Nutritional Interventions for IBS

Transforming Patient Outcomes with Diet

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Disclaimer

- Azora Therapeutics (consultant, equity)

Objectives

- To understand the mechanisms that link diet to symptoms of IBS
- To describe different dietary interventions and their relative efficacy for IBS
- To list dietary supplements that may be effective to treat IBS

Outline

- What is Irritable Bowel Syndrome?
- Why Diets for IBS?
- What Diets for IBS?
- What About Dietary Supplements?

What is Irritable Bowel Syndrome?

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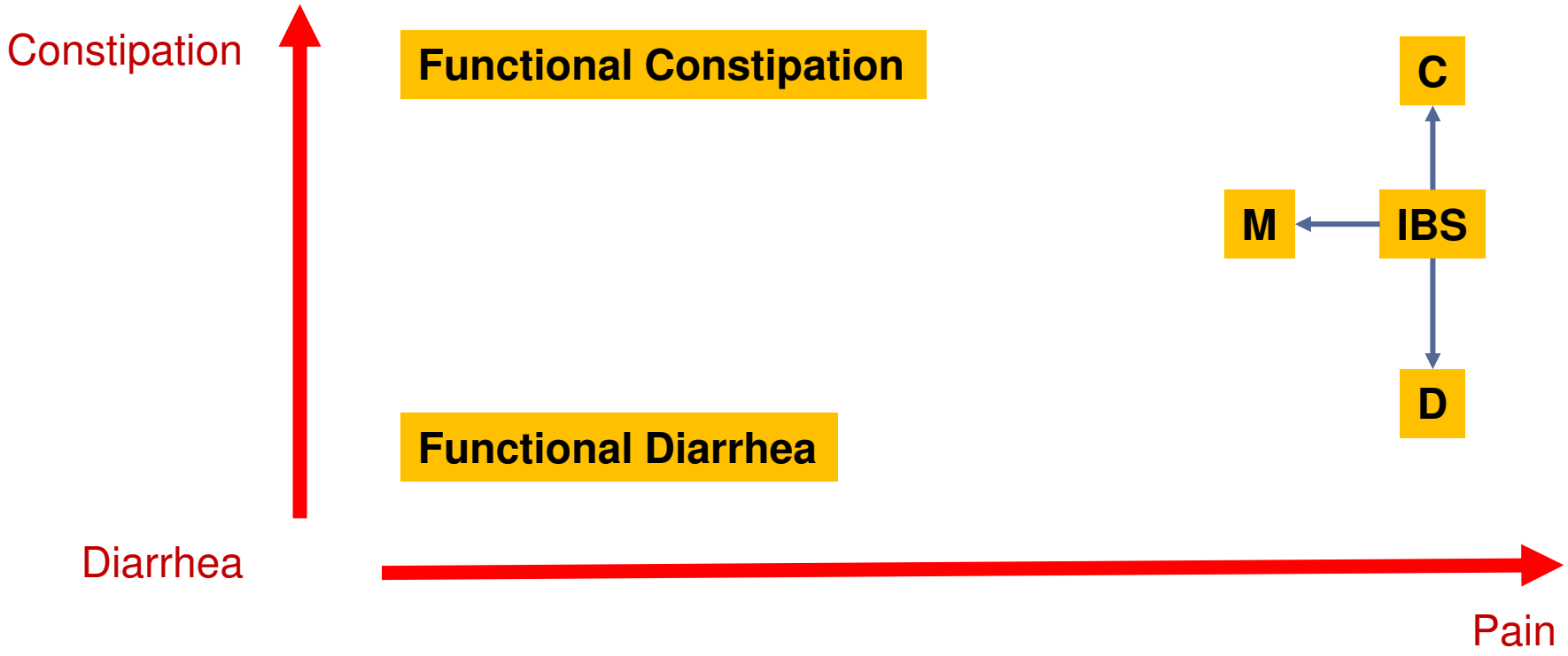
What is Irritable Bowel Syndrome?

Functional GI Disorders → Disorders of Gut-Brain Interaction (DGBI)



Lacy *et al. Gastroenterology* 2016;150:1393-1407

What is Irritable Bowel Syndrome: Rome IV Criteria

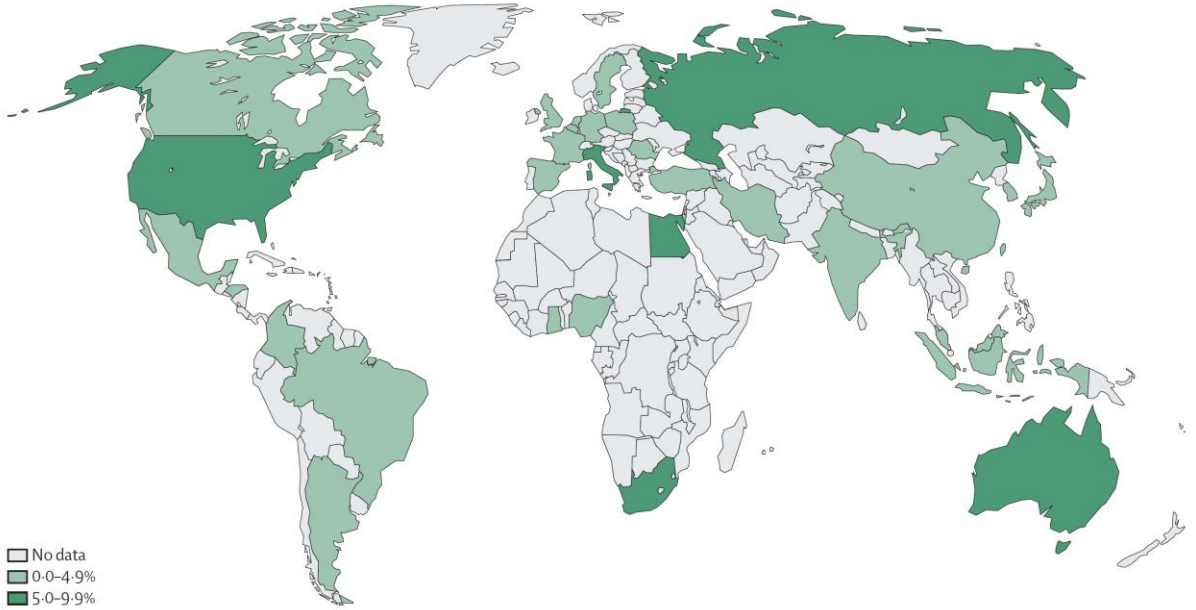
Recurrent abdominal pain, on average, at least **1 day per week** in the **last 3 months** with symptom onset at least **6 months** prior to diagnosis, associated with 2 or more of the following criteria:

- Related to defecation
- Associated with a change in stool frequency
- Associated with a change in stool form (appearance)

Sperber. *Aliment Pharmacol Ther* 2021;54(Suppl 1):S1-11

The Burden of IBS

- Pooled global prevalence
  - DGBI: 40.3%
  - IBS (Rome IV): 3.8% to 4.1%
- Prevalence in US:
  - DGBI: 39.9%
  - IBS: 5.3%

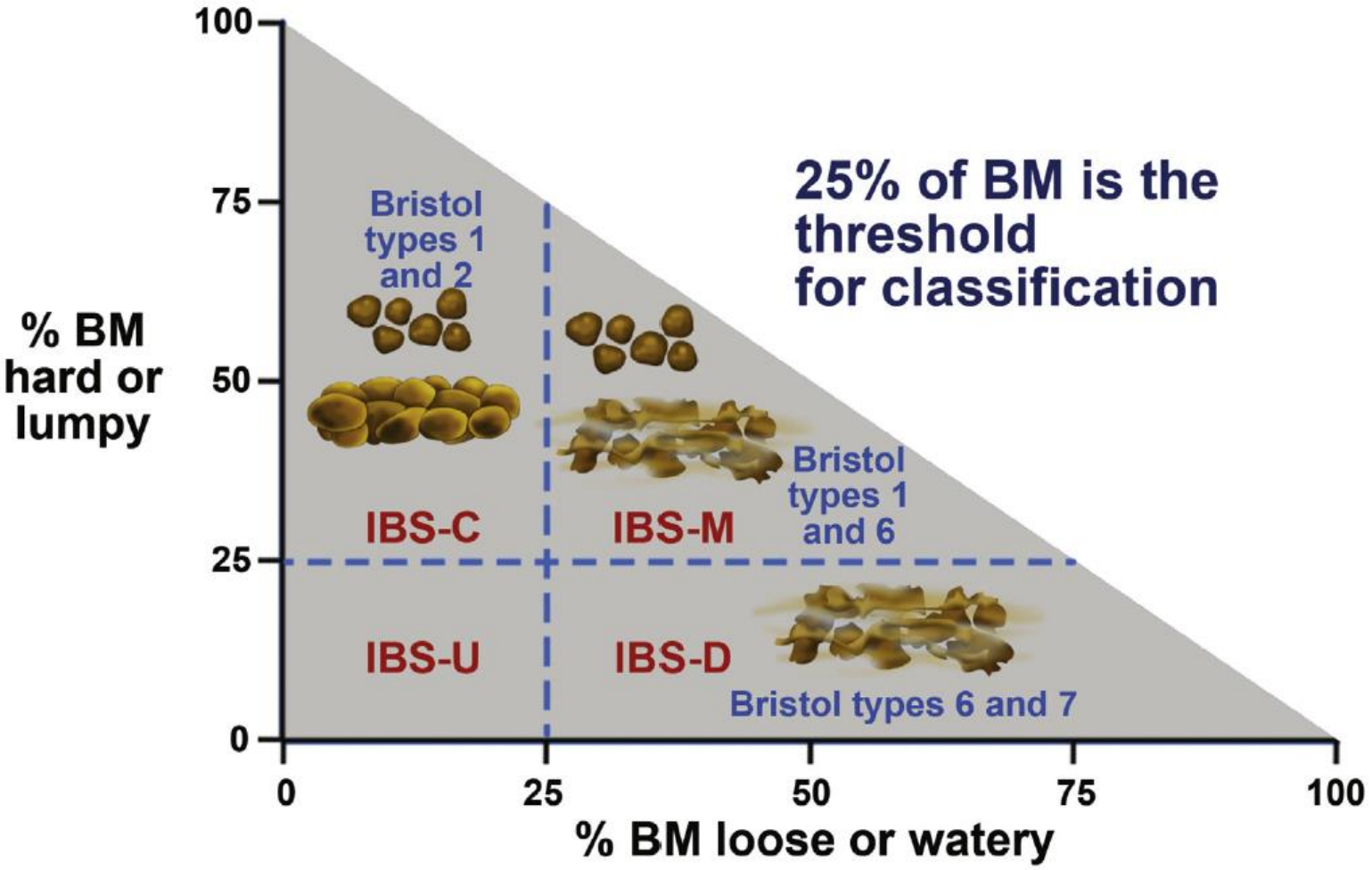


- 2-to-3 times more common in women than men
- 5.3% (18- to 39-year old), 3.7% (40- to 60-year old), 1.7% (>60-year old)

