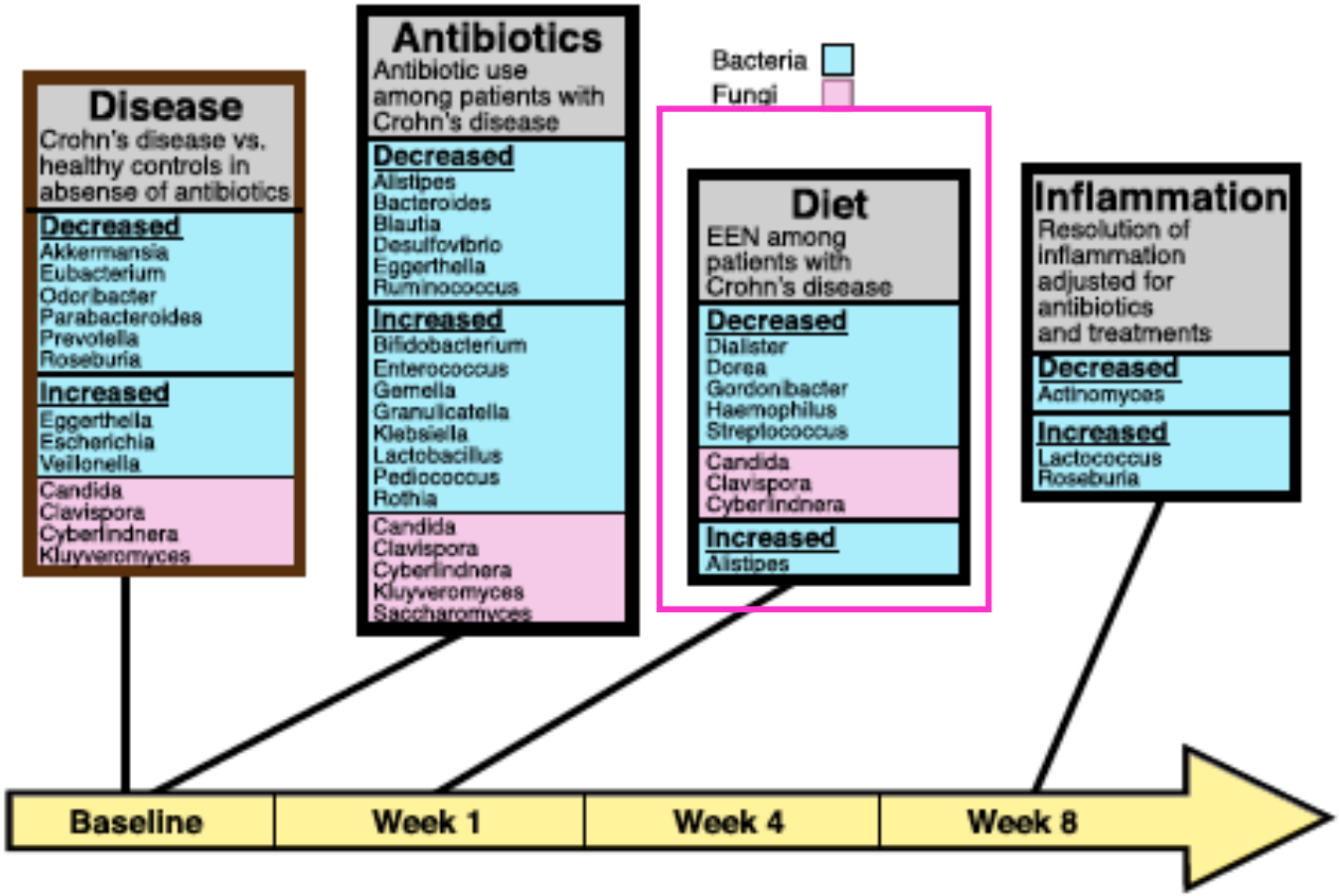
Emulsifiers Increase Permeability





Chassaing, *et al* (2015). *Nature*

Diet, Antibiotics, and Inflammation Independently Impact GI Microbiota



Lewis, et al (2015). *Cell Host Microbe*

How Do We Define Enteral Therapy?

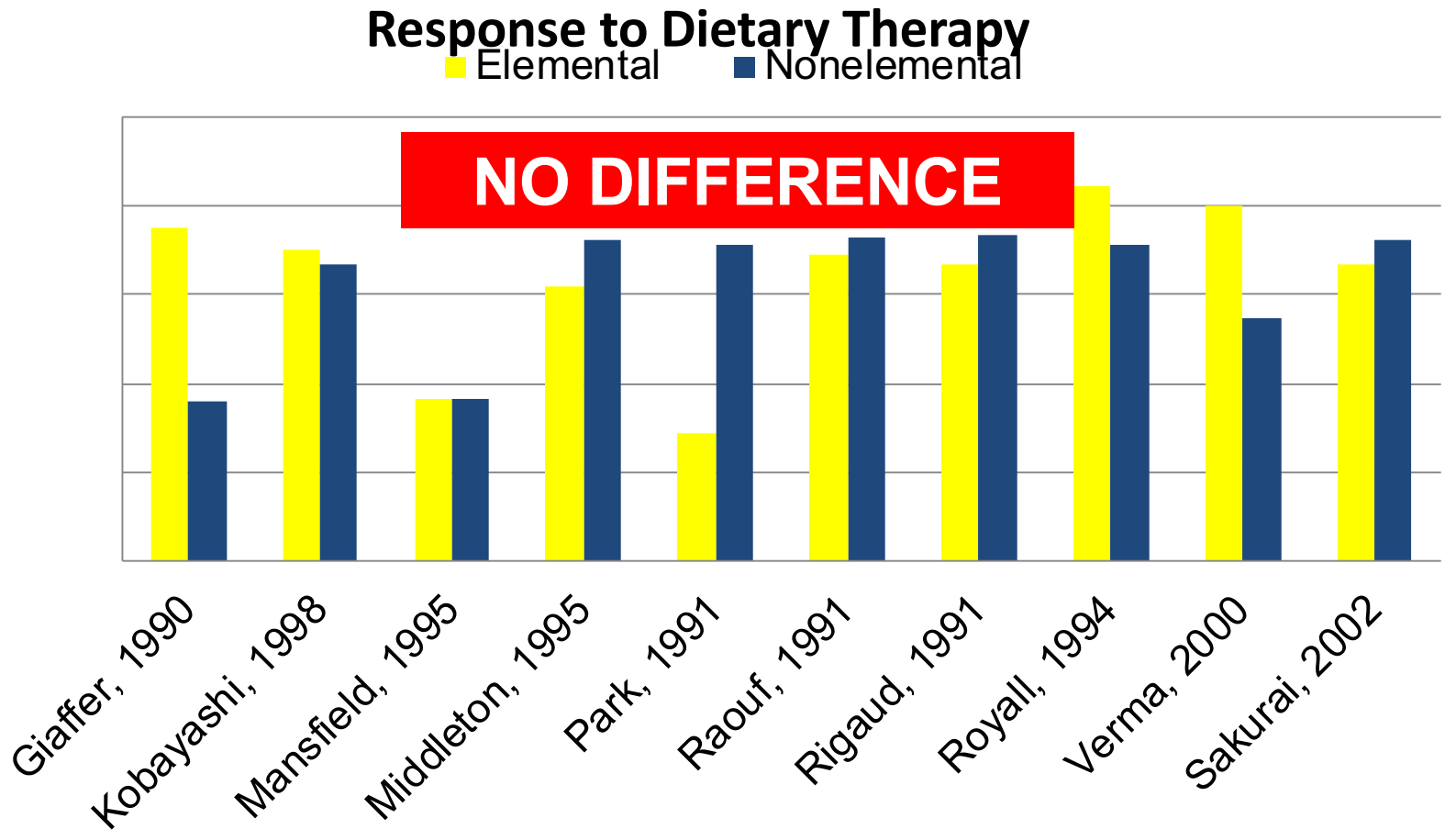
- Enteral nutrition/therapy (EN): Liquid formulas to treat Crohn's disease
- Exclusive enteral nutrition (EEN): Utilizing enteral nutrition as a sole source of nutrition to induce remission in Crohn's disease
- Partial enteral nutrition (PEN): Utilizing enteral nutrition as the majority or portion of nutrition (in addition to regular foods) to induce remission, maintain remission, or improve nutrition status

ECCO/ESPGHAN Guidelines

- Evidence – based review of existing data
- Individualized treatment algorithms
- EEN first choice for induction therapy in children who have not finished growth over corticosteroids
- Predictors for poor outcomes with EEN
  - Severe perianal fistulizing disease
  - Severe stricturing/penetrating disease
  - Severe growth failure
  - Pan-enteric disease

Ruemmele, et al (2014). *J Crohns Colitis*

Is Elemental Formula Better than Polymeric Formula?



