UC IRVINE 12TH ANNUAL GI & HEPATOLOGY SYMPOSIUM

29 FEBRUARY 2020

Nutritional Therapies for IBD

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UCLA Health

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Disclaimers

- Scientific advisor for Azora Therapeutics

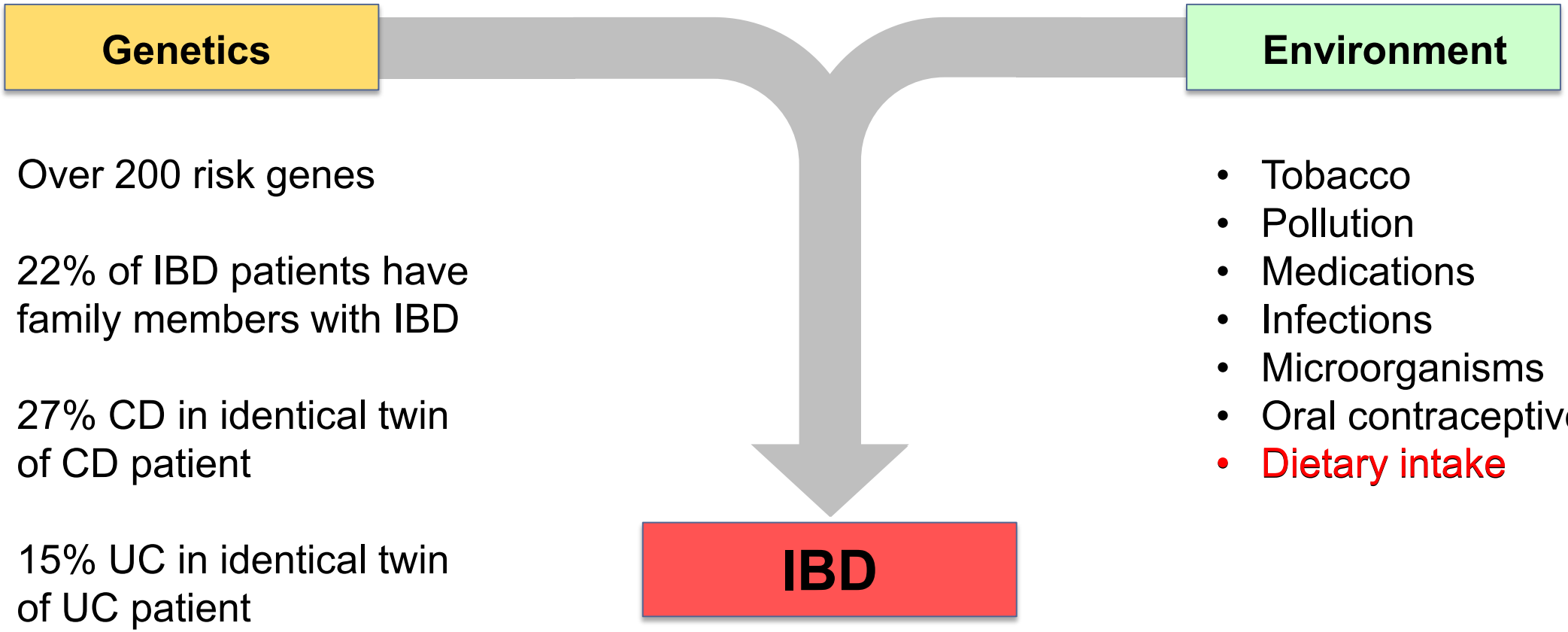
Outline

- Does the Diet Matter?
- Bidirectional Relationship
- Enteral Nutrition
- Solid Food Diets
- Dietary Supplements

- This presentation will broadly touch on major themes and is not intended to be comprehensive
- A lot of research is still needed

Image: Wikipedia

Does the Diet Matter?



- Over 200 risk genes
- 22% of IBD patients have family members with IBD
- 27% CD in identical twin of CD patient
- 15% UC in identical twin of UC patient

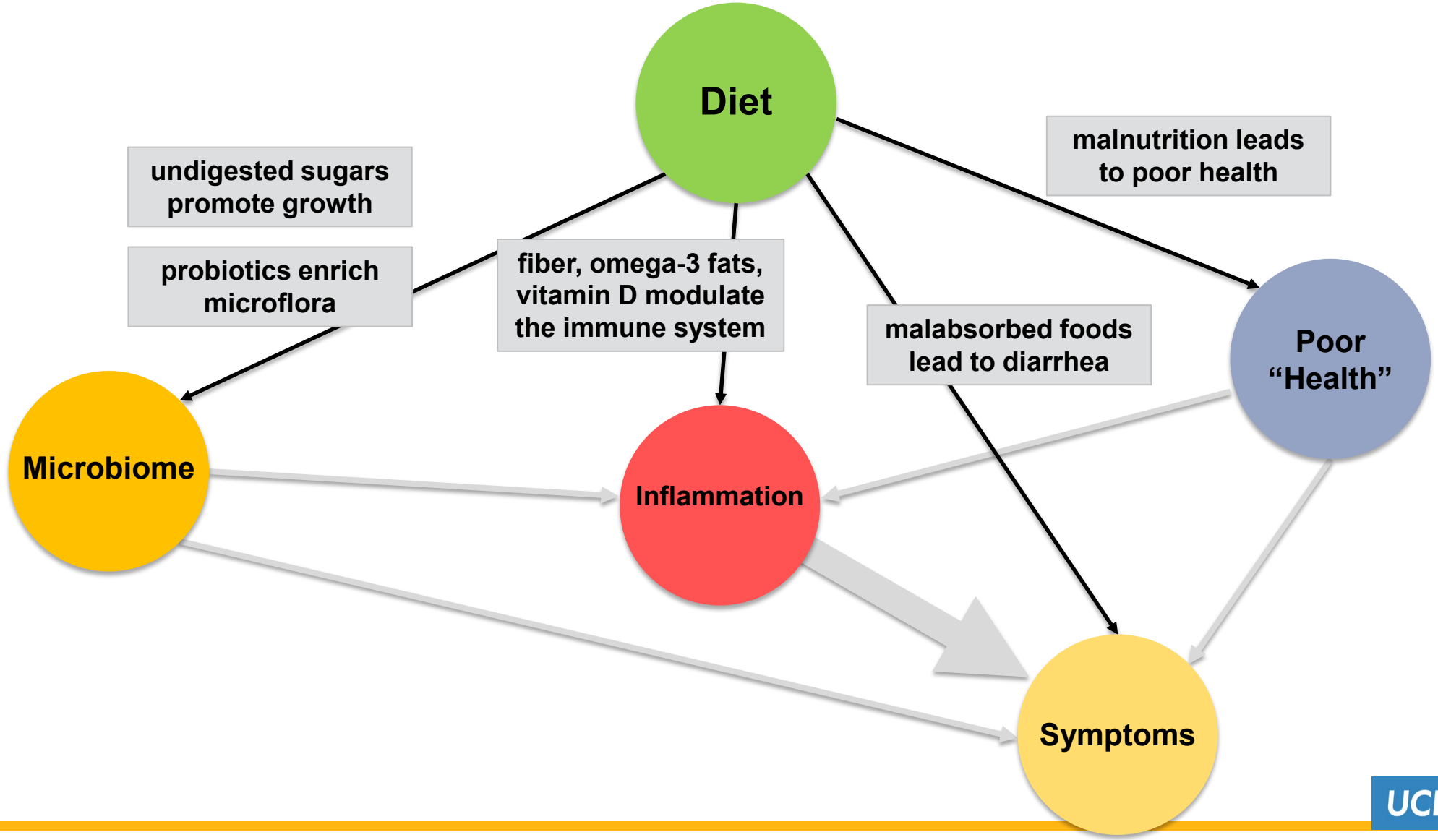
- Tobacco
- Pollution
- Medications
- Infections
- Microorganisms
- Oral contraceptives
- Dietary intake