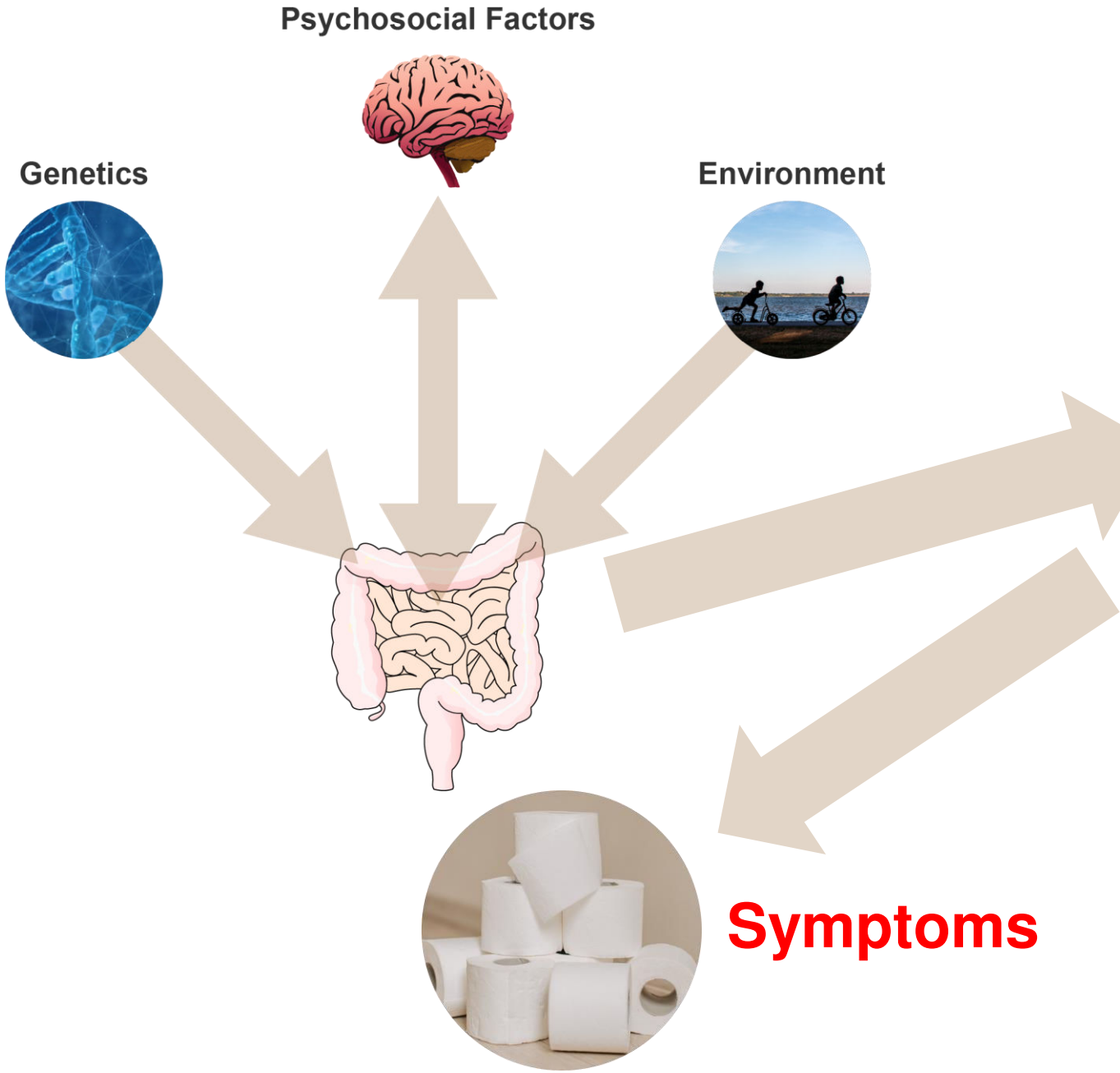
- 43.1% who meet criteria for IBS do not have a formal medical diagnosis

Sperber. *Aliment Pharmacol Ther* 2021;54(Suppl 1):S1-11
Oka *et al. Lancet Gastroenterol Hepatol 2020;5:908-17*
Sayuk *et al. Am J Gastroenterol* 2017;112(6):892-9

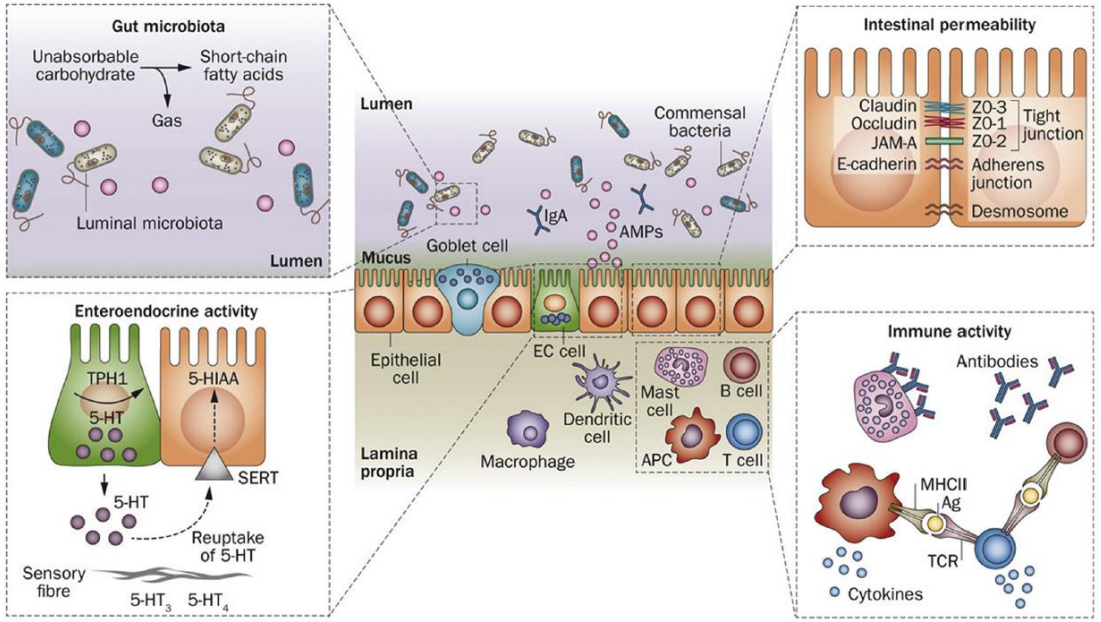
What is Irritable Bowel Syndrome: Subtypes



Oka *et al. Lancet Gastroenterol Hepatol 2020;5:908-17*
Lacy *et al. Gastroenterology* 2016;150:1393-1407



- Altered GI motility
- Visceral hyperalgesia
- Altered enteroendocrine activity
- Increased intestinal permeability
- Enteric immune activation
- Altered gut microbiota
- Gut-brain dysregulation



Lacy *et al. Gastroenterology* 2016;150:1393-1407
Chang *et al. Gastroenterology* 2016;151:e1-8

Overall Management of IBS

- Counseling and reassurance
- Lifestyle modification
  - Exercise, stress reduction, attention to impaired sleep
- Medications
  - IBS-D: rifaximin, alosetron, loperamide, TCAs, antispasmodics
  - IBS-C: tenapanor, plecanatide, linaclotide, tegaserod, lubiprostone, PEG, TCAs, antispasmodics
- Diet

Lacy *et al. Gastroenterology* 2016;150:1393-1407
Lembo *et al. Gastroenterology* 2022;163:137-51
Chang *et al. Gastroenterology* 2022;163:118-36

Why Diets for IBS?