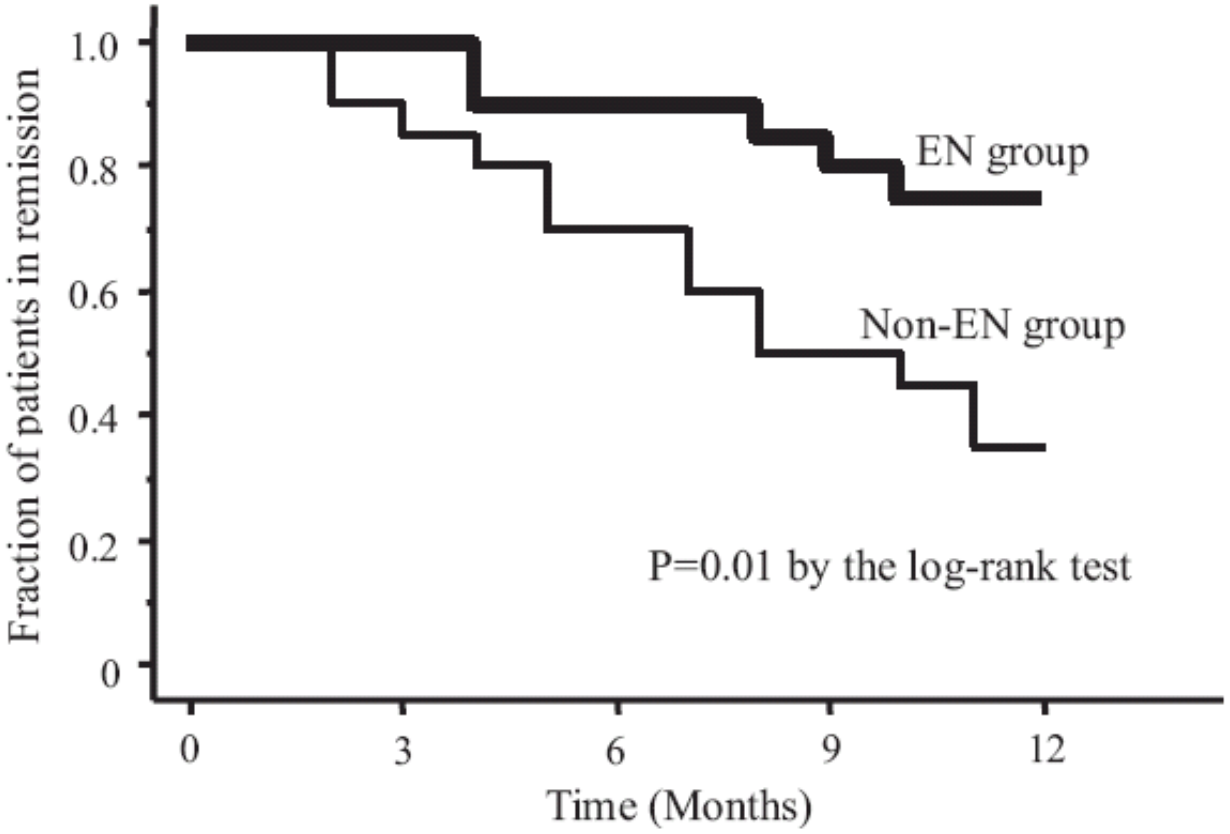
Adapted from Zachos M (2007). *Cochrane Review*

Enteral Therapy in Crohn's Disease

- Effective in children and adults with Crohn's disease for induction and maintenance (50-75%)
- EN vs. corticosteroids in pediatric Crohn's
  - 5 prospective randomized clinical trials: EN (4-8 wks) vs. corticosteroids (1-3 wks)
  - Better remission rates
  - *Mucosal healing
  - *Positive effect on growth
- EN may be more effective in children than adults
- Efficacy has not been demonstrated in UC

1. Lochs, *et al. (*1991).Gastroenterology
2. Seidman, *et al. (*1993).Gastroenterology (Abstract)
3. Griffiths, *et al. (*1995).Gastroenterology
4. Borreilli, *et al (2006). Clin Gastro Hepatol*
5. Day, *et al*.(2008). *Aliment Pharmacol Ther*
6. Zachos, *et al* (2007). *Cochrane Database*
7. Gupta, *et al* (2013). *Inflamm Bowel Dis*

Maintenance Therapy with Enteral Nutrition for Crohn's Disease

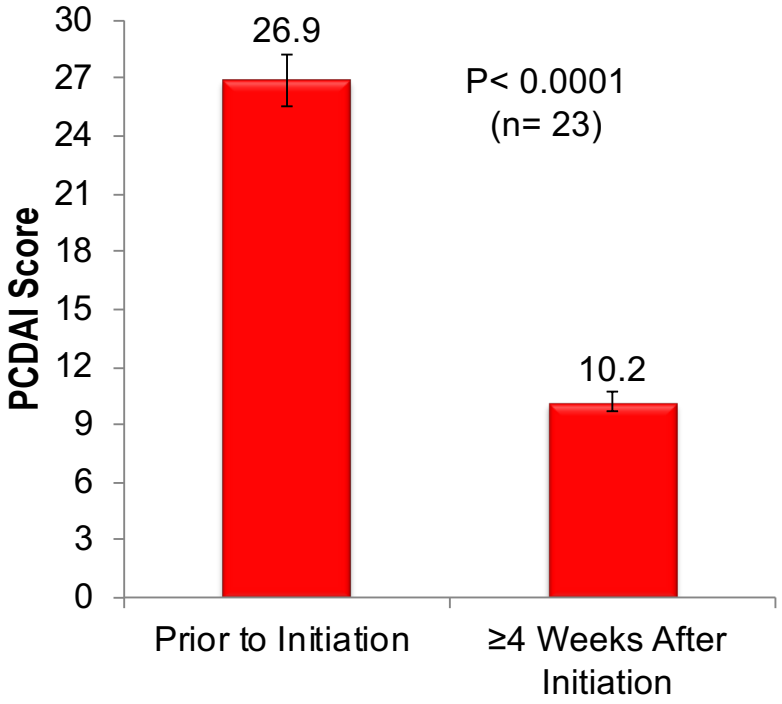


- Prospective study: Adult CD pts in remission (CDAI<150)
- Proportion in remission higher in EN group (p=0.01)
  - Lower endoscopic inflammation
  - Decreased mucosal TNF, IL-6

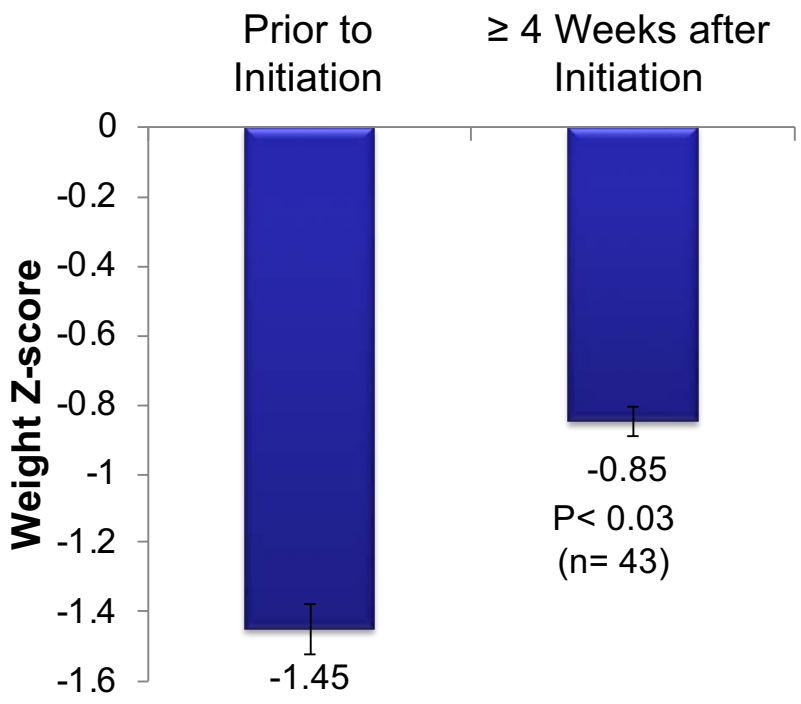
Yamamoto, et al.2007. *Inflamm Bowel Dis*