Jostins *et al*. *Nature* 2012;491(7422):119-124
Halfvarson *et al*. *Inflamm Bowel Dis* 2011;17(1):6-12
Lashner *et al*. *Gastroenterology* 1986;91(6):1396-400

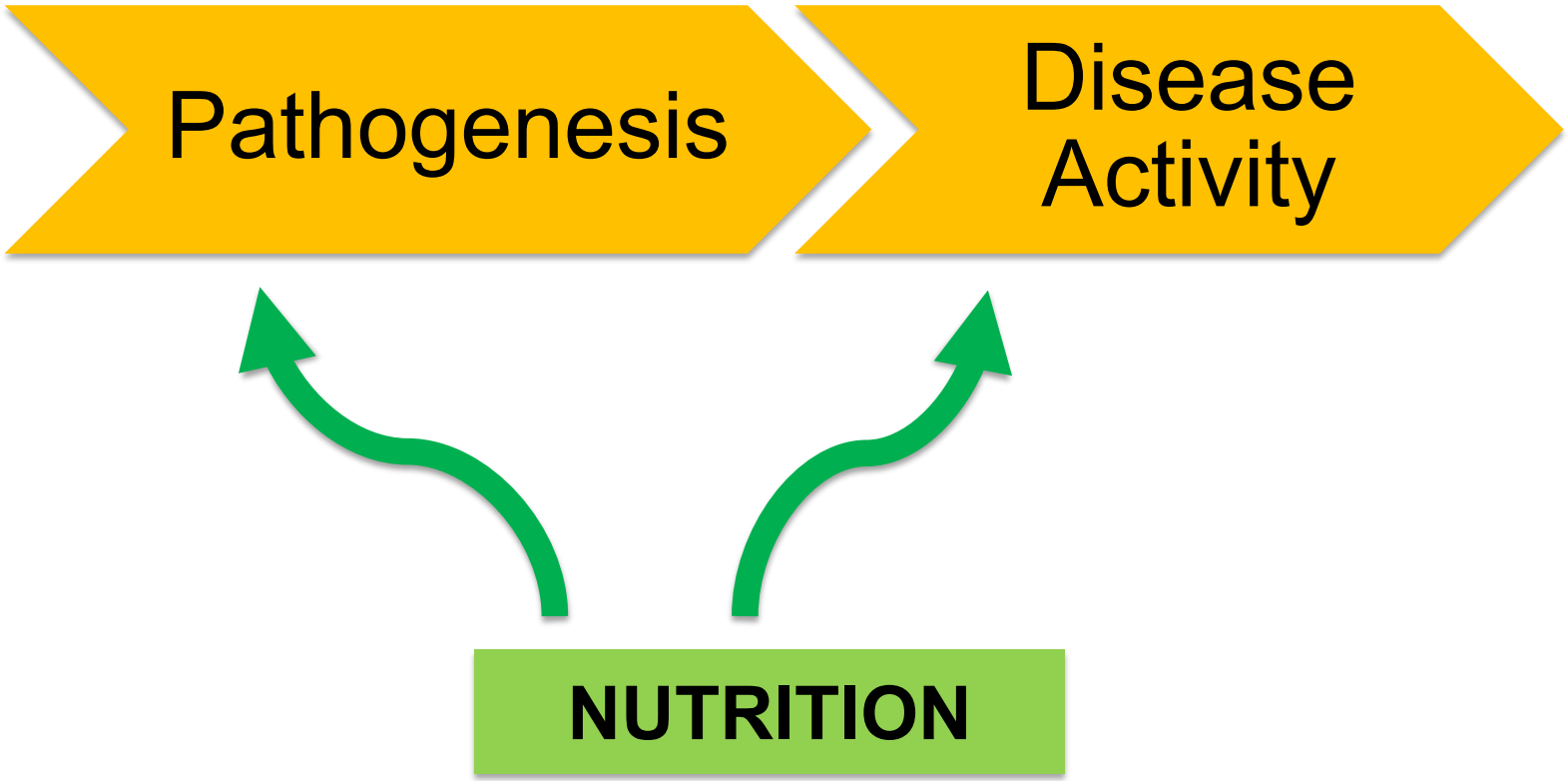
Does the Diet Matter?

- Japanese Survey
  - Surveys of up to 68,000 Japanese (1966-1985)
  - 242 CD patients had ↑ animal protein, ↑ omega-6, ↓ omega-3
- European Prospective Investigation into Cancer
  - Surveys of 203,193 Europeans (1991-1998)
  - 126 UC patients had ↑ omega-6
- Nurses' Health Study
  - Surveys of up to 170,000 women
  - Fiber was associated with ↓ risk of CD but not UC
  - Vitamin D was associated with ↓ risk of CD but not UC

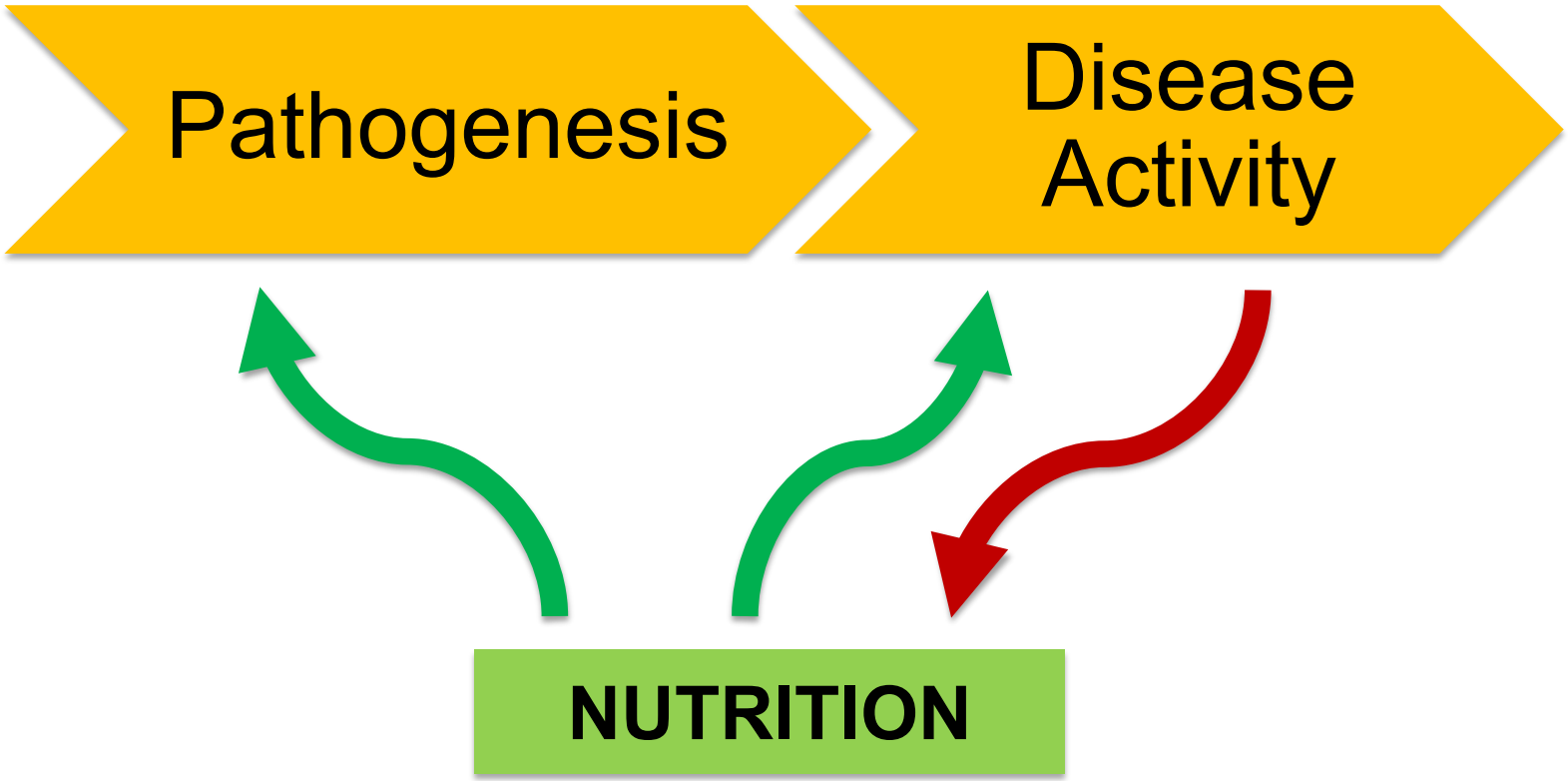
How Does Diet Affect Disease Activity?