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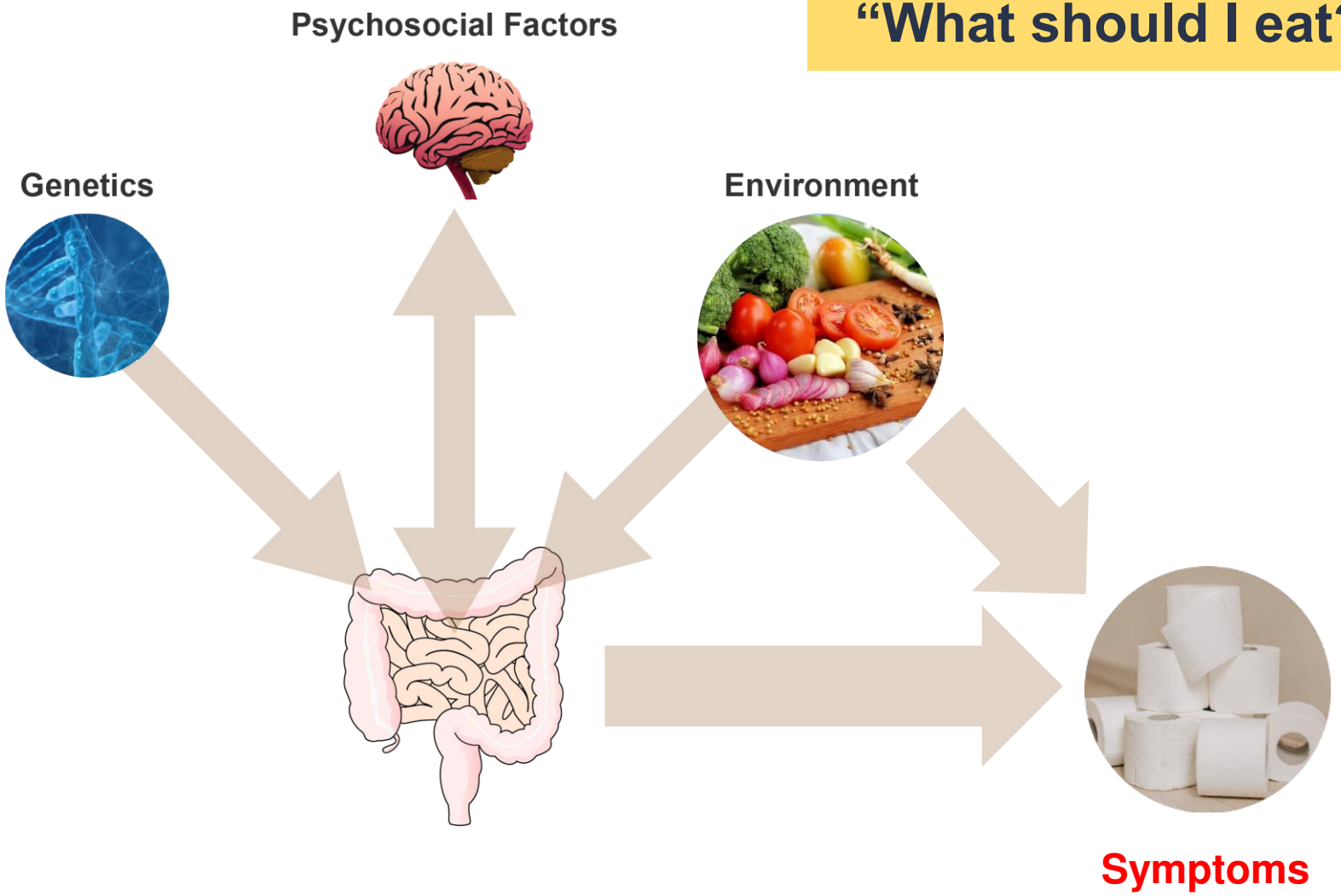
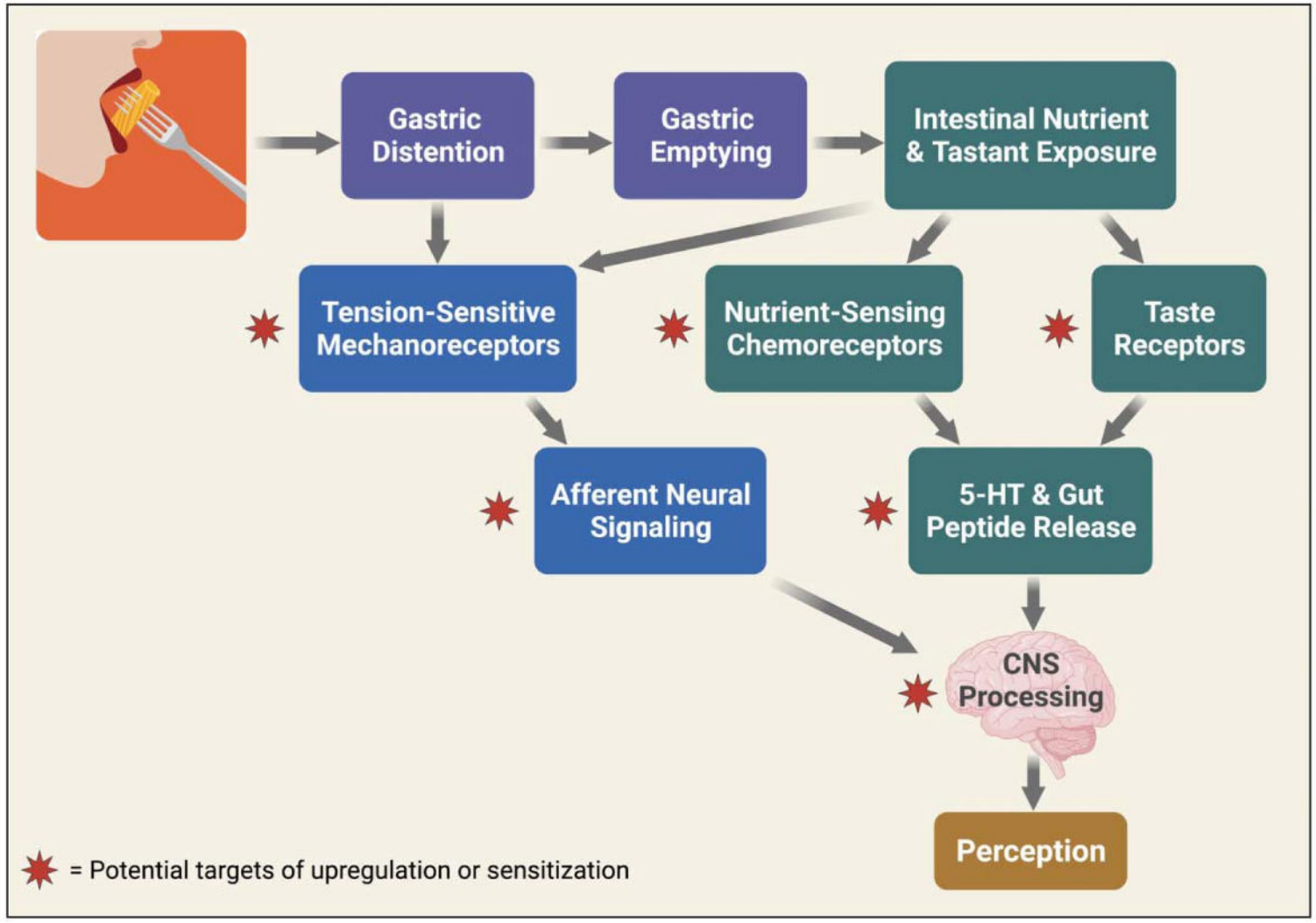
Why Diet for IBS?

The most common question (63%) asked by patients with IBS is **“What should I eat?”**



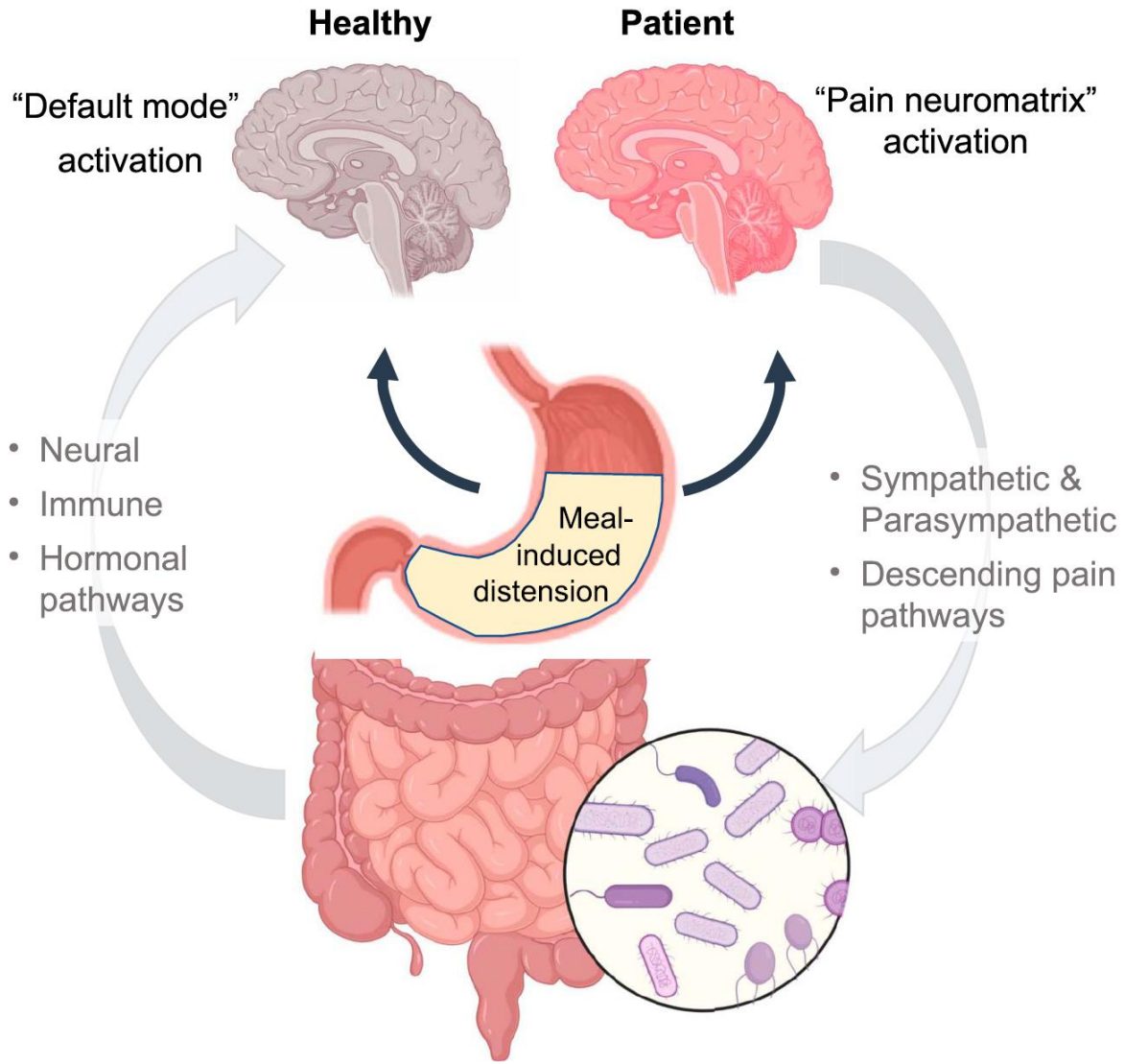
Halpert *et al. Am J Gastroenterol* 2007;102:197-82

Why Diet for IBS?



van den Houte *et al. Am J Gastroenterol* 2022;117:937-46

Why Diet and IBS?