CHOP Enteral Nutrition Experience

Mean Change: PCDAI Score



Mean Change: Weight Z-score

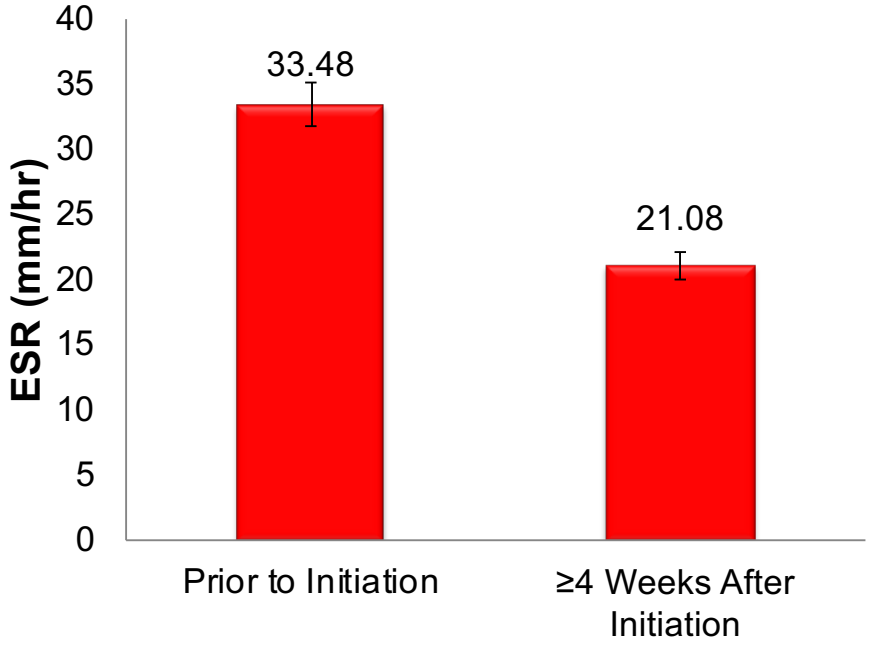


Gupta. *et al (*2013). *Inflamm Bowel Dis*

CHOP Enteral Nutrition Experience

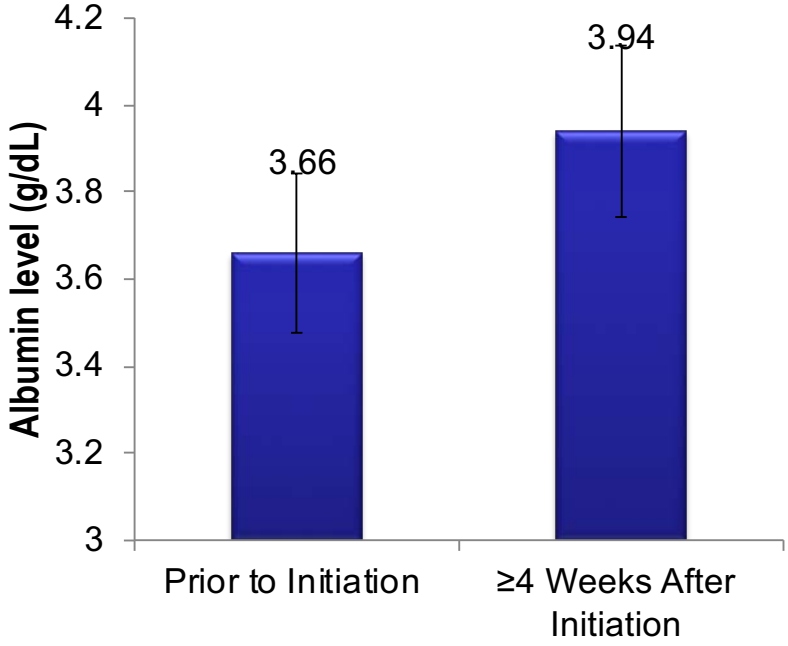
Mean Change: ESR

p=0.0001
n=43



Mean Change: Albumin

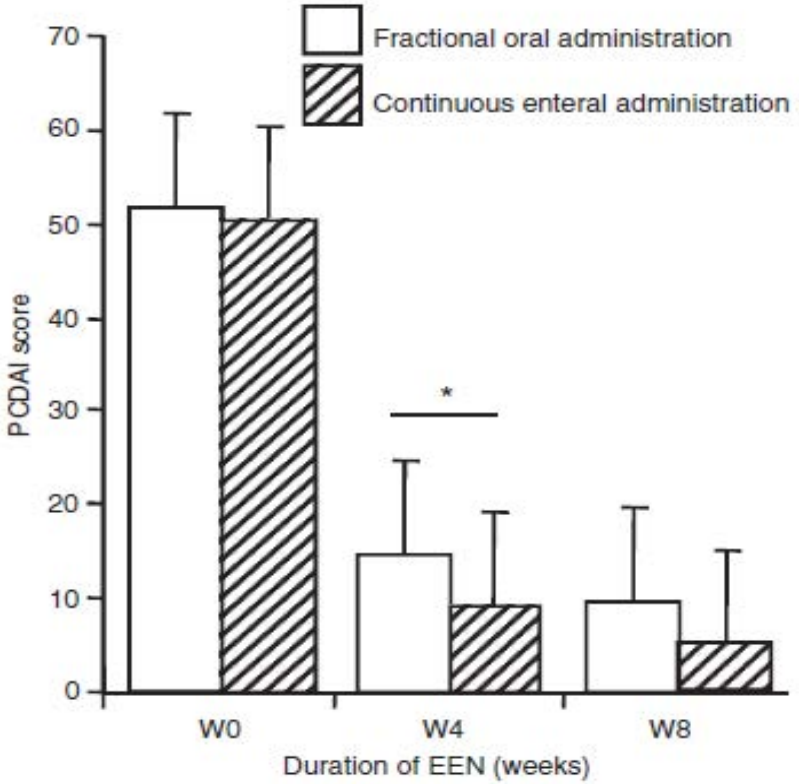
p=0.03
n=43



Gupta. *et al* (2013). *Inflamm Bowel Dis*

Oral vs. Nasogastric EEN in Pediatric Crohn's Disease

- Retrospective review
- Oral route (n=45) or overnight NG continuous feeds (n=61)
- Remission rates similar at 8 wks
  - Continuous>oral at 4 weeks
- All patients had improvement in:
  - Growth and weight gain
  - Laboratory indices
- Similar compliance rates
  - 87% vs. 90%



Rubio, *et al. (*2011). *Aliment Pharmacol Ther*

Comparative Effectiveness: Enteral Nutrition (Partial and Exclusive) and anti-TNF

- Prospective study
  - N = 90
  - Anti-TNF (n=52), EEN (n=22), or PEN (n=16)
- Clinical remission
  - PCDAI: Anti – TNF (84%); EEN (88%); PEN (64%)
  - Calprotectin $\leq$250 μg/g: Anti – TNF (62%); EEN (45%); PEN (14%)
- QOL improved with EEN in body image (p=0.03) and anti – TNF in emotional domain (p=0.04)

Lee *et al* (2015). *Inflamm Bowel Dis*

Preoperative EEN Reduce Post-operative Complications in Active Crohn's Disease

- Patients undergoing resection for fibrostenotic ileal +/- colonic Crohn's
  - N = 81 (EN = 42; non – EN = 39)
  - No other treatments for 3 months pre-operatively
- Post – operative complications
  - Significantly less infectious ($p < 0.03$) and non-infectious ($p < 0.02$) in EN vs. non - EN patient groups
- Cumulative recurrence
  - Endoscopic (Rutgeerts): 3 vs 10 (6 months; $p<0.03$); 20 vs 22 (24 months; $p<0.43$); clinical recurrence rates similar at all points