Bidirectional Relationship of Nutrition and IBD



Bidirectional Relationship of Nutrition and IBD

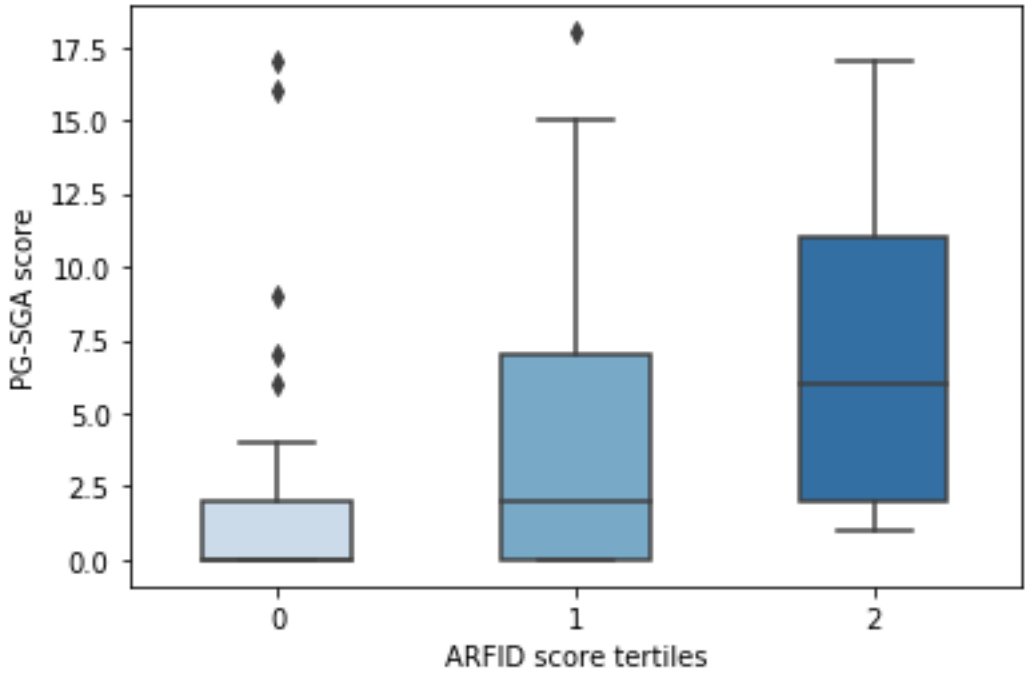


High Risk of Restrictive Eating Behaviors

- 58% had characteristics of restrictive eating

- Most commonly reported symptoms influencing intake: pain (14%), diarrhea (12%), fatigue (12%)

- Restrictive eating patterns associated with malnutrition



Yelencich *et al* 2020

What are Dietary Strategies for IBD?

Established Evidence

- Enteral nutrition

Emerging Evidence

- Solid food diets
- Probiotics

Extrapolated Evidence

- Omega-3 fatty acids
- Fiber

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Enteral Nutrition

- Specialized liquid formulae that are either delivered orally or through a feeding tube

Premise

- Provides a supplementary source of calories
- Reduces intake of “pro-inflammatory” substances
- Preserves integrity of bowel
- Modulates gut immune system

Enteral Nutrition

Crohn's Disease

- Effective for induction and maintenance of remission in CD
- Can be used as monotherapy when corticosteroids not possible (Grade A evidence)

Ulcerative Colitis

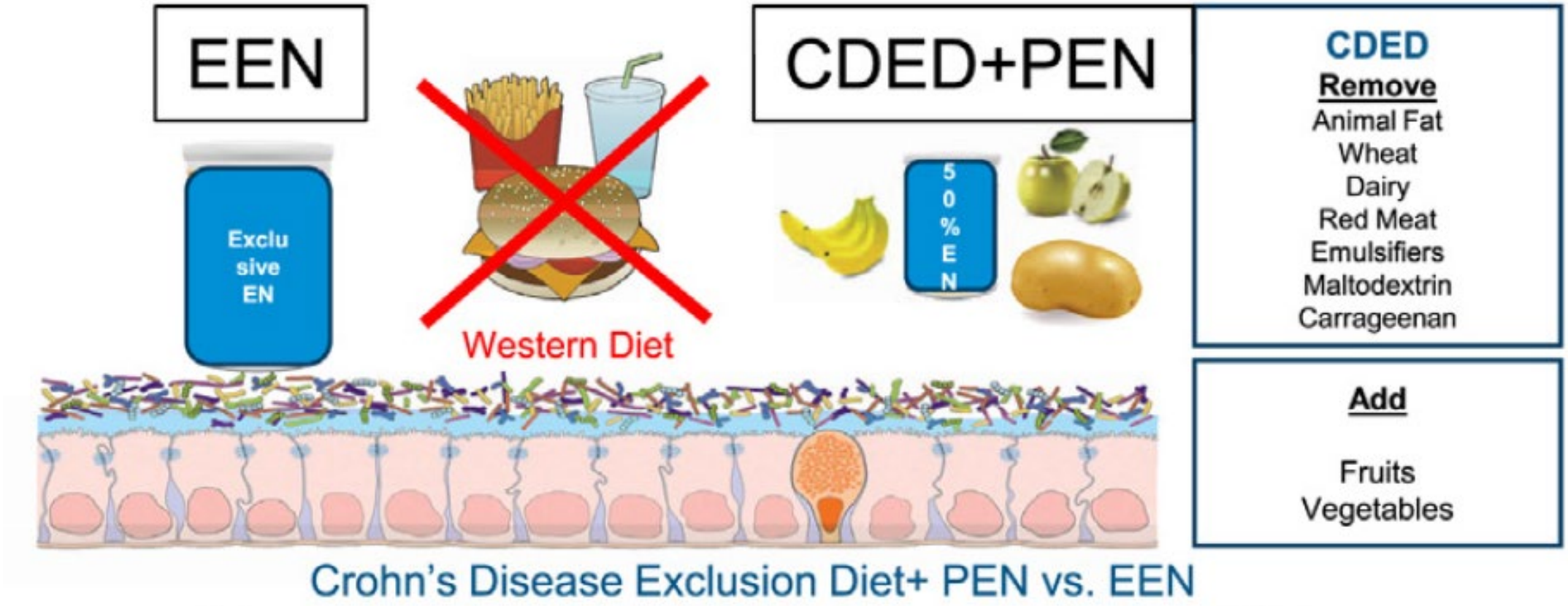
- No clear benefit

But …

- Adherence is very challenging due to discomfort, distaste, social reasons, insurance coverage, etc.

Loch *et al*. Clin Nutr 2006;25(2);260-74

What about *Partial* Enteral Nutrition?