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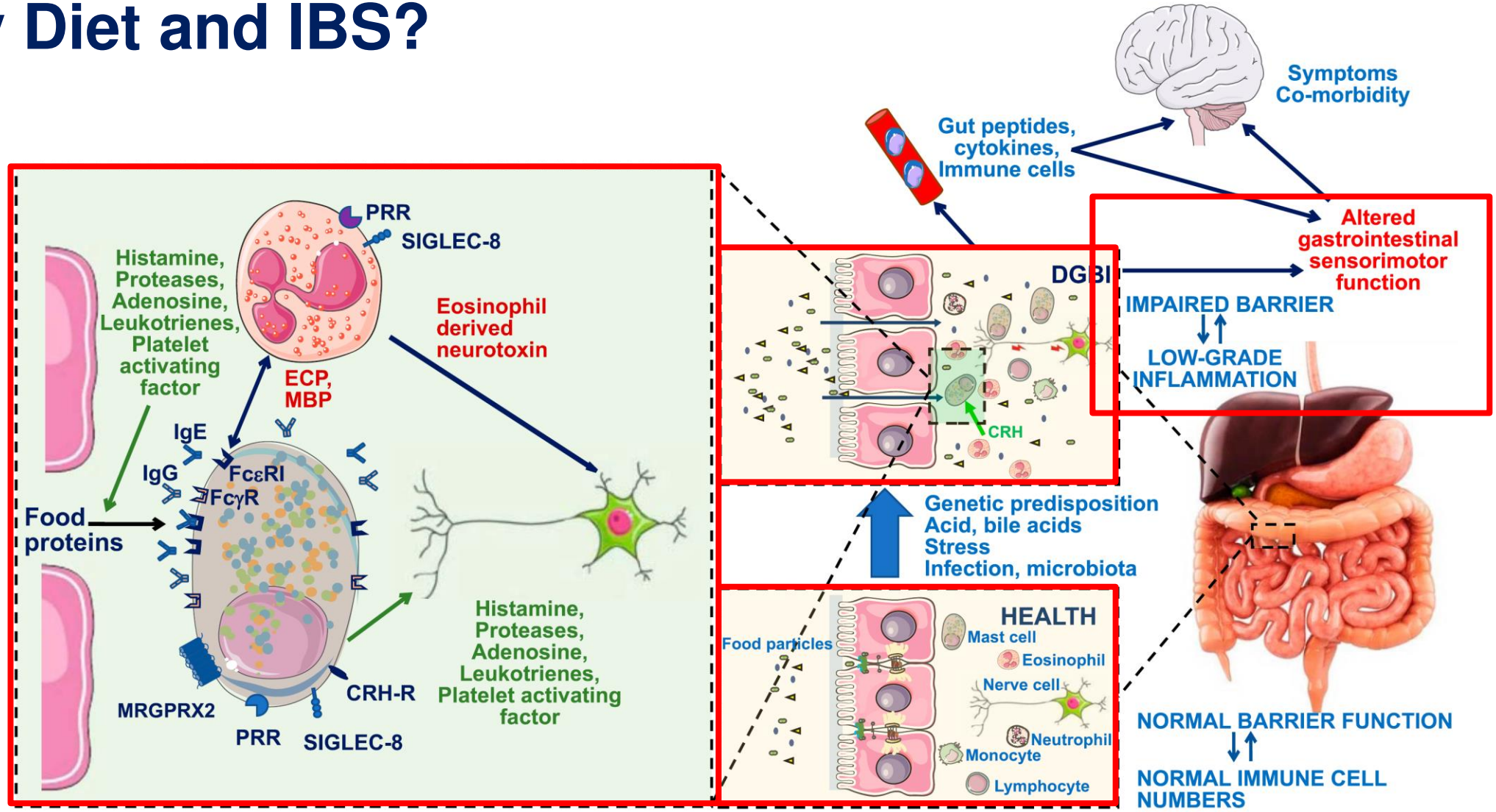

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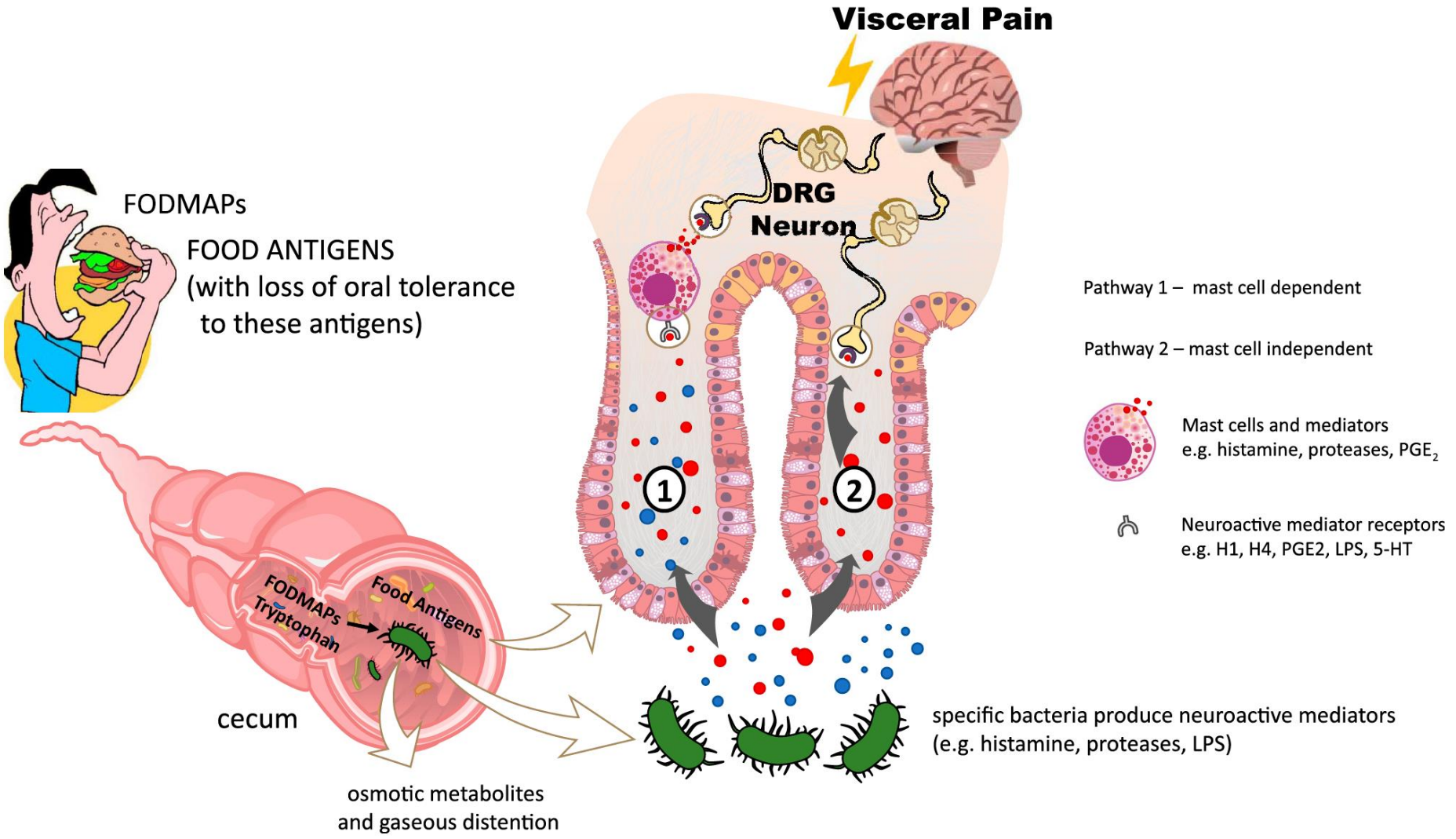
Why Diet and IBS?



van den Houte *et al. Am J Gastroenterol* 2022;117:937-46

What Diets for IBS?

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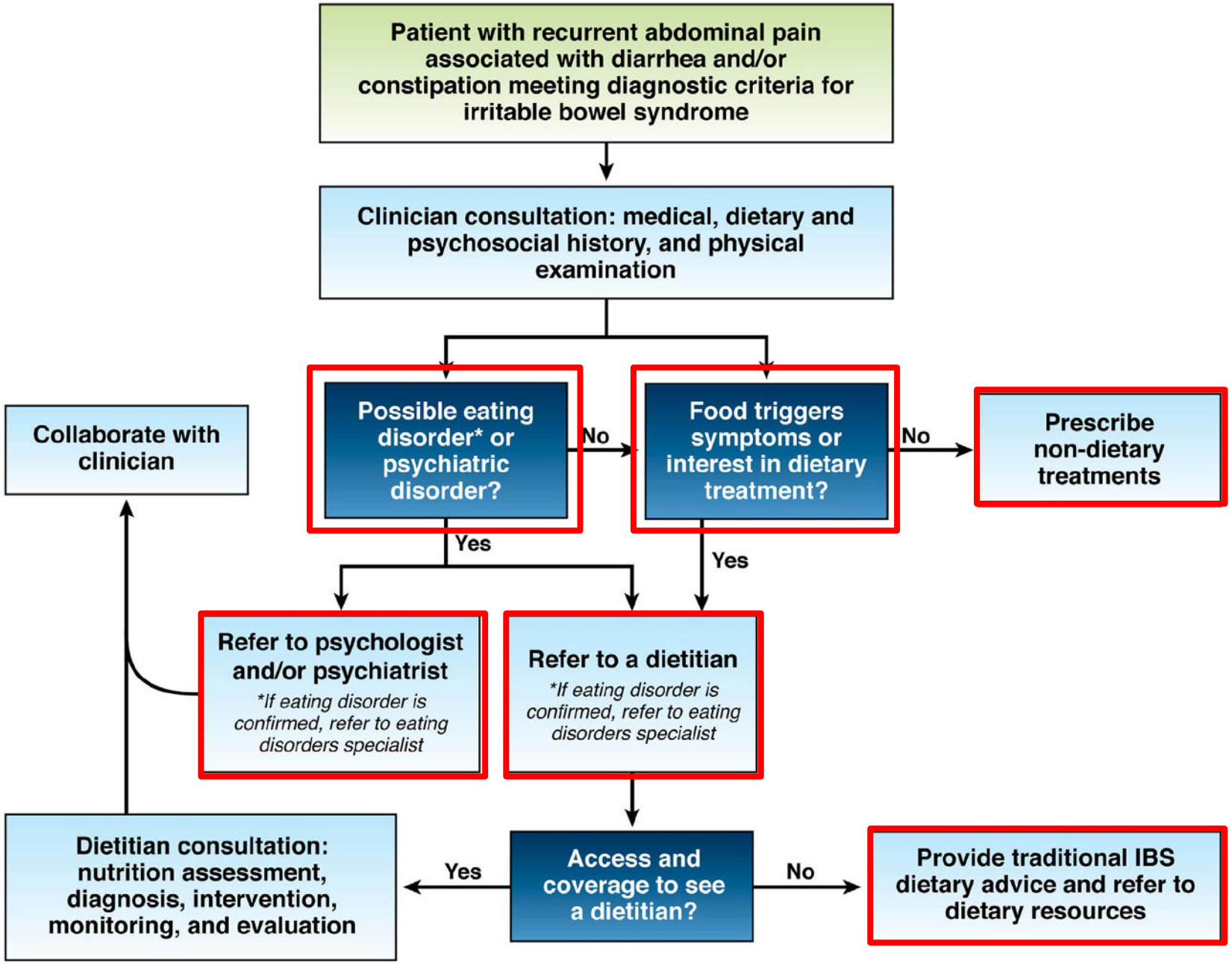