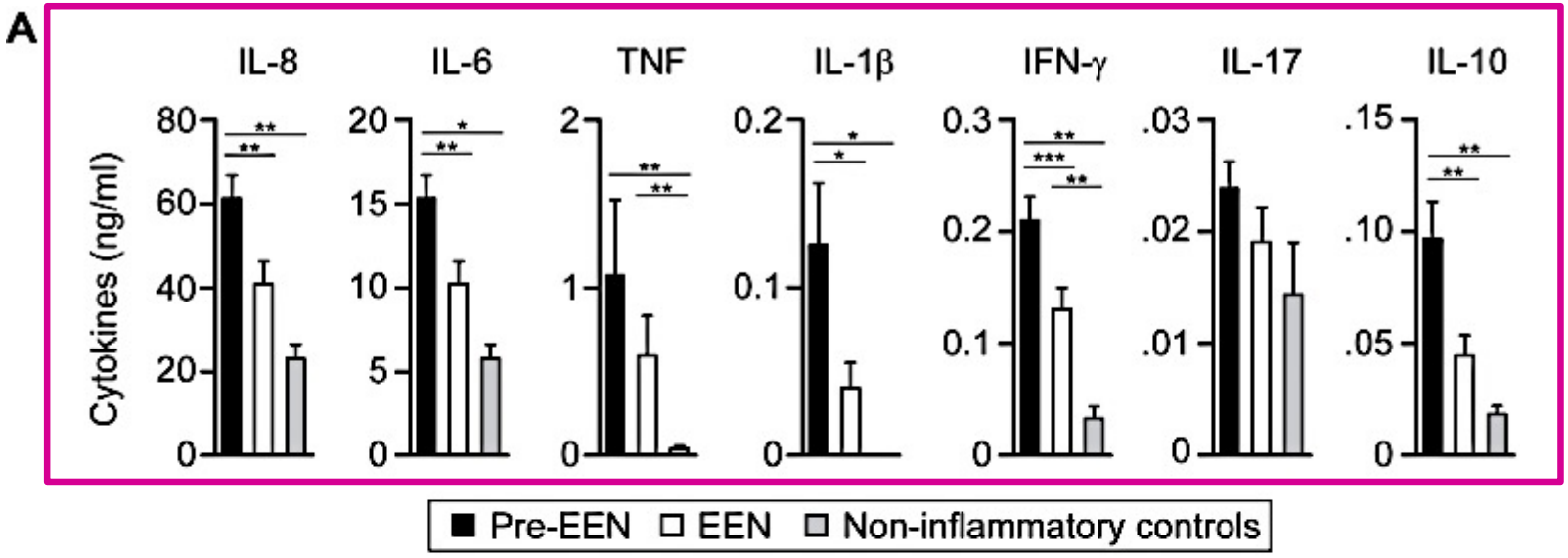
Wang, *et al* (2016). *World J Gastro*

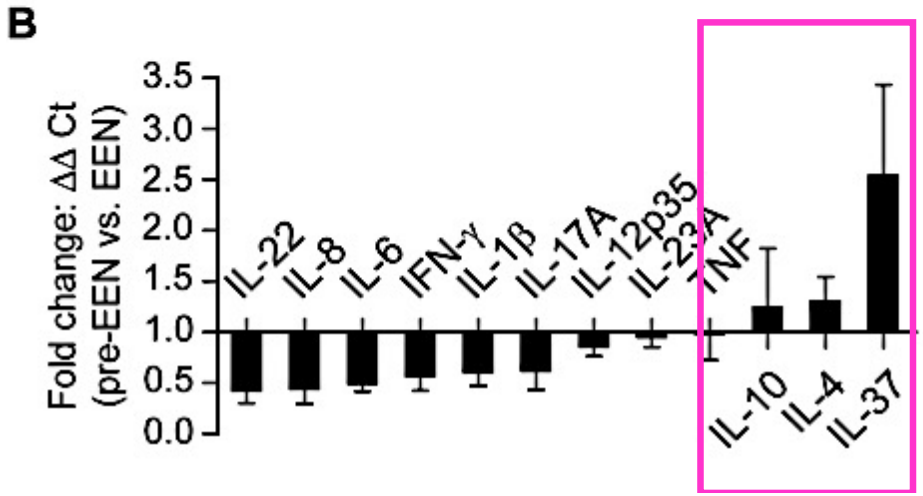
Enteral Therapy and the Impact on Microbial Diversity

- Potential efficacy of EEN on fecal microbiota
- Recent studies show decrease/little change in overall microbial diversity in children on EEN
- Changes in specific species associated with disease activity (increases in *Firmicutes, Ruminococcia*e)
  - Includes decrease in presumed protective bacteria *(F. prausnitizii)*
- While EEN does affect composition, need additional studies to look at associative vs. causative role

1. Gerasimidas, *et al (*2014). *Inflamm Bowel Dis*
2. Kaakoush, *et al* (2015). *Clin Transl Gastro*
3. Schwerd*, et al* (*2016). JACI*