Levine *et al*. Gastroenterology 2019;157:440-50

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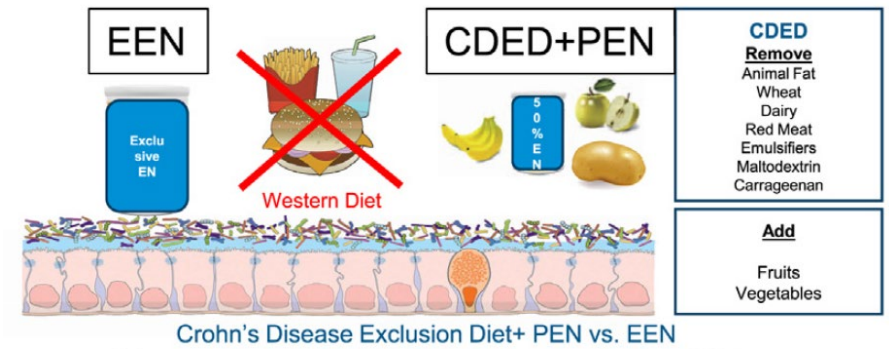
What about *Partial* Enteral Nutrition?



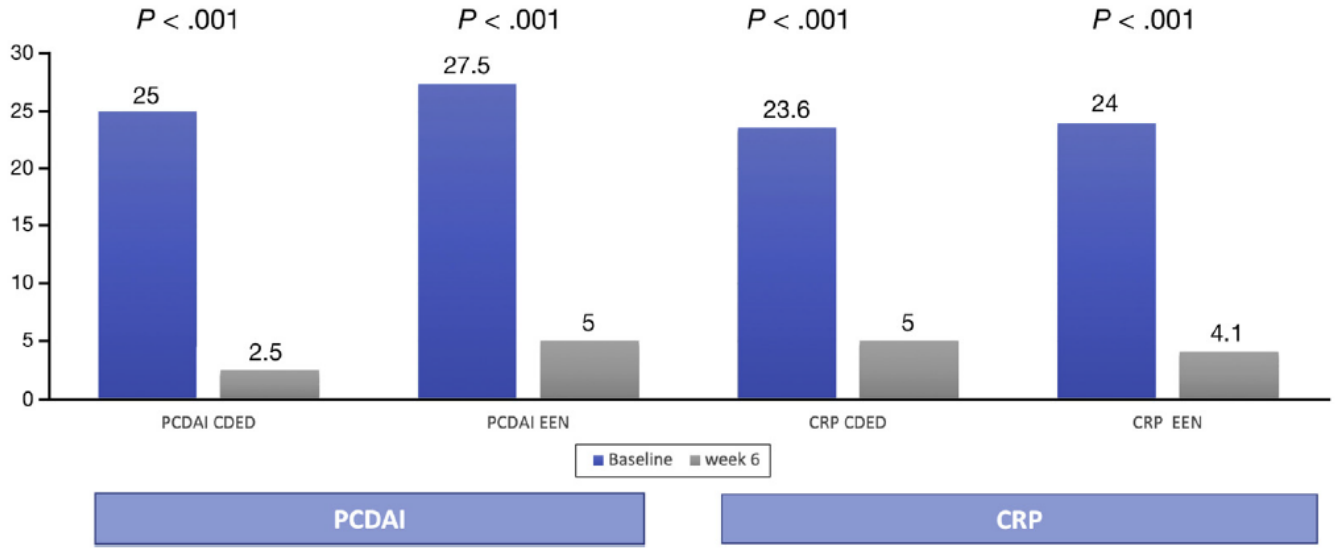
Week 1 - 6

EEN (100%)
(n = 34)

PEN (50%)
CDED (50%)
(n = 40)

Findings

- PEN and EEN improved symptoms and CRP



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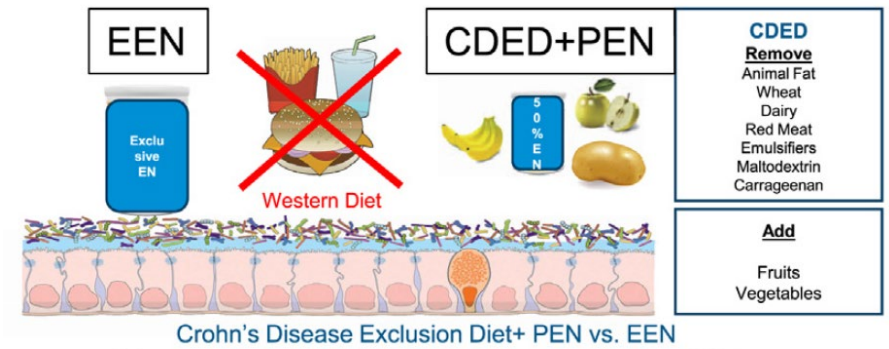


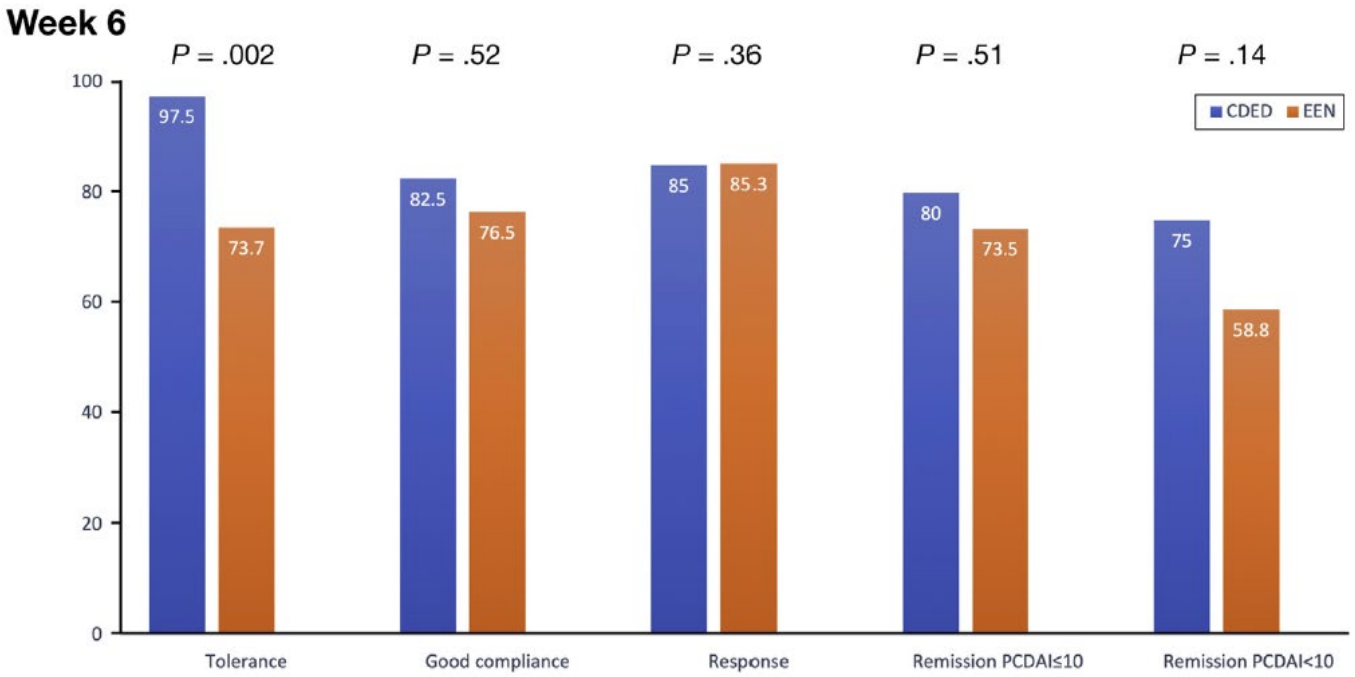
Week 1 - 6

EEN (100%)
(n = 34)

PEN (50%)
CDED (50%)
(n = 40)

Findings

- PEN was more tolerable than EEN
- PEN ~ EEN for achieving 6-week response and remission