Chey *et al*. *Gastroenterology* 2022;162:1737-45

Candidates for Dietary Intervention

Ideal Candidates

- Insight into meal-related GI symptoms
- Motivated to make necessary changes

Suboptimal Candidates

- Consuming few culprit foods
- Risk for malnutrition
- Food insecure
- Eating disorder
- Uncontrolled psychiatric disorder

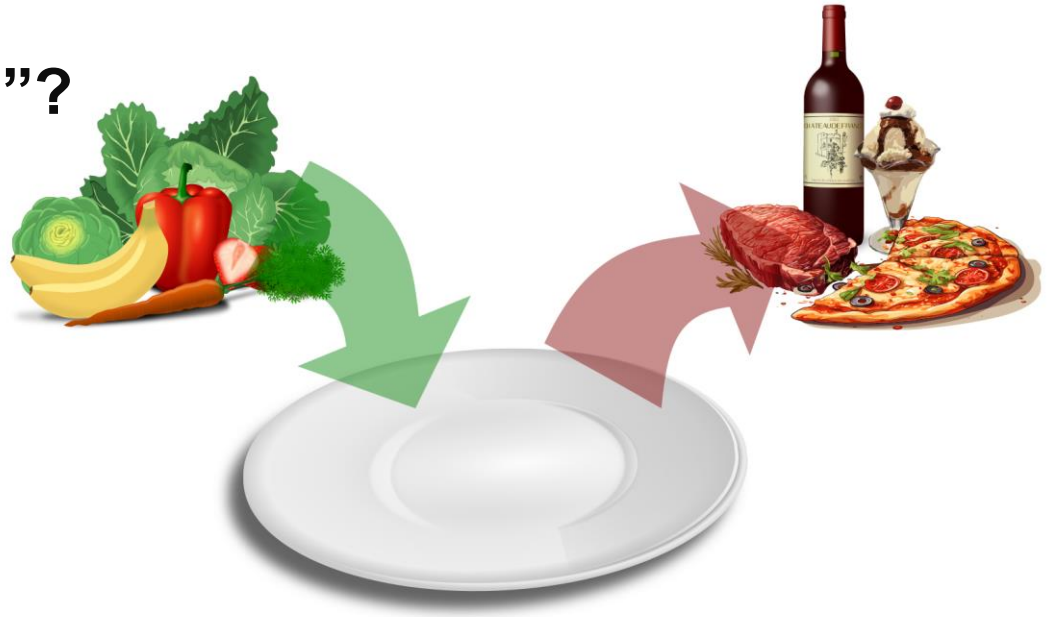
Routine screening for disordered eating is critical, because they are common and often overlooked in GI conditions

Chey *et al*. *Gastroenterology* 2022;162:1737-45

What Diets for IBS?

Add what is “good”?

- Fruits
- Vegetables
- Omega-3



Remove what is “bad”?

- Refined sugars
- Red meats
- Gluten
- Alcohol
- Additives
- Emulsifiers
- Ultra-processed foods

↓ dietary antigens
↑ favorable microbiome
↓ pro-inflammatory metabolites
↑ anti-inflammatory metabolites
↑ intestinal barrier
↓ inflammasome

Mechanistic Approach to Diets for IBS

Putative Mechanism	Possible Dietary Approaches
Loss of oral tolerance with food IgE generation	Specific food elimination
Atypical intestinal food allergy	Specific food elimination
Diet-microbial interactions	Specific food elimination
Exaggerated response to nutrient chemosensing	Nutrient elimination
Exaggerated mechanosensitivity	Low residue meal Small volume meals
Defective processing	Carbohydrate reduction (lactose, fructose, sucrose, starch)
Osmotic and fermentation effects of non-absorbed carbohydrates	Low FODMAP diet Lactose elimination diet

van den Houte *et al. Am J Gastroenterol* 2022;117:937-46

Traditional Dietary Advice (NICE)

- Restrict **tea** and **coffee** to three cups a day
- Reduce intake of **alcohol** and **fizzy** drinks
- Limit intake of **high-fiber foods** (e.g., whole meal or high-fiber flour and breads, cereals high in bran, wholegrains such as brown rice)
- Avoid **insoluble fiber** (e.g., bran) in favor of soluble fiber (e.g., ispaghula, oats)
- Reduce "**resistant starch**"
- Limit **fresh fruit** to three portions (80 g) per day
- For those with diarrhea, avoid **sorbitol**
- Consider low **FODMAP** diet

- For those with bloating and gassiness, eat oats and linseeds

Hookway *et al. BMJ* 2015;350:h701

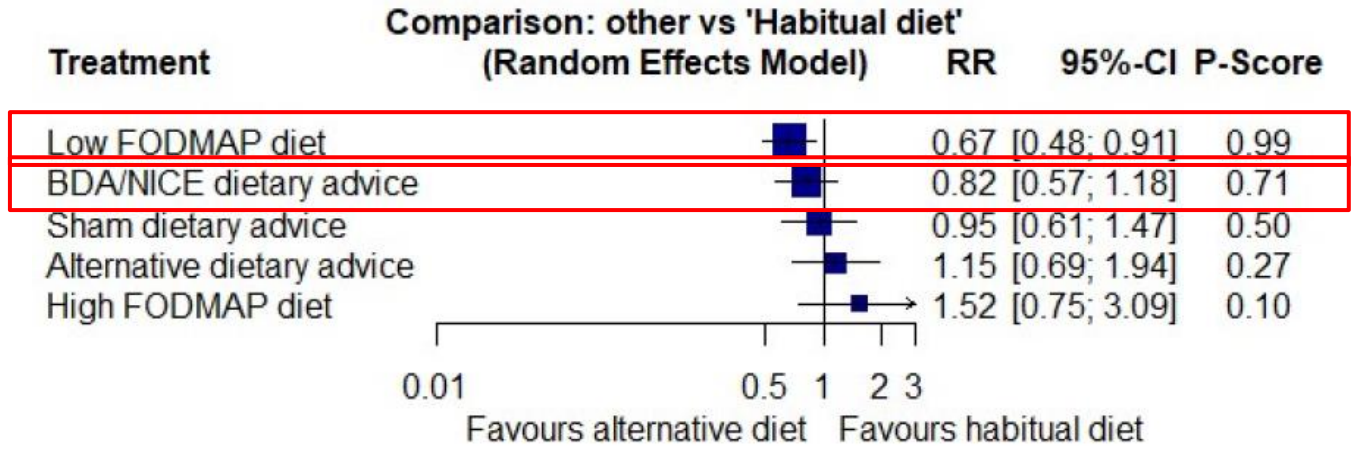
Traditional Dietary Advice (BDA)

- Moderate **alcohol** intake
- Restrict **spicy foods** if associated with symptoms
- Restrict **fats foods** if associated with symptoms
- Low **lactose** diet if associated with symptoms
- Avoid **wheat bran** to treat IBS. Do not increase from usual intake
- Consider low **FODMAP** diet

- Can try probiotic
- For IBS-C, try linseeds (2 tbsp/day x 3 month trial)
- No recommendation on gluten, caffeine, or fluids