Enteral Therapy is Associated With Decreased Pro-inflammatory Cytokines

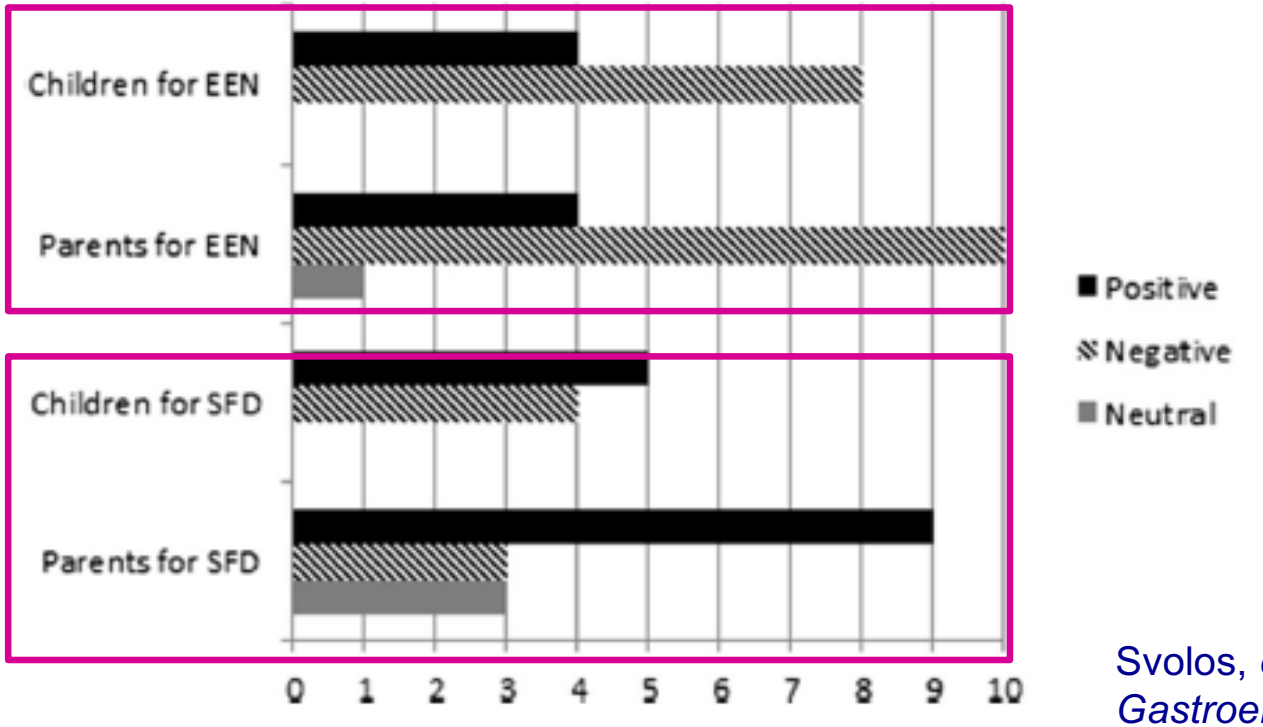




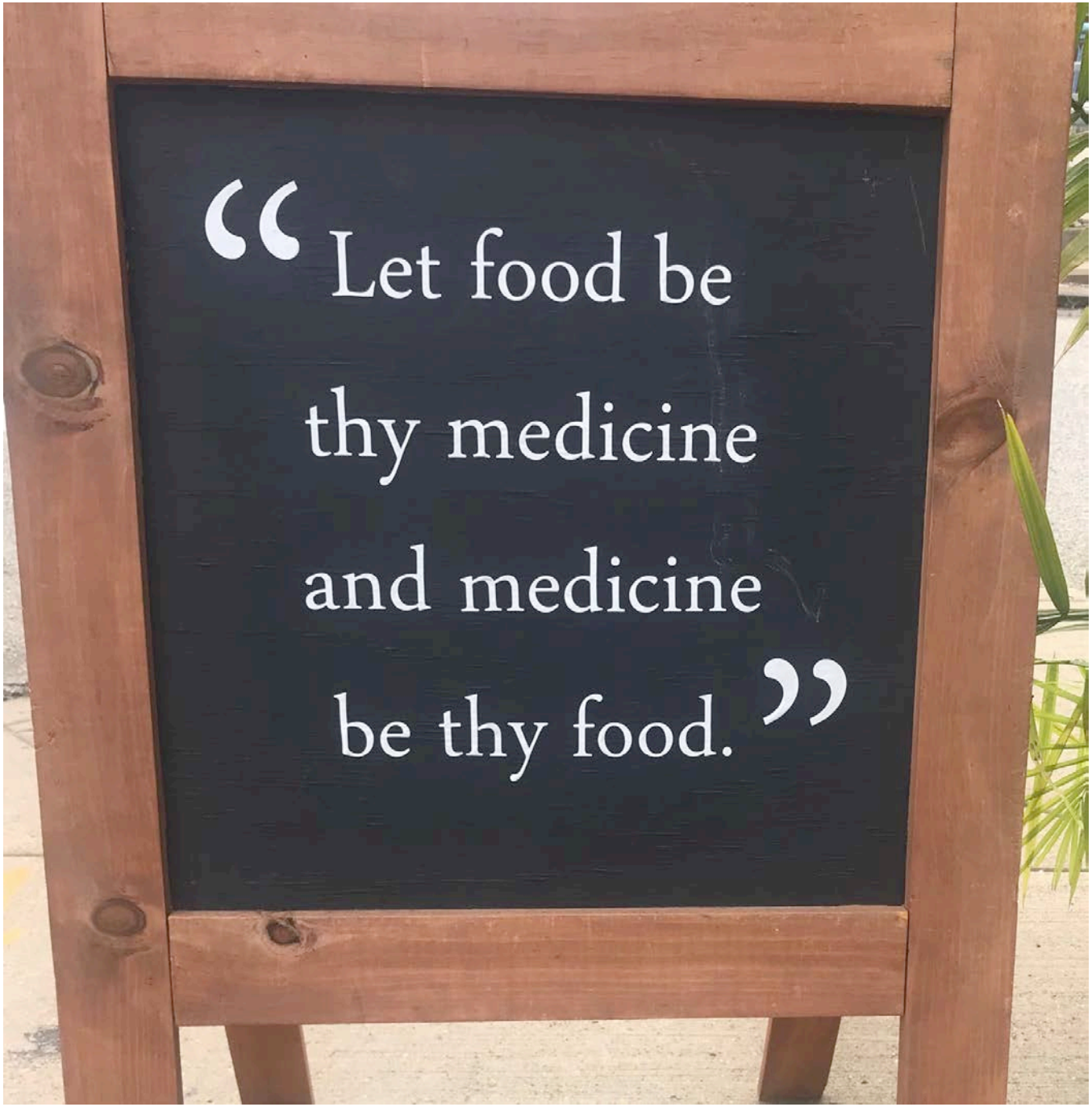
Schwerd, *et al. JACI* 2016

Family Perceptions on EEN vs. Solid Food Diet Alternatives

- Survey – families with children treated with EEN (N=58)
- Majority (59%) positive on additional EEN course
- Preference for SFD vs EEN (Pts: 66%; Parents: 72%)



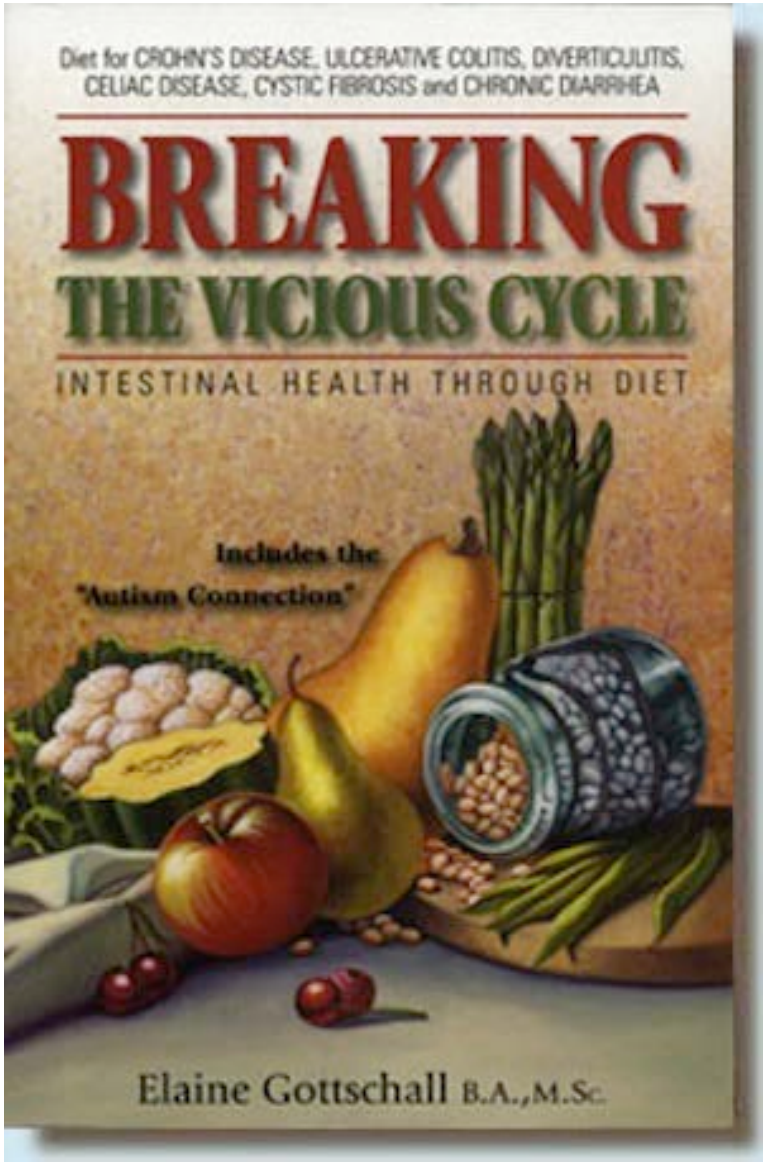
Svolos, *et al* (2017). *BMC Gastroenterology*


“Let food be
thy medicine
and medicine
be thy food.”

Defined Dietary Approaches in IBD Management

- Exclusive enteral nutrition (EEN, polymeric diet)
- ***Specific carbohydrate diet (SCD)***
- ***CD-TREAT***
- ***Crohn's disease exclusion diet (CDED)***

Specific Carbohydrate Diet (SCD)



- The SCD is a grain-free, low sugar and low lactose diet.
- Almost all foods are made from scratch with whole, non-processed ingredients, including fruits and vegetables, meats, nuts and nut flours, fermented dairy, oils and honey.

Specific Carbohydrate Diet in Crohn's

Crohn's disease										
Parameter	Before diet		2–6 wk		4–6 mo		7–11 mo		12 mo	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
PCDAI (all)	14.5	16.4	8.5	13.4	3.1	5.1	7.5	6.5	0	
PCDAI (diet initiated during active disease)	32.8	13.2	20.8	16.6	8.8	8.5	10	8.7	0	
ESR (mm/h)	19	15.9	12.2	7.6	9.5	5.2	11.8	10.1	14	16.1
CRP (mg/dL)	1.8	1.0	1.3	1.1	0.9	0.2	1.3	1.6	0.9	0.3
Albumin (mg/dL)	4.1	0.5	4.3	0.3	4.3	0.3	4.2	0.5	4.4	0.5
Hematocrit (%)	35.6	2.9	37.3	3.5	39.3	2.4	38.3	3.6	39.3	3.3
Calprotectin (mcg/g)	685	205.5	212.6	235	504	540.6				
Vitamin D, 25-hydroxy	31.1	4.7	30.7	10.6	37.5	26.2	34.3	13.6	24.5	3.5
BMI	17.3	2.3	17.9	2.3	16.7	2.9	16.9	3.12	18.3	4
Ulcerative colitis										
PUCAI (all)	20	11.4	12.5	13.7	12	24.1	10	–	0	–
PUCAI (diet initiated during active disease)	28.3	10.3	20	17.3	18.3	31.7	10	–	0	–
ESR (mm/h)	15.6	7.0	11.4	6.9	8.5	3.5	7	–	7	–
CRP (mg/dL)	1.0	0.5	0.7	0.3	0.9	0.3	0.8	–	0.8	–
Albumin (mg/dL)	4.2	0.4	4.5	0.2	4.4	0.3			4.1	–
Hematocrit (%)	35.1	2.6	38.9	3.2	37.5	3.0	35.5	–	38.5	–
Vitamin D, 25-hydroxy	25.5	3.5	28	0						
BMI	17.2	2.1	17.6	1.6	18.0	1.9	18.9	–	20.1	–

- 12/26 patients improved (clinical and inflammatory markers)
- Potential component of therapeutic regimen