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Established Evidence

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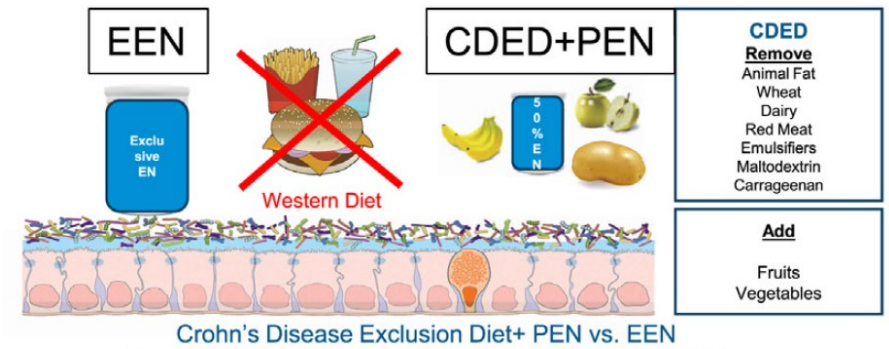
Emerging Evidence

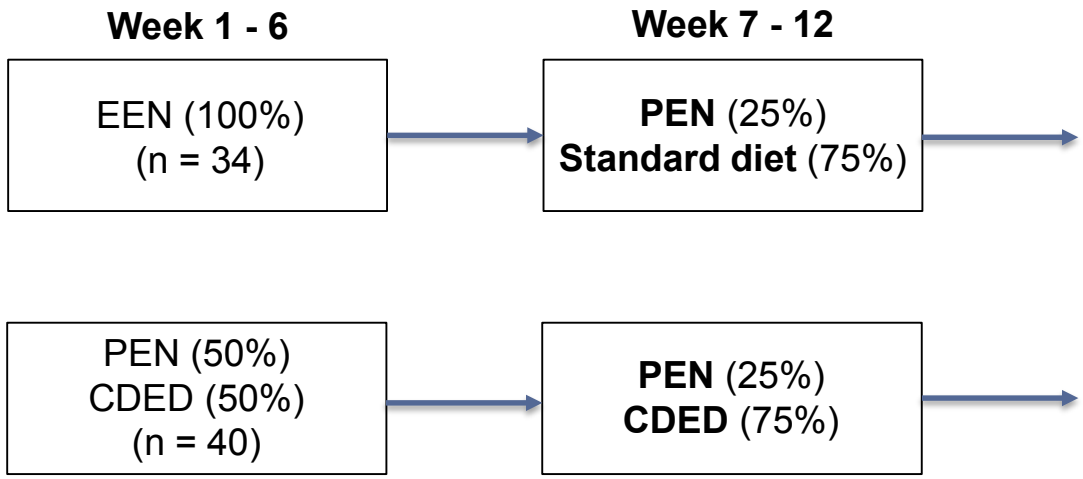
- Solid food diets
- Probiotics

Extrapolated Evidence

- Omega-3 fatty acids
- Fiber

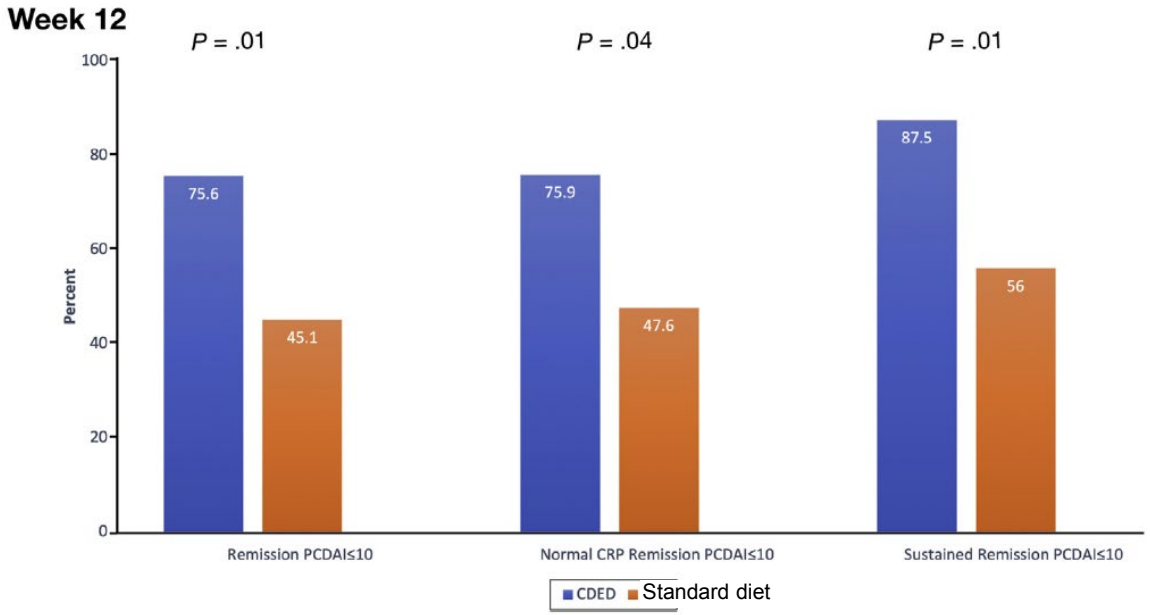
What about *Solid Food* Diets?





Findings

- CDED was superior to standard diet for sustained remission



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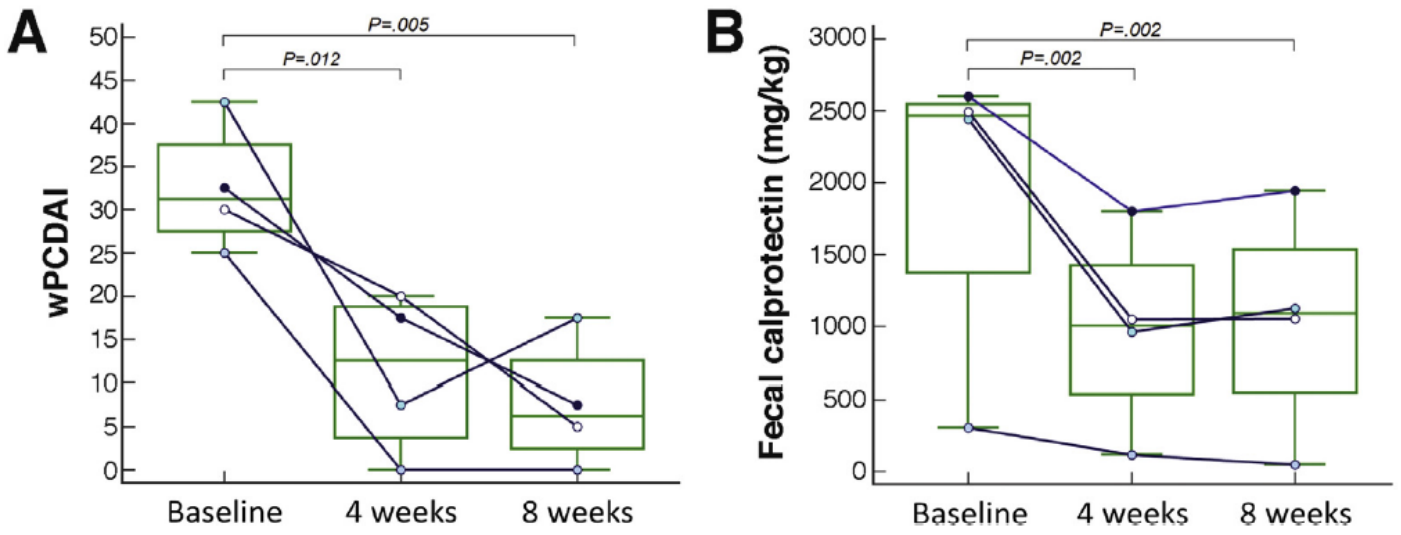
CD Exclusion Diet