McKenzie *et al. J Hum Nutr Diet* 2016;29:549-75

Network Meta-Analysis of Diets: Global Symptoms

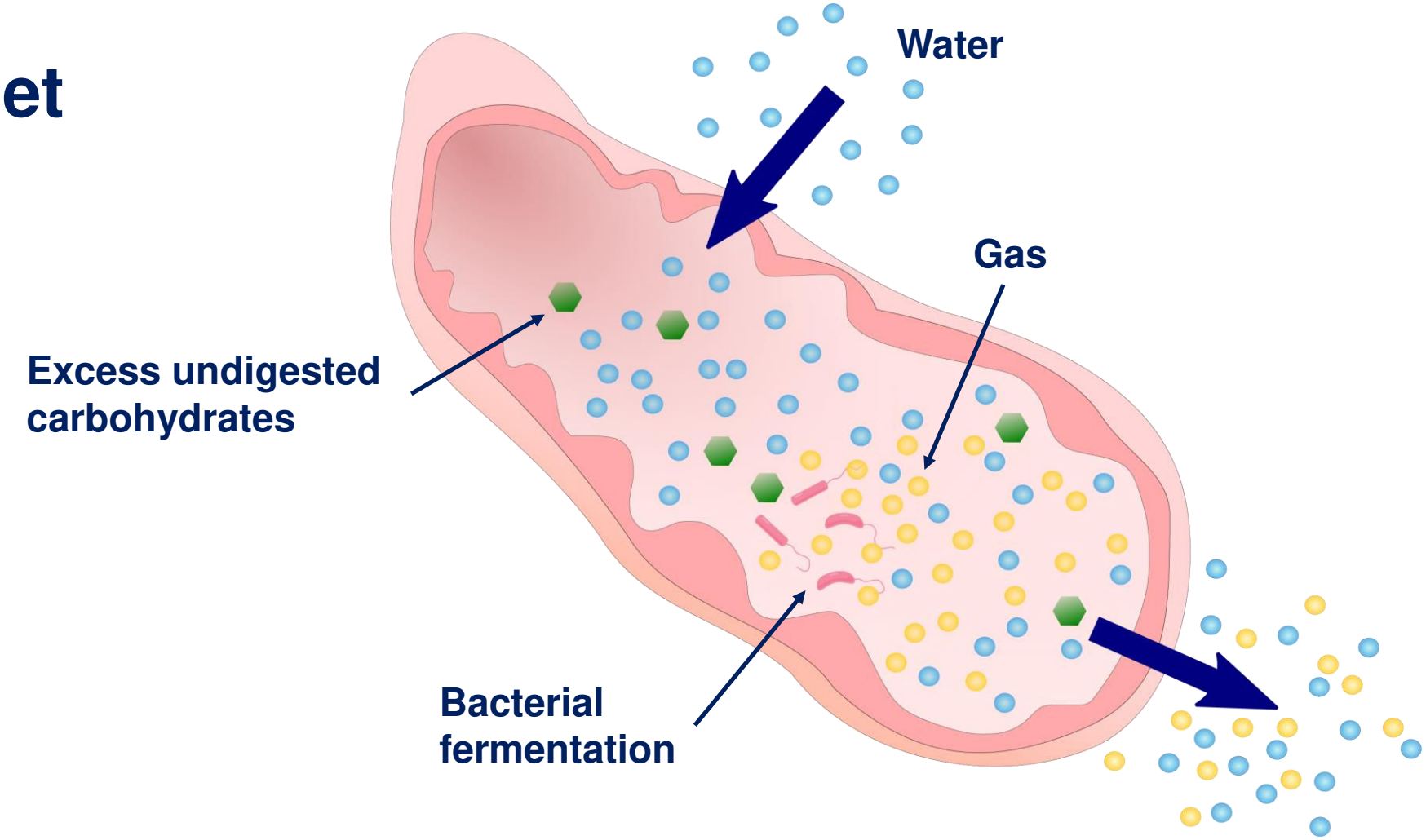


BDA/NICE dietary advice				
0.87 (0.61 to 1.23)	**Sham dietary advice**			
0.82 (0.57 to 1.18)	0.95 (0.61 to 1.47)	**Habitual diet**		
0.71 (0.45 to 1.12)	0.82 (0.49 to 1.37)	0.87 (0.52 to 1.46)	**Alternative dietary advice**	
0.54 (0.28 to 1.05)	0.62 (0.31 to 1.26)	0.66 (0.32 to 1.34)	0.76 (0.36 to 1.62)	**High FODMAP diet**

Black *et al. Gut* 2022;71:1117-26

Low FODMAP Diet

Fermentable
Oligosaccharides
Monosaccharides
Disaccharides
And
Polyols



- **Alteration of intestinal microbiota**
- **Bacterial growth and overgrowth**
- **Low-grade inflammation**

Low Lactose

CHEESE (2 servings)
Brie, camembert, Colby, cheddar, goat, feta, Havarti, Haloumi, manchego, Monterey jack, mozzarella, parmesan, pecorino, soy cheese, Swiss, queso fresco, lactose-free cottage + cream cheese, rinsed fresh mozzarella and burrata

BEVERAGES
Almond milk, Coconut milk UHT (<1/2 cup), Lactose free cow's milk, hemp milk, macadamia nut milk, pea protein milk, quinoa milk, rice milk

OTHER
Coconut yogurt, lactose-free ice cream, lactose-free sour cream, lactose-free yogurt, nut milk creamers, whipped cream

No Excess Fructose

FRUIT (1 serving)
Banana (small green), dried banana chips, clementine, coconut, cranberry juice, dragon fruit, grapes (6), guava (ripe), kiwi, lemon, lime, orange, papaya, passionfruit, pineapple, plantain, raspberries, rhubarb, star fruit, strawberries (5), tangelo

SWEETENERS
Brown sugar, cane sugar, palm sugar, raw sugar, pure maple syrup, dairy-free chocolate, rice malt syrup, stevia, vanilla extract

ALCOHOL (1 serving)
Beer, gin, vodka, whiskey, wine

Low Fructan / GOS

VEGETABLES
Alfalfa, artichoke hearts (canned), arugula, bamboo shoots, bean sprouts, beets (canned/pickled), butternut squash (1/3 c), bell pepper (yellow, red, orange), broccoli (florets only), bok choy, carrots, cabbage (common, Chinese, red), capers, cassava, celeriac, chayote, chives, collard greens, corn (canned kernels or baby), cucumber, daikon, eggplant, endive, fennel bulb, green beans, ginger, hearts of palm (canned), jicama, kabocha squash, kale, kohlrabi, leeks (green portion only), lettuces (all varieties), okra, olives, parsnip, pattypan squash, pumpkin (1/3 c canned), white potato, radish, rutabaga, seaweed, scallions (green portion only), spaghetti squash, spinach, Swiss chard, summer squash, taro (½ c), tomatillos, tomatoes, turnip, water chestnut, watercress, zucchini (1/3 c)

FRUIT
Honeydew (½ c), pineapple (<1 c), pomegranate seeds (<¼ c), dried cranberries or raisins (1T), dried coconut and other dried fruit (<½ c), blueberries (<¼ c), cantaloupe (3/4 c)

GRAINS
Almond meal (¼ c), buckwheat (groats, flour), corn tortillas/masa, gluten-free bread, gluten-free pasta, millet, oats (½ c), polenta, quinoa, rice, slow-leavened sourdough bread (spelt and wheat), soba noodles, sorghum, teff, yam flour

NUTS & SEEDS (1 handful or 1 tbsp. butters)
Almonds (10), brazil nuts, chestnuts, chia seed, hazelnuts (20), hemp seeds, macadamias, peanuts, pecans, pine nuts, poppy seeds, pumpkin seeds, sesame seeds, sunflower seeds, walnuts

LEGUMES
Chickpeas (¼ c, canned, drained, well-rinsed), edamame (1 c), lentils (½ c, canned, drained, well-rinsed), tempeh, tofu (firm)

OTHER
All herbs (except garlic/onion and chipotle), teas (black, green, white, herbals except listed on high list), coffee, espresso, oil infused with garlic or onion, soy sauce

Low Polyols

FRUIT
Banana (small green), banana chips (dried), cranberry juice, coconut meat (<2/3 c), dragon fruit, grapes (6), guava, kiwi, lemon, lime, orange, papaya, passionfruit, pineapple, plantain, raspberries, rhubarb, star fruit, strawberries (5), tangel0

VEGETABLES
1/8 avocado, butternut squash (1/3 c), cabbage, celery (¼ stalk), bok choy, green bell pepper (<¼), sweet corn (½ cob) , sweet potato (½ c), oyster mushrooms, canned champignon mushrooms

SWEETENERS
Brown sugar, cane sugar, palm sugar, raw sugar, pure maple syrup, dairy-free chocolate, rice malt syrup, stevia, vanilla extract

***** All animal proteins and fat sources are safe*****

Source: UCLA Division of Digestive Diseases

Phases of Low FODMAP Diet

Strict elimination of FODMAPs (4-6 weeks)

Elimination

- Consider daily MVI

Progressive reintroduction of FODMAPs (6-10 weeks)

Reintroduction

- Increase dose every 3 days

Individualized selection of FODMAPs to continue

Personalization

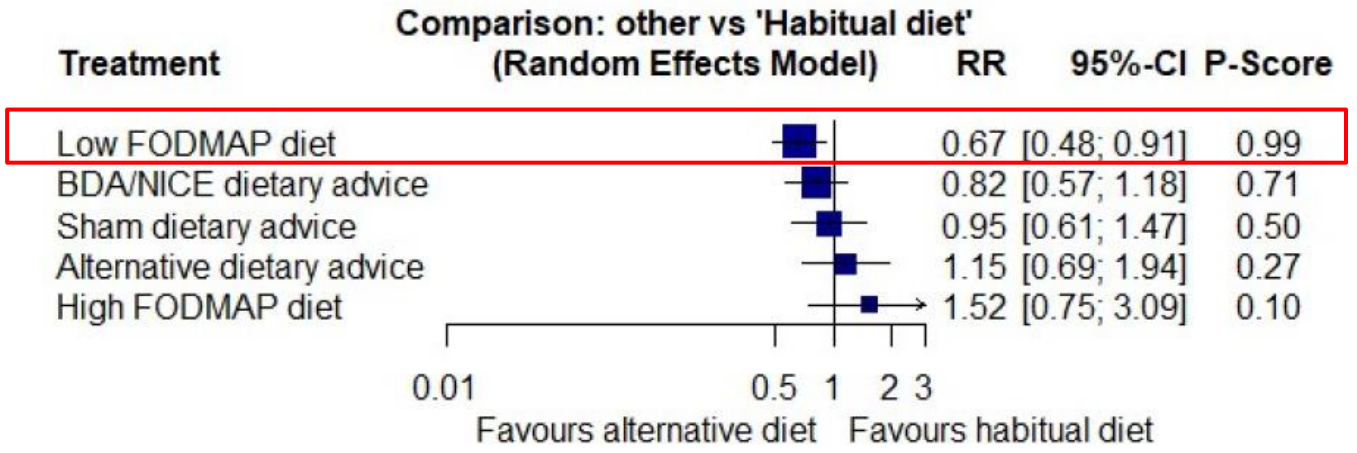
- Use re-introduction data to liberalize diet
- >80% can liberalize