Obih, *et al* (2016). *Nutrition*

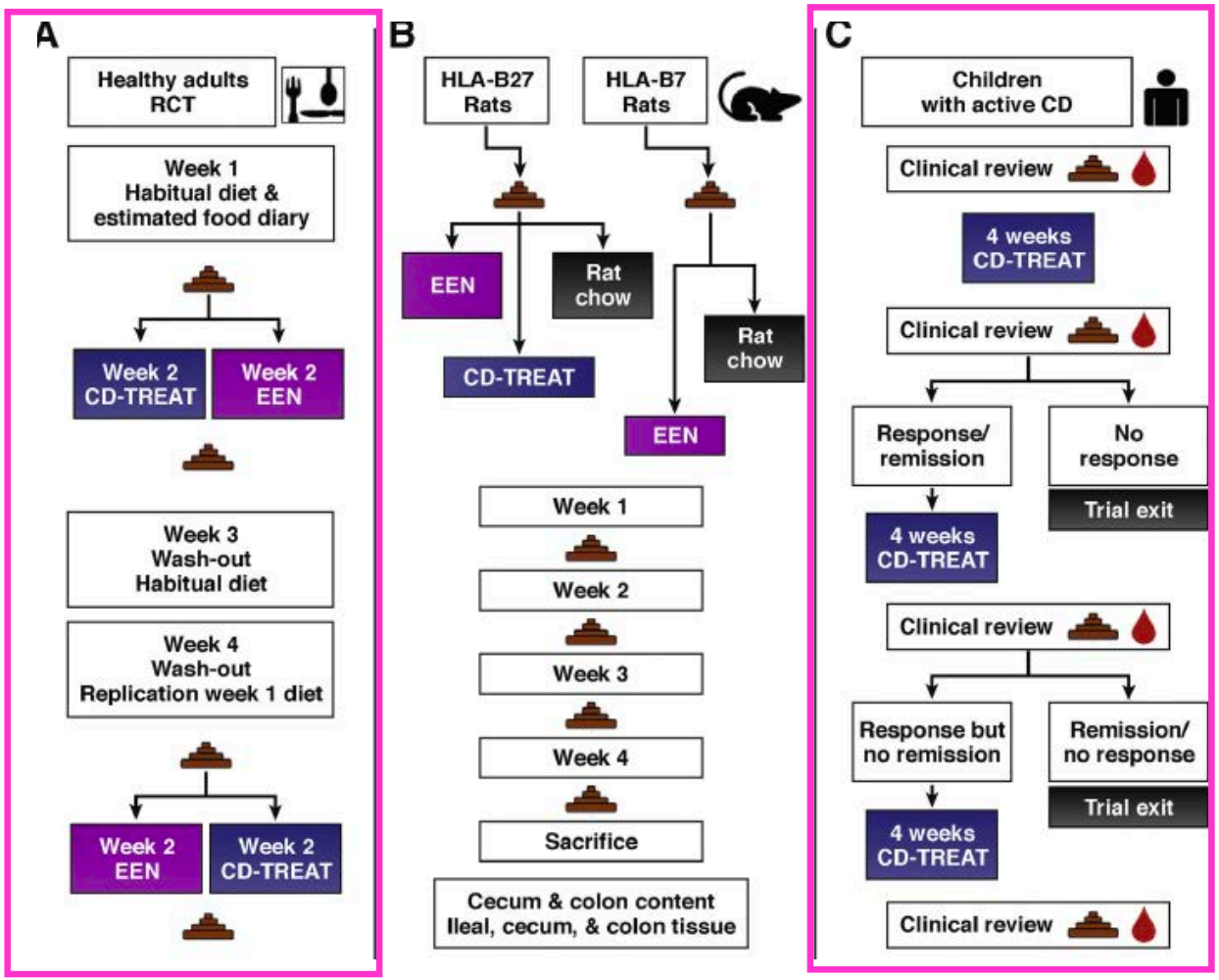
SCD: Lack of Mucosal Healing in Crohn's

	SES-CD*		UGI ulcers		Phenotype†		Behavior			
Patient	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Complete mucosal healing‡	Duration of SCD, mo
1	0	5	Yes	Yes	L4	L1L4	B1	B1	No	26
2	5	5	No	N/A	L3	L3	B1	B2	No	13
3	16	11	Yes	No	L3L4	L2	B1	B1	No	62
4	9	10	No	Yes	L2L4	L3L4	B1p	B2	No	15
5	9	24	Yes	Yes	L2L4	L3L4	B1	B1	No	34
6	20	0	Yes	Yes	L3L4	L4	B1p	B1	Yes	27
7	8	3	Yes	No	L1L4	L1	B1	B1	No	22

- N = 7 with Crohn's
- Improved clinical symptoms and normalizing labs (albumin and CRP)
- However, complete mucosal healing not noted

Wahbeh, *et al* (2017). *JPGN*

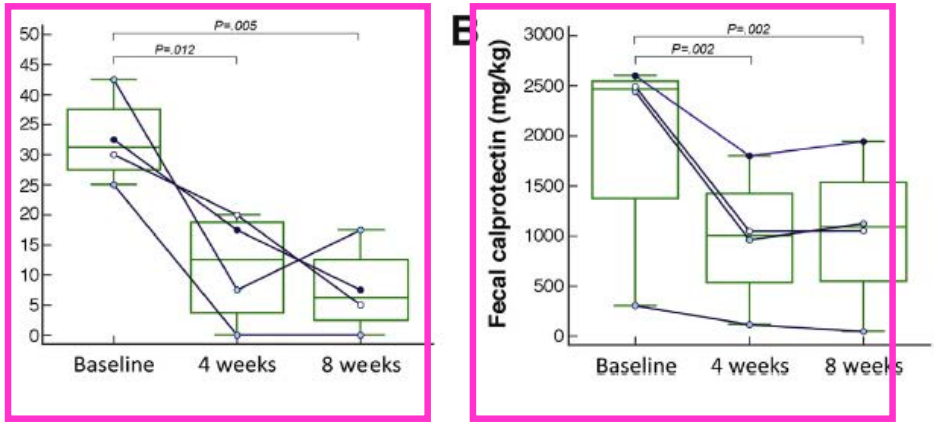
CD-TREAT: Replicating EEN in a Defined Food Diet



Svolos, *et al* (2019). *Gastroenterology*

CD-TREAT

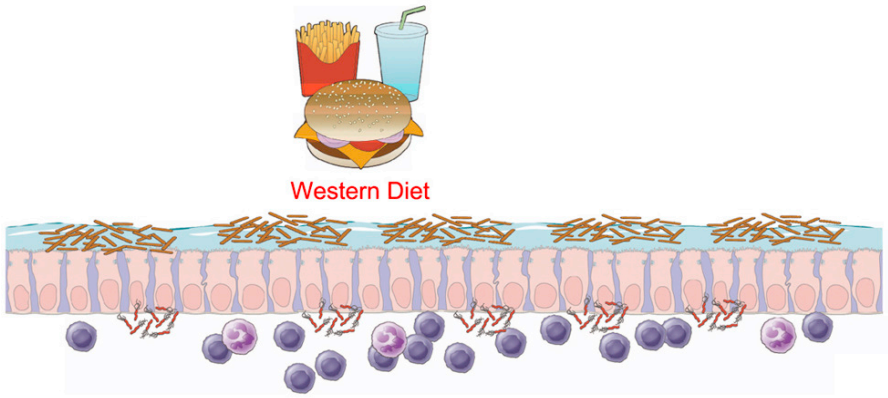
- Adult participants: similar caloric intake and nutrient composition with CD-TREAT and EEN
  - Easier to follow
  - Less reported GI symptoms with CD-TREAT
  - Similar changes in microbiome
- Children with active CD



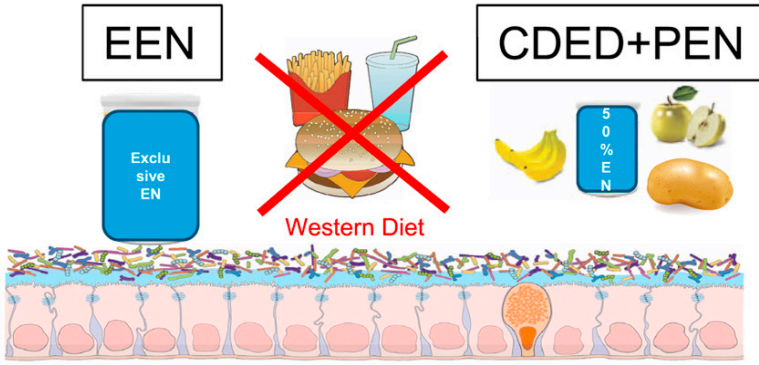
Svolos, *et al (*2019). *Gastroenterology*

Crohn's Disease Exclusion Diet

Dietary Therapy: Crohn's Disease Exclusion Diet + Partial Enteral Nutrition vs. Exclusive Enteral Nutrition



Habitual Diet Triggering Crohn's Disease
Increased Proteobacteria Dysbiosis, Intestinal permeability, Inflammation,
Active Disease



CDED
Remove
Animal Fat
Wheat
Dairy
Red Meat
Emulsifiers
Maltodextrin
Carrageenan

Add
Fruits
Vegetables

Crohn's Disease Exclusion Diet+ PEN vs. EEN
Primary endpoint: CDED+PEN is better tolerated than EEN
Secondary endpoints:
Both CDED+PEN and EEN are effective to achieve remission at week 6
CDED+PEN is superior to sustain remission and reduce inflammation at week 12
CDED+PEN: associated with reduction in Proteobacteria and Intestinal Permeability