“Forbidden Foods”
Dairy products, margarine
Wheat, breakfast cereals, breads and baked goods, yeast for baking
Gluten products, soy products, potato or corn flour
Processed or smoked meats and fish
Sauces, salad dressings, syrups and jams
Canned products, dried fruits
Packaged snacks
Soft drinks, fruit juices, sweetened beverages, alcoholic beverages, coffee
Candies, chocolate, cakes, cookies, and gum

CD-TREAT Diet

- Aim to develop solid food diet that recapitulates the microbiome changes from using exclusive enteral nutrition
- Diet components still proprietary
- Tested on 5 children with mild-to-moderate CD



Svolos *et al*. Gastroenterology 2019;156

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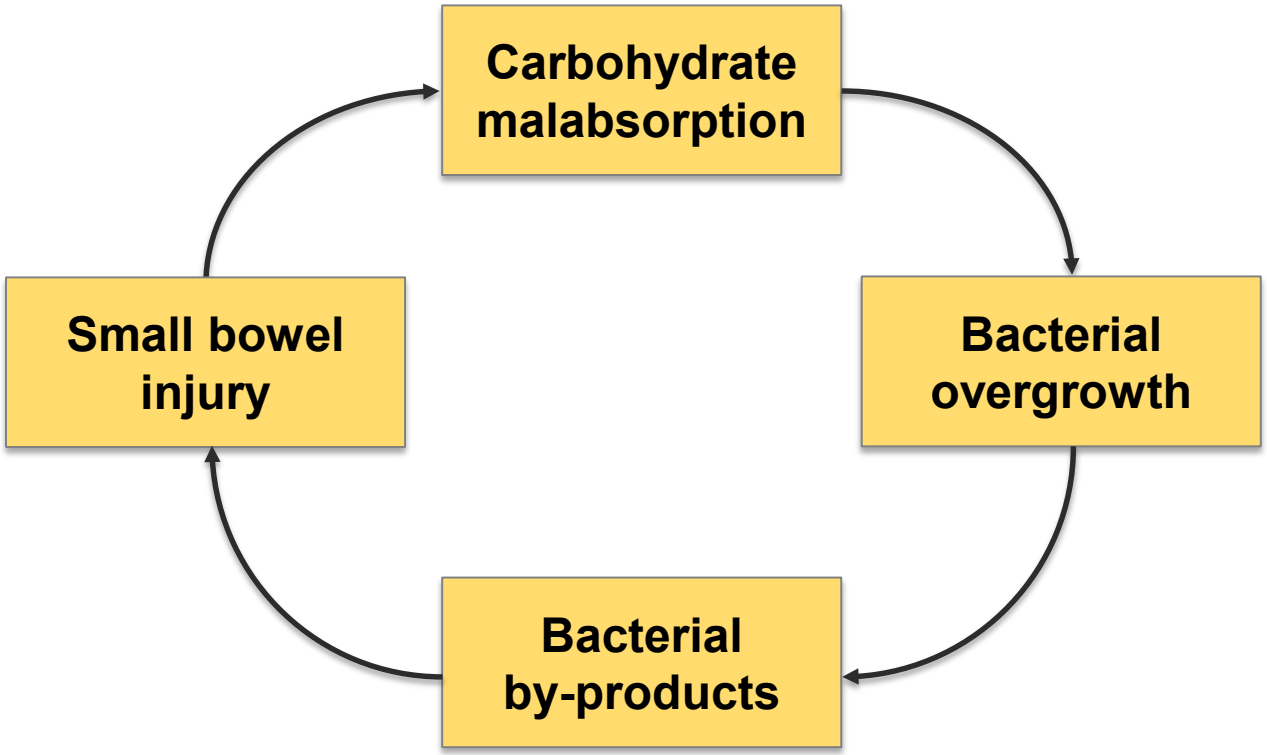
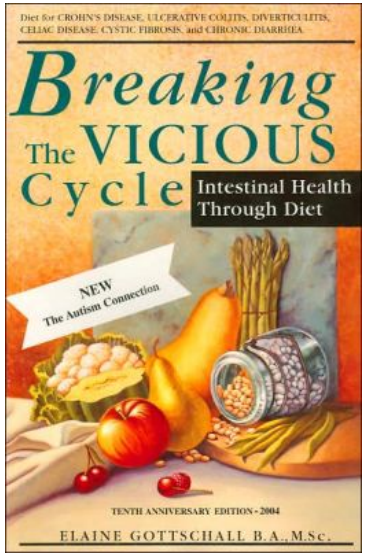
Specific Carbohydrate Diet

- Originally developed to treat celiac disease
- Popularized by the book “Breaking the Vicious Cycle”
- Elimination of di-, oligo-, and polysaccharides





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Specific Carbohydrate Diet

Allowed (“Legal food”)	Not Allowed (“Illegal food”)
All fresh meats, fish, shellfish	Packaged, deli, preserved meats
Most vegetables	Potatoes, corn, starchy vegetables. Tapioca starch, cornstarch
Most fruits	Canned fruits, Green bananas, plantains and young coconut
All fats and oils, including butter	
Cheeses (aged >30days)	Cream, ricotta, mozzarella, other soft un-aged cheeses
Lactose free yogurt	Milk, store- bought yogurt
Honey	All other sweeteners (cane sugar, artificial sweeteners, agave, maple syrups)
Legumes (soaked) (lentils &most beans)	Grains (wheat, rye, oats, rice, buckwheat, quinoa) Bean sprouts, fava beans, garbanzo beans, soy beans
Nuts : Almonds, pecans, hazelnuts, walnuts, cashews, chestnuts, peanuts, brazil nuts	Not candied, salted, flavored nuts
Drinks: weak tea/coffee, water, mineral water, club soda, dry wine, gin, scotch, bourbon, vodka	Instant coffee, fruit juices, milk, soda, sweet wines, flavored liqueurs, brandy, sherry, beer

Specific Carbohydrate Diet

Seattle Children's Hospital (2014)

- 7 CD patients had normalization of symptoms, albumin, and CRP by 3 months
- Stool inflammation markers significantly improved
- No concurrent medications

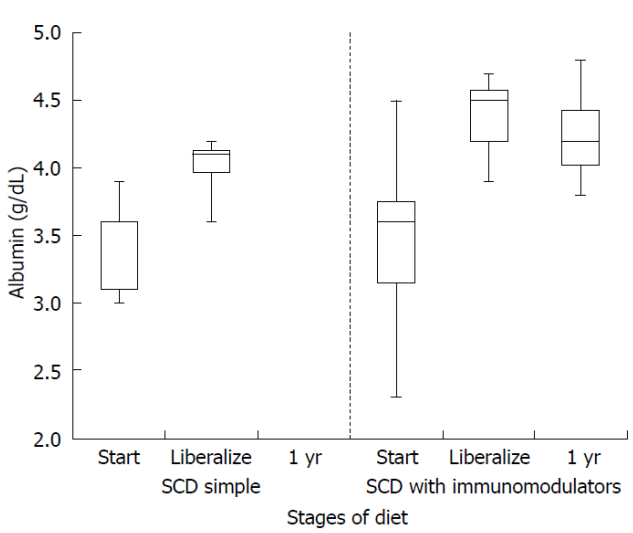
Children's Healthcare of Atlanta (2014)

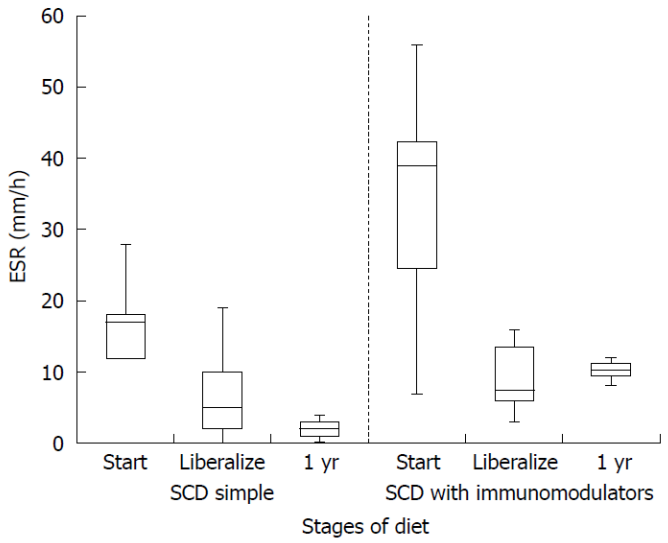
- 6/9 CD patients had clinical remission by 3 months
- No changes to existing medications

Specific Carbohydrate Diet

Stanford Children's Hospital (2016)

- 11 CD pediatric patients
- Albumin, ESR, height, weight improved and remained stable
  - … even after progressive liberalization of diet





What are Dietary Strategies for IBD?