No benefit

Other

Chey *et al. Gastroenterology* 2022;162:1737-45

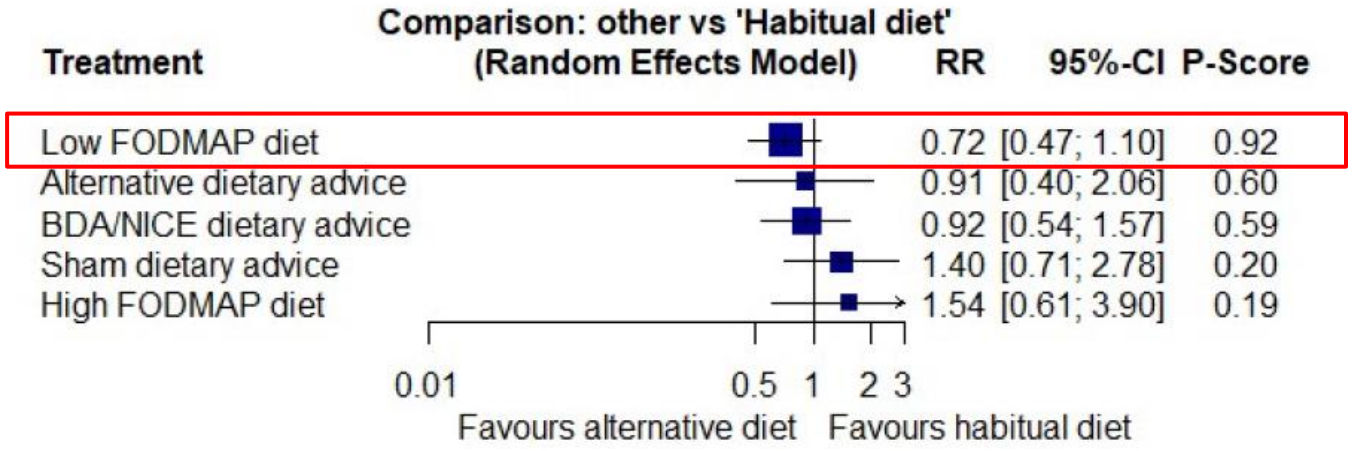
Network Meta-Analysis of Diets: Global Symptoms



Low FODMAP diet					
0.81 (0.67 to 0.97)	**BDA/NICE dietary advice**				
0.70 (0.52 to 0.95)	0.87 (0.61 to 1.23)	**Sham dietary advice**			
0.67 (0.48 to 0.91)	0.82 (0.57 to 1.18)	0.95 (0.61 to 1.47)	**Habitual diet**		
0.58 (0.38 to 0.87)	0.71 (0.45 to 1.12)	0.82 (0.49 to 1.37)	0.87 (0.52 to 1.46)	**Alternative dietary advice**	
0.44 (0.23; 0.83)	0.54 (0.28 to 1.05)	0.62 (0.31 to 1.26)	0.66 (0.32 to 1.34)	0.76 (0.36 to 1.62)	**High FODMAP diet**

Black *et al. Gut* 2022;71:1117-26

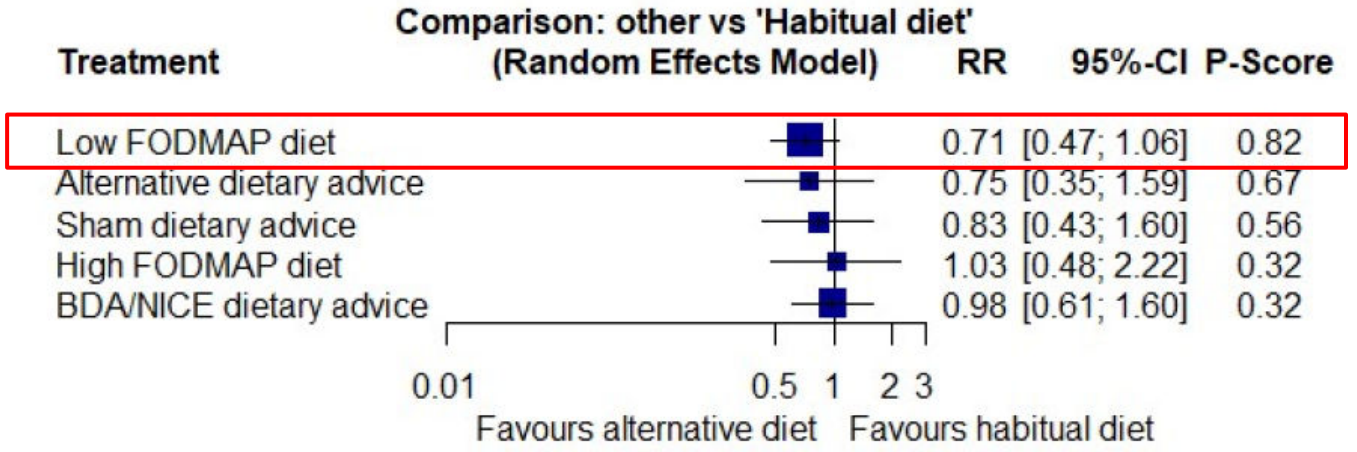
Network Meta-Analysis of Diets: Abdominal Pain



Low FODMAP diet					
0.79 (0.39 to 1.59)	**Alternative dietary advice**				
0.78 (0.57 to 1.06)	0.98 (0.46 to 2.11)	**BDA/NICE dietary advice**			
0.72 (0.47 to 1.10)	0.91 (0.40 to 2.06)	0.92 (0.54 to 1.57)	**Habitual diet**		
0.51 (0.30 to 0.87)	0.65 (0.27 to 1.56)	0.66 (0.35 to 1.22)	0.71 (0.36 to 1.41)	**Sham dietary advice**	
0.47 (0.20 to 1.07)	0.59 (0.20 to 1.74)	0.60 (0.25 to 1.45)	0.65 (0.26 to 1.65)	0.91 (0.34 to 2.44)	**High FODMAP diet**

Black *et al. Gut* 2022;71:1117-26

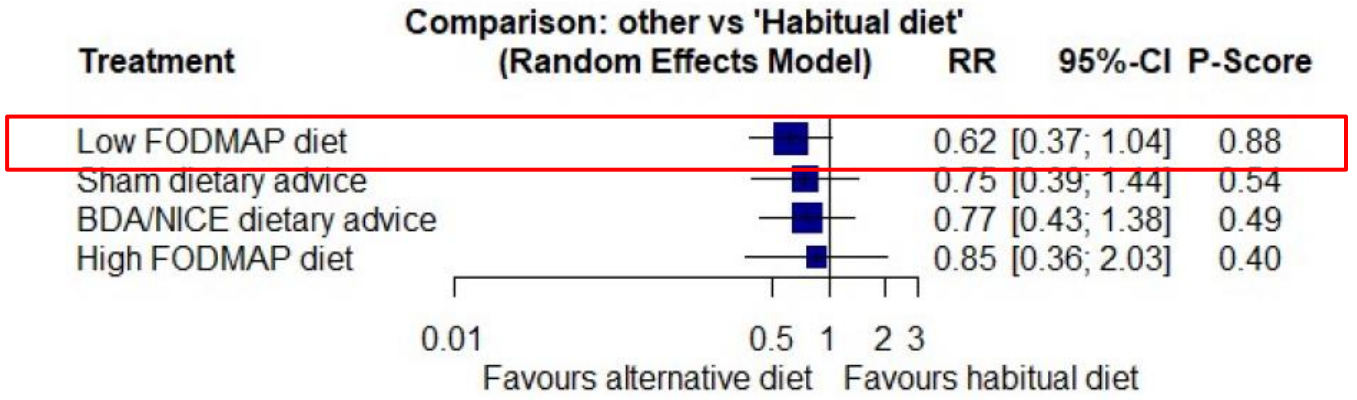
Network Meta-Analysis of Diets: Distention



Low FODMAP diet					
0.95 (0.50 to 1.79)	**Alternative dietary advice**				
0.85 (0.51 to 1.43)	0.90 (0.40 to 2.05)	**Sham dietary advice**			
0.69 (0.36 to 1.32)	0.73 (0.29 to 1.81)	0.81 (0.35 to 1.86)	**High FODMAP diet**		
0.72 (0.55 to 0.94)	0.76 (0.38 to 1.52)	0.84 (0.47 to 1.52)	1.05 (0.51 to 2.13)	**BDA/NICE dietary advice**	
0.71 (0.47 to 1.06)	0.75 (0.35 to 1.59)	0.83 (0.43 to 1.60)	1.03 (0.48 to 2.22)	0.98 (0.61 to 1.60)	**Habitual diet**

Black *et al. Gut* 2022;71:1117-26

Network Meta-Analysis of Diets: Bowel Habits



Low FODMAP diet				
0.83 (0.55 to 1.25)	**Sham dietary advice**			
0.81 (0.61 to 1.07)	0.97 (0.59 to 1.60)	**BDA/NICE dietary advice**		
0.73 (0.36 to 1.48)	0.88 (0.39 to 1.99)	0.90 (0.42 to 1.93)	**High FODMAP diet**	
0.62 (0.37 to 1.04)	0.75 (0.39 to 1.44)	0.77 (0.43 to 1.38)	0.85 (0.36 to 2.03)	**Habitual diet**