Gastroenterology

Levine, *et al (*2019). *Gastroenterology*

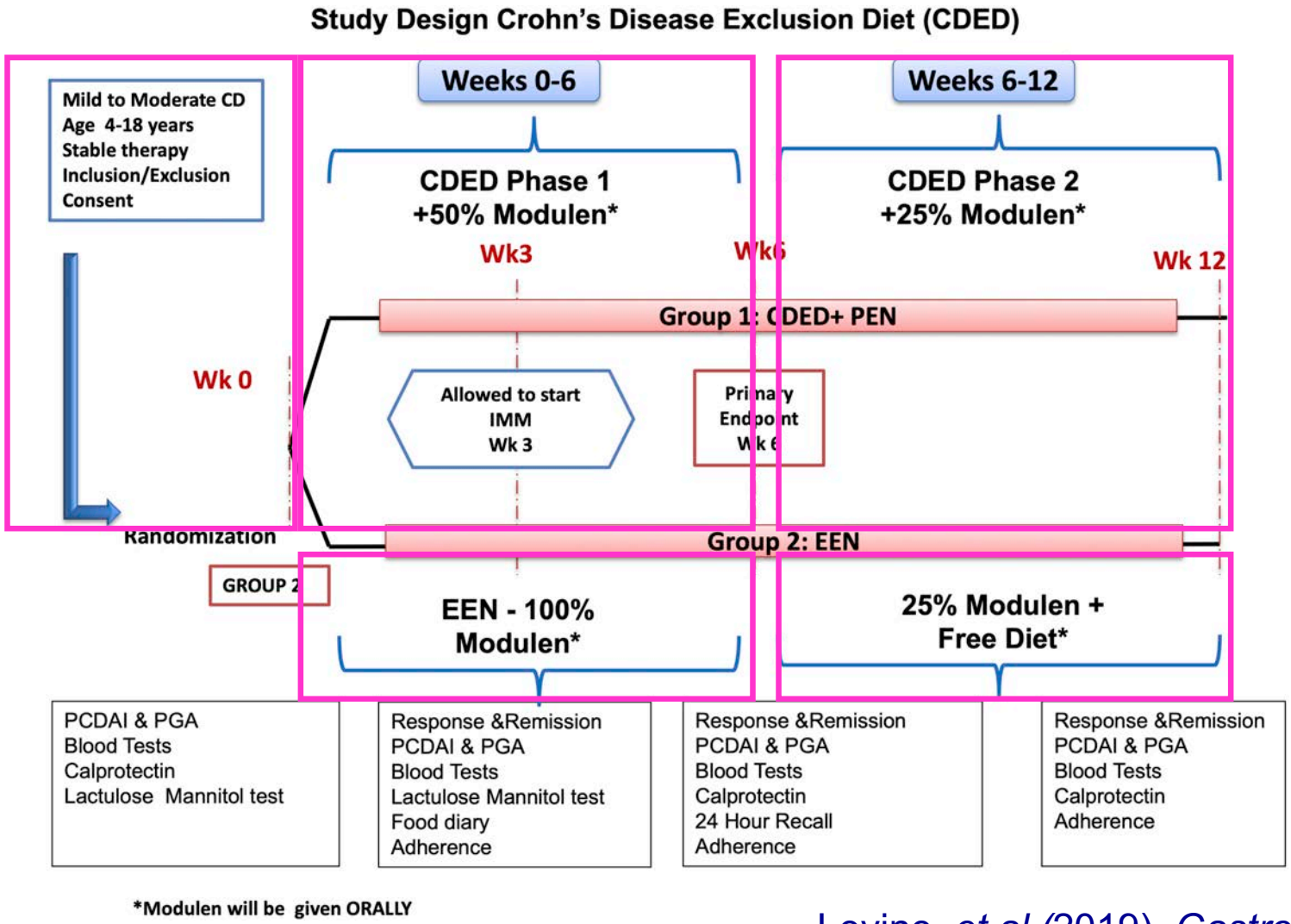
Induction Therapy with Partial Enteral Nutrition for Crohn's Disease

N = 36	Week 0	Week 12	*P*
HBI, mean	5.9 ± 2.7	0.75 ± 1.75	0.000
HBI, median (range)	6.0 (0–13)	0.0 (0–6)	0.000
PCDAI (n = 24)	25.7 ± 8.9	6.44 ± 8.07	0.000
CRP	2.3 ± 2.3	0.81 ± 0.64	0.002
ESR	25.7 ± 12.7	17 ± 8.2	0.001
Hemoglobin	12.0 ± 1.4	12.6 ± 1.3	0.1
Albumin	3.8 ± 0.42	4.12 ± 0.39	0.000

Pairwise comparisons only in subjects with parameters at both time points. Abnormally distributed variables are present as median values. HBI (used in all patients). PCDAI calculated only for children and adolescents through age 18 years.
PCDAI, pediatric Crohn's disease activity index.

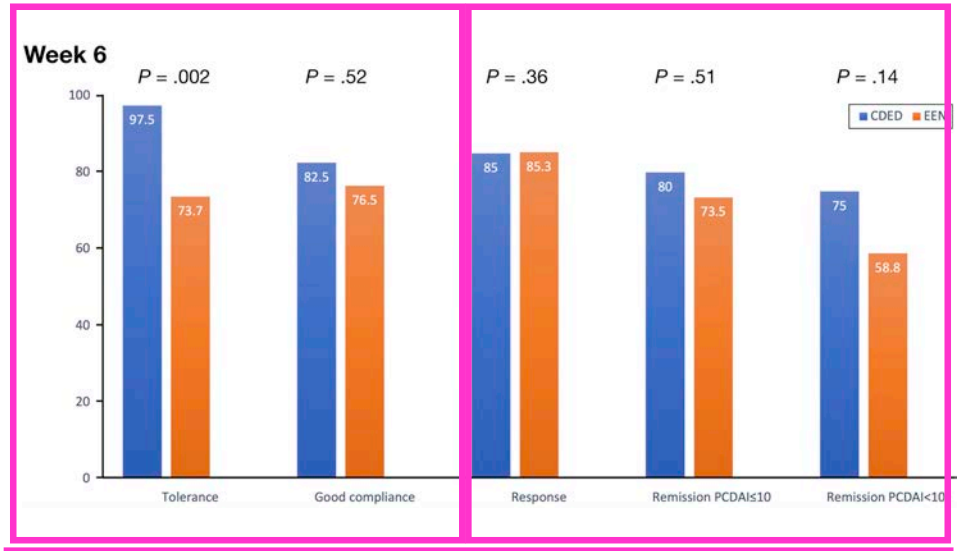
Sigall-Boneh, *et al* (2014). *Inflamm Bowel Dis*