Established Evidence

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Emerging Evidence

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Extrapolated Evidence

- Omega-3 fatty acids
- Fiber

Where Do We Stand with Probiotics?

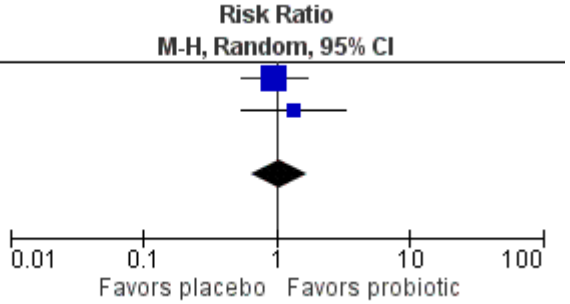
Crohn's Disease

- No known benefit

Study or Subgroup	Probiotic Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Schultz 2004	4	5	5	6	71.6%	0.96 [0.55, 1.69]
Steed 2010	8	19	5	16	28.4%	1.35 [0.55, 3.31]
Total (95% CI)		**24**		**22**	**100.0%**	**1.06 [0.65, 1.71]**
Total events	12		10			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.57$, df = 1 (P = 0.45); $I^2 = 0\%$

Test for overall effect: Z = 0.23 (P = 0.82)



Ulcerative Colitis

- Potential benefit from multi-strain probiotics in the *induction* and *maintenance* of remission

Pouchitis

- Potential benefit from multi-strain probiotics

Limketkai *et al*. 2020

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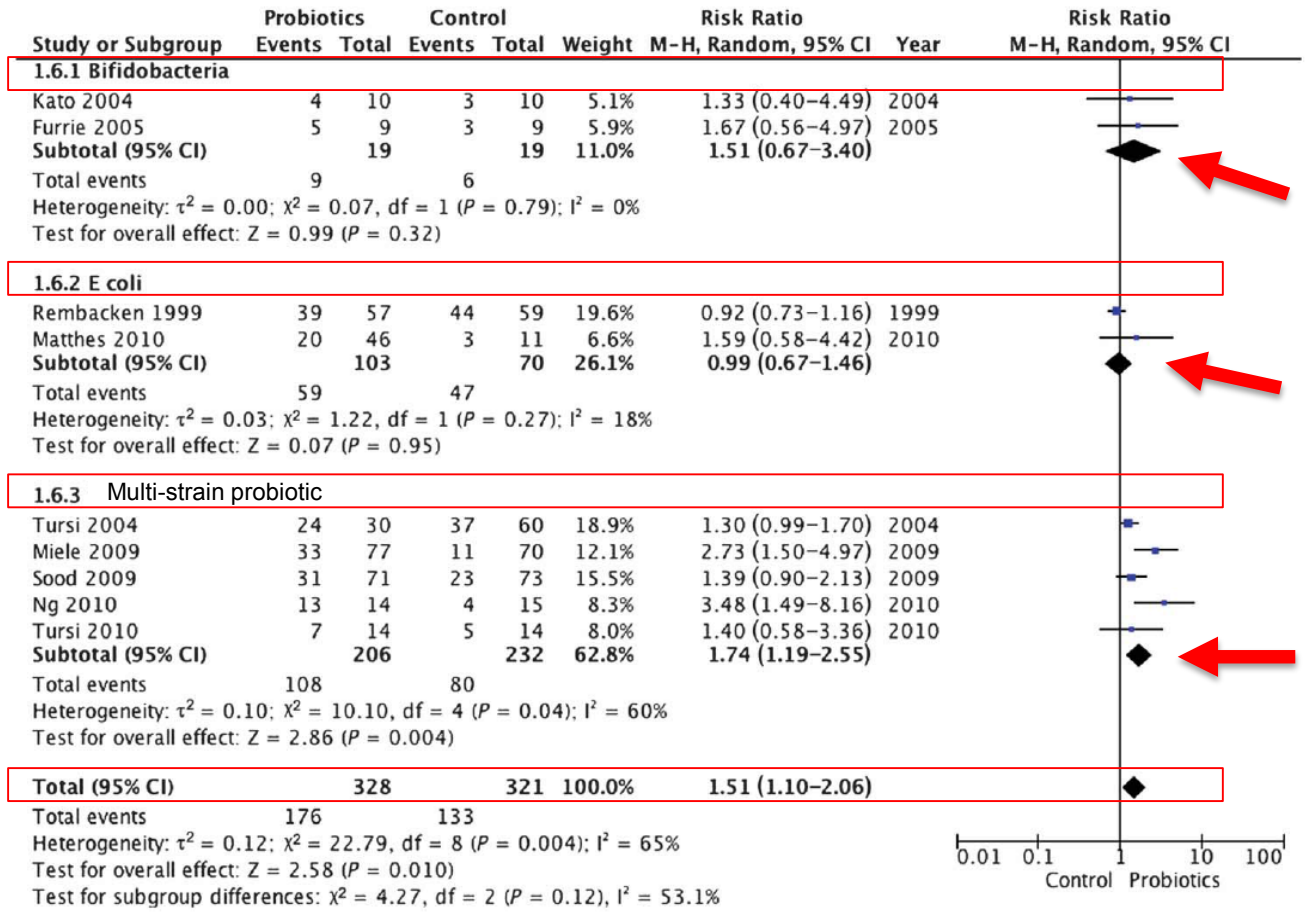
Probiotics for *Induction* of Remission



Shen J *et al*. *Inflamm Bowel Dis* 2014;20:21-35

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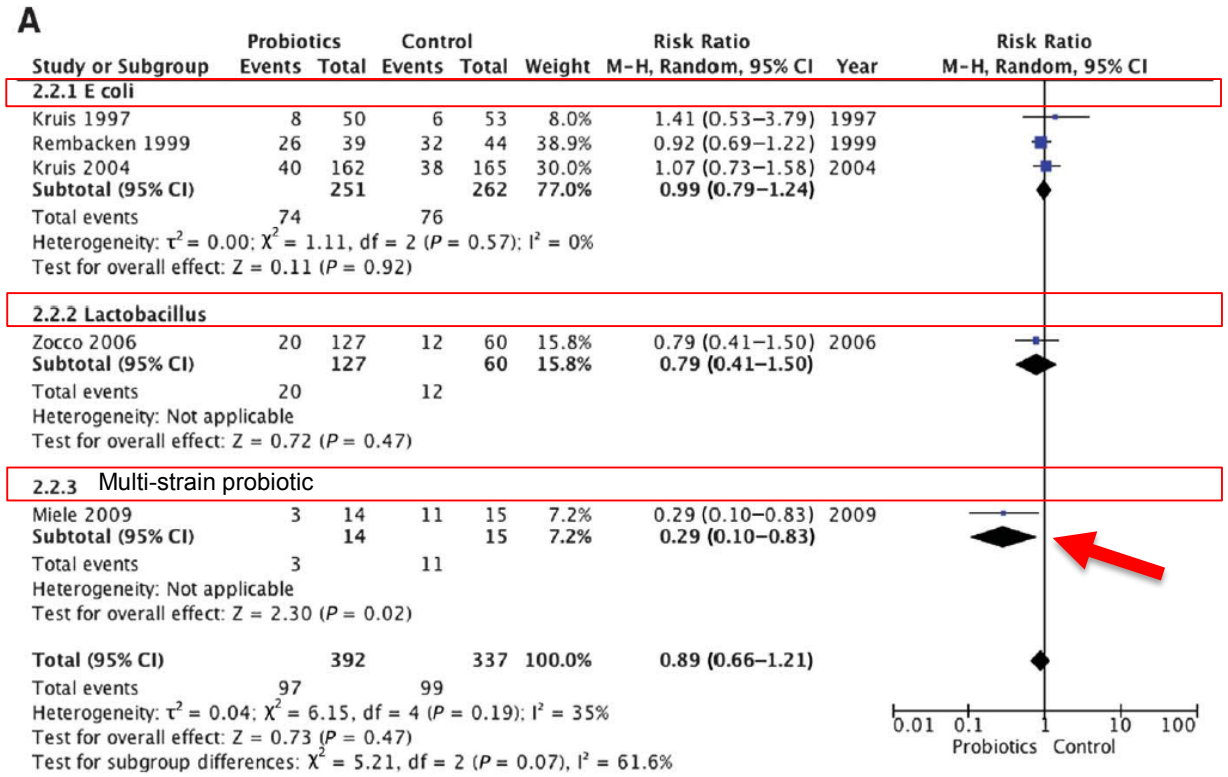
Probiotics for *Maintenance* of Remission



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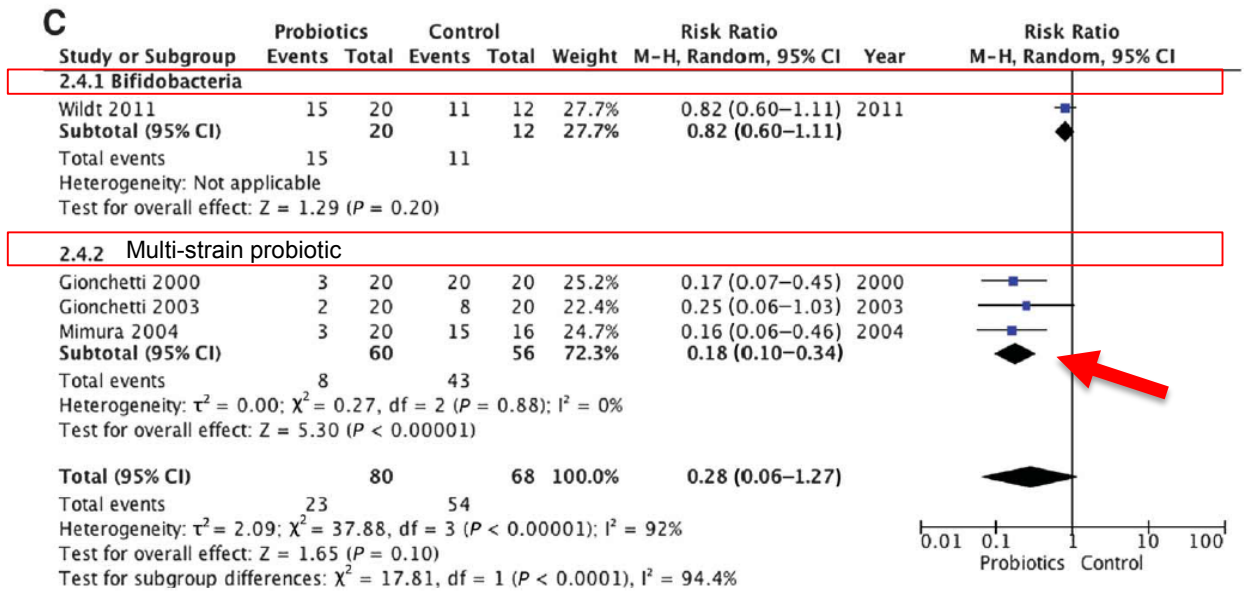
Probiotics for Pouchitis



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Where Do We Stand with Probiotics?

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Ulcerative Colitis

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Emerging Evidence

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Extrapolated Evidence

- Omega-3 fatty acids
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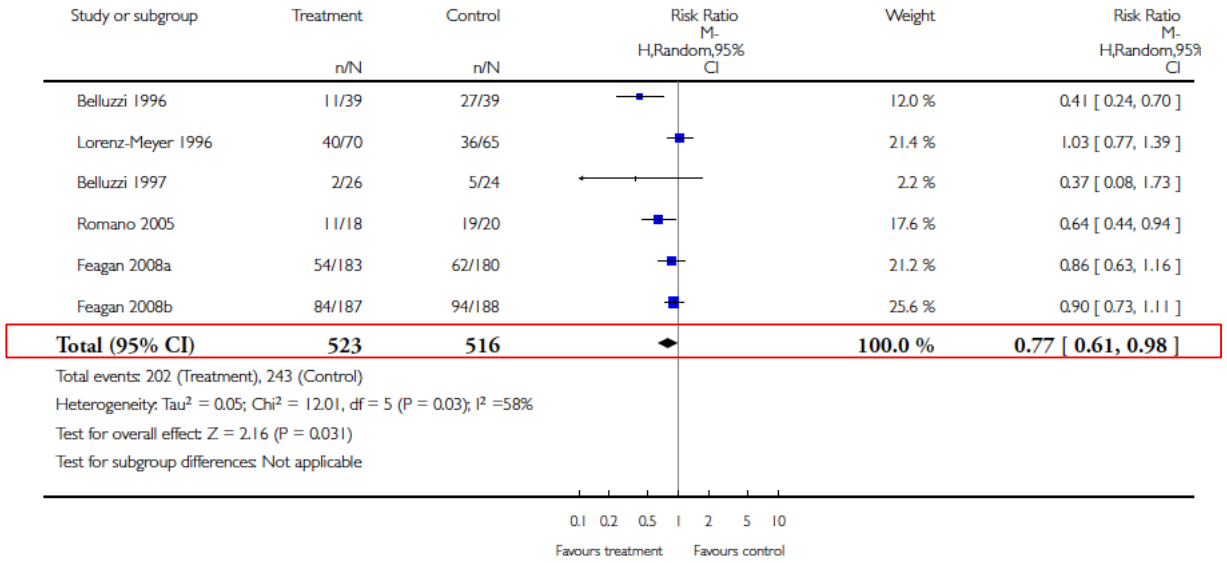
Omega-3 Fatty Acids

Crohns' Disease

- Induction: No trials
- Maintenance:
  - Cochrane review of 1039 patients → marginal benefit



Ulcerative Colitis

- Induction
  - Inconsistent results
  - Largest study (86 patients) → no difference
- Maintenance
  - 3 trials (138 patients) → no difference in 1-2 year relapse rates

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Fiber

- Fiber is non-digestible plant-based substance

- Premise
  - Converted to short chain fatty acids (SCFA)
  - SCFA serve as fuel for colonocytes
  - SCFA enhances microbial diversity toward a favorable profile
  - SCFA has anti-inflammatory properties

- Current Evidence
  - Inconsistent data with lack of high-quality studies
  - Solid food diets with some data of benefit encourage use of **fiber** (fruits + vegetables)

Summary

- Maintain good hydration
- Eat “healthy” balanced diet (plant-based diet? Mediterranean diet?)
  - Sounds simple, but research up to 2019 supports this principle for IBD
  - Current data suggest the benefit of **exclusion** (red meat? processed foods? refined carbohydrates? emulsifiers?) and **inclusion** (fruits and vegetables)
- Consider fiber (if not at risk of obstruction)
- Consider probiotics (UC)
- Much more research is needed!

Thank You

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