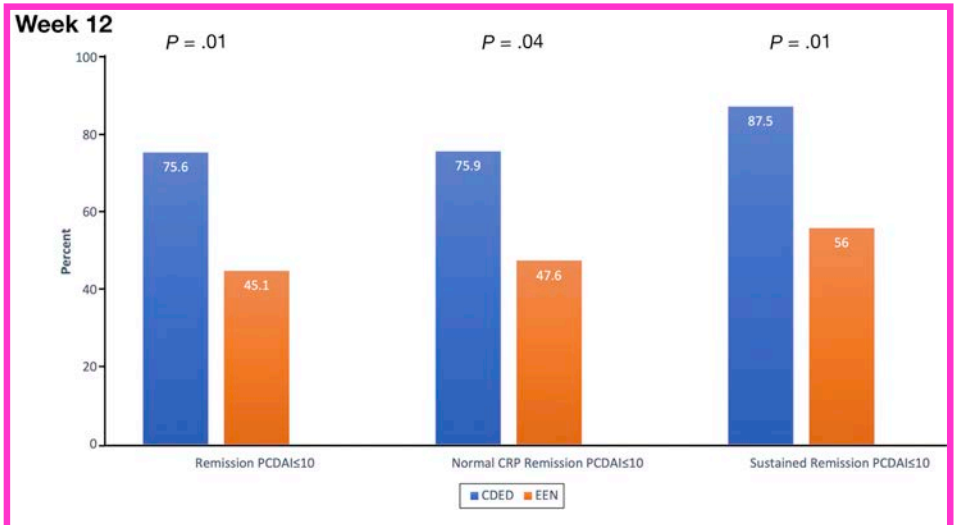
CDED: Clinical Efficacy

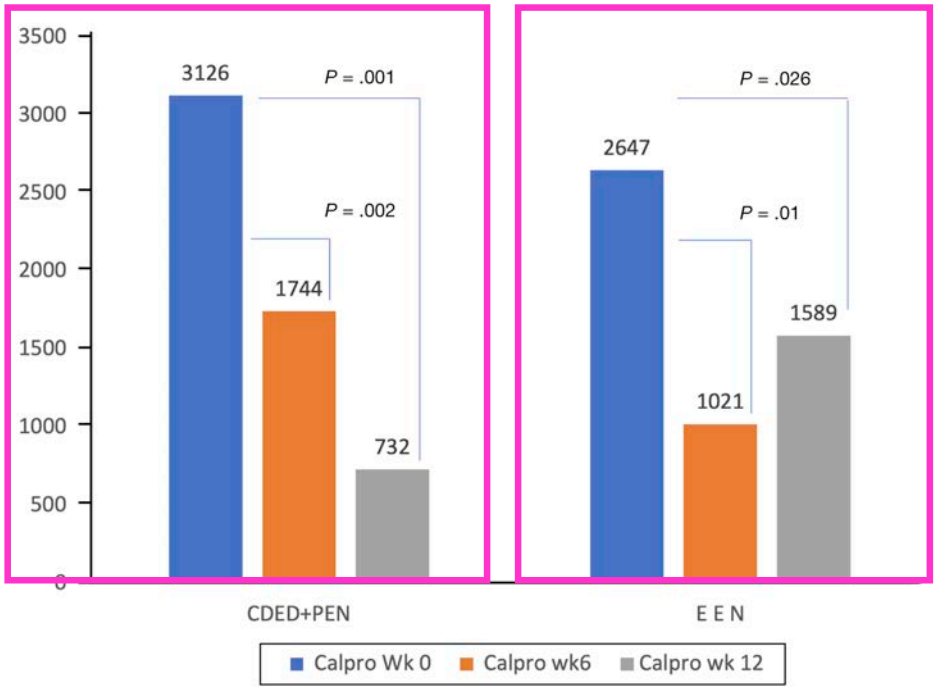


Levine, *et al (*2019). *Gastroenterology*

CDED Induces Clinical and Biochemical Remission

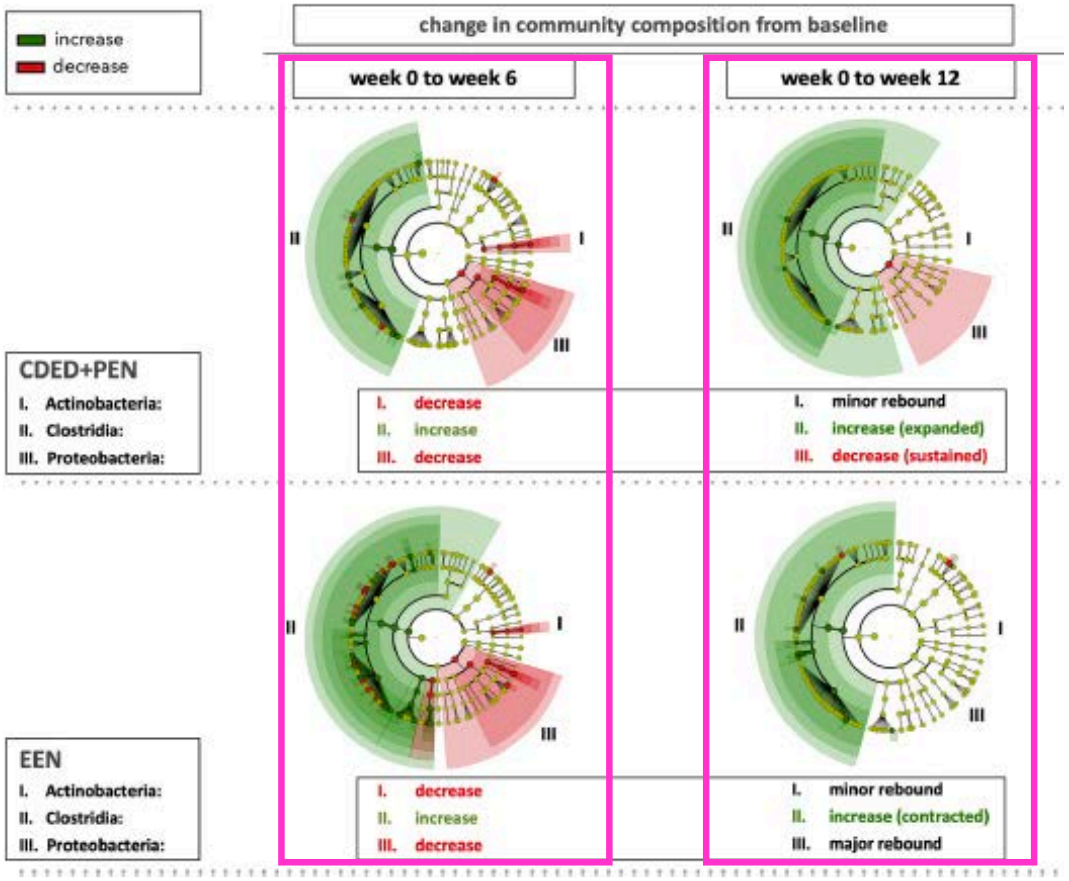






Levine, *et al* (2019). *Gastroenterology*

Microbiome Changes Are Sustained With CDED + PEN



Levine, *et al* (2019). *Gastroenterology*

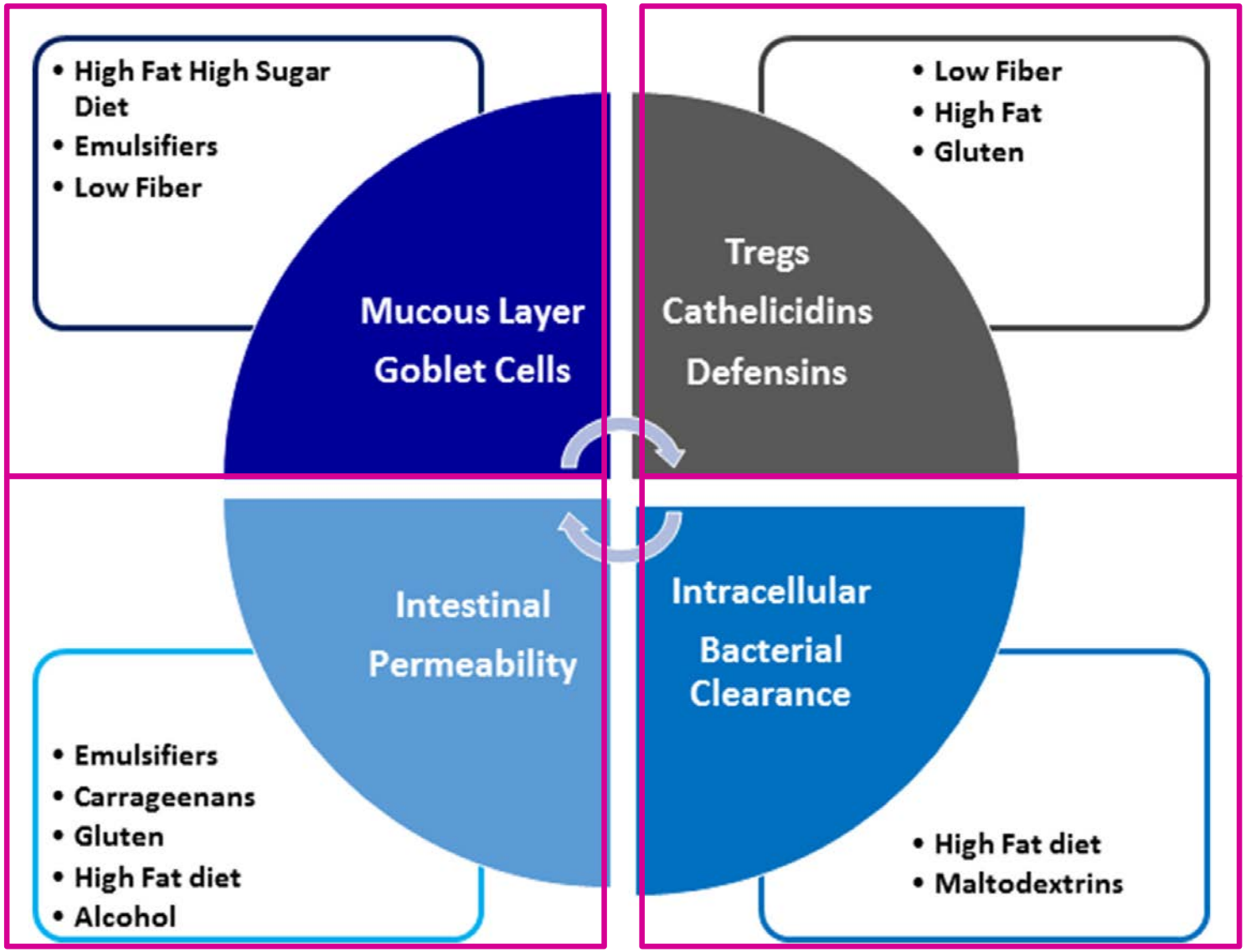
Partial Enteral Nutrition in Patient's Who Have LOR to Anti-TNF Agents

Table 3. Dietary therapy for induction of remission.

Dietary therapy	Remission [n = 13]	Failures [n = 8]
CDED + PEN, n [%]	7 [54%]	5 [62.5%]
CDED alone, n [%]	3 [23%]	1 [12.5%]
Modified EEN + CDED, n [%]	3 [23%]	2 [25%]
Total, n [%]	13 [62%]	8 [38%]

Sigall-Boneh, *et al* (2017). *J Crohn's Colitis*

Impact of Diet on the GI Tract



Adapted from Levine, *et al*. *Gut* 2018

Summary and Take Home Points

- The impact of dietary factors on IBD is multifactorial
  - GI tract permeability
  - Immune cell activation
  - Food antigen recognition
- Enteral therapy is effective as both induction and maintenance regimens in pediatric Crohn's disease
- Specific diets like CDED may be effective in some forms of IBD (primary and adjunct)

Future Directions

- Clinical research
  - Larger scale studies on elimination diets +/- EEN looking at mucosal healing
- Basic/translational research
  - Delineate the specific protective and inflammatory components of diet (i.e. which food additives)
  - Define how different diets impact the microbiome and metabolome
- Health care delivery
  - Improve accessibility
  - Financial issues

Thank You!