Black *et al. Gut* 2022;71:1117-26

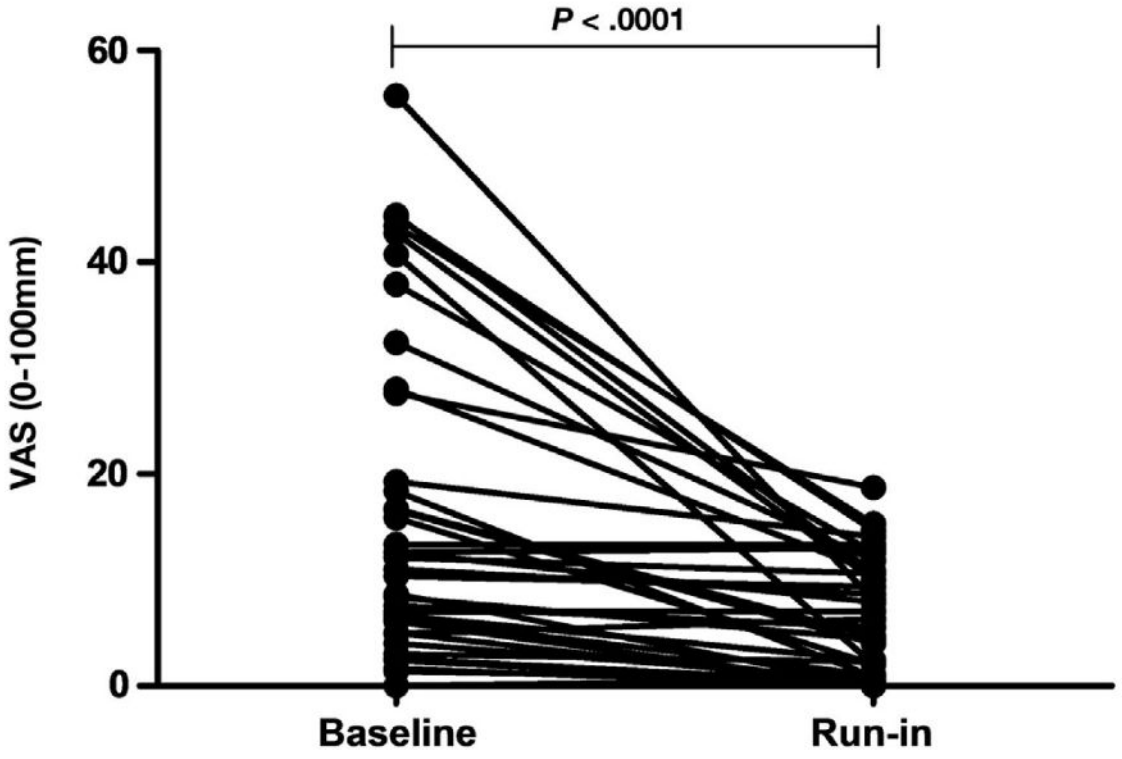
Drawbacks of Low FODMAP Diet

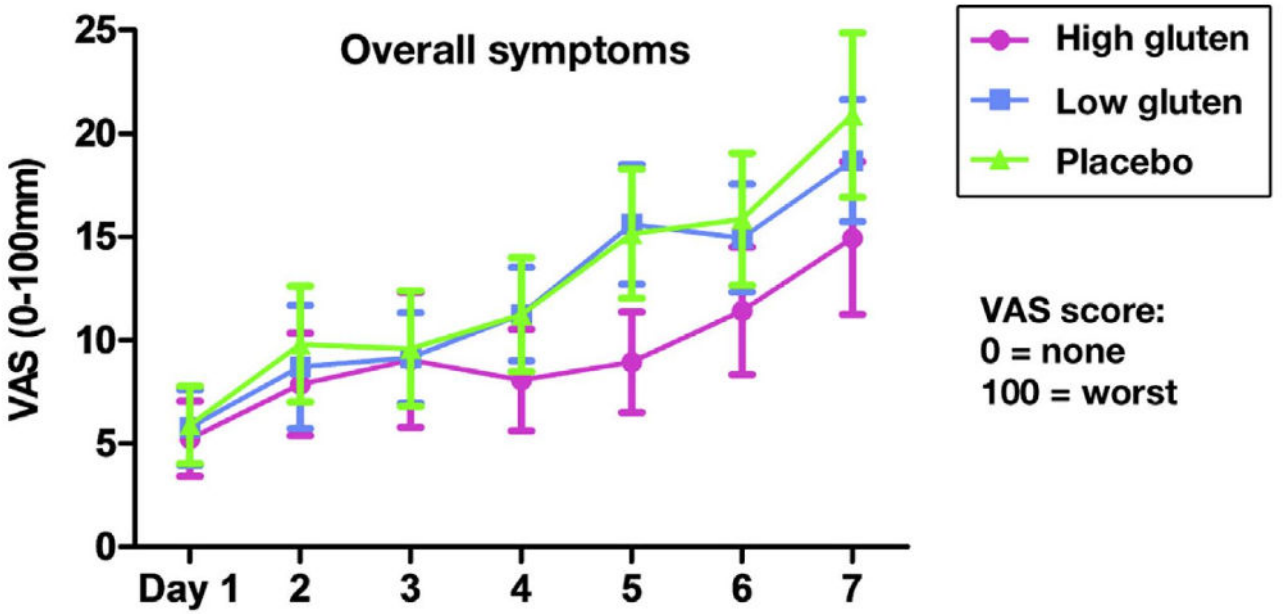
- Partial efficacy
- Cost to patient
- Patient adherence/feasibility
  - 40% complete all phases
- Consequences of long-term dietary restriction
  - Conditioned food avoidance/restriction
  - Nutrient inadequacy
  - Altered gut microbiome

Gluten Avoidance

- Gluten is a protein found in wheat, barley, rye
- Gluten avoidance is dietary treatment for celiac disease
- Reduces abdominal pain, bloating, diarrhea
- Popularized for other digestive disorders

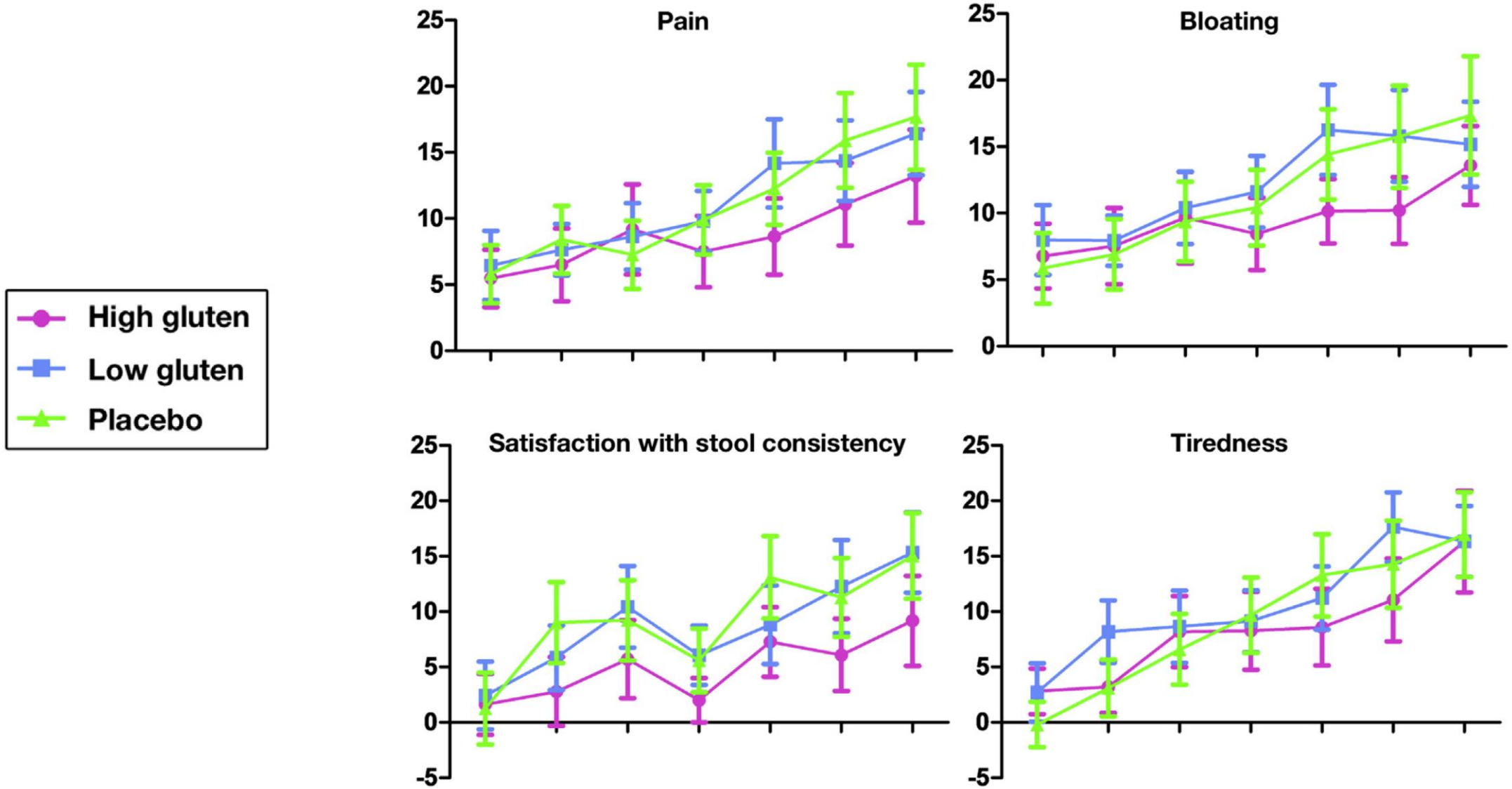
Low vs. High Gluten Consumption in IBS





Biesiekierski *et al. Gastroenterology* 2013;145:320-8

Low vs. High Gluten Consumption in IBS



Biesiekierski *et al. Gastroenterology* 2013;145:320-8

Low vs. High Gluten Consumption in IBS

	High gluten	Low gluten	Placebo
Celiac serology, *U/mL*			
Whole gliadin (IgA)	19 ± 3.6 (21)	19 ± 3.4 (13)	17 ± 1.6 (13)
Whole gliadin (IgG)	11 ± 2.9 (8)	9.4 ± 1.8 (5)	11 ± 2.1 (8)
Deamidated gliadin (IgA)	16 ± 1.4 (8)	15 ± 1.4 (3)	14 ± 1.2 (5)
Deamidated gliadin (IgG)	8.7 ± 1.5 (8)	8.8 ± 1.6 (11)	9.3 ± 1.5 (11)
Human β-defensin-2, *ng/mL*	35 ± 4.9 (21)	33 ± 4.8 (24)	34 ± 5.6 (29)
Eosinophil cationic protein, *ng/mL*	3.6 ± 0.6 (3)	3.5 ± 0.6 (3)	3.4 ± 0.5 (3)
Radioallergosorbent test, *kU/L*	0.09 ± 0.05 (0)	0.07 ± 0.02 (0)	0.07 ± 0.02 (0)
Frequency, *times/d*, median (range)	1 (0–4)	1 (0–3)	1 (0–4)
Output, *g wet wt/d*	127 ± 14	113 ± 11.5	124 ± 13
Dry wt/d, %	25 ± 1.3	25 ± 1.1	26 ± 1.1
Fecal pH	6.9 ± 0.06	6.9 ± 0.07	6.9 ± 0.06
Fecal ammonia, *μg/L*	316 ± 23	328 ± 24	336 ± 25
Calprotectin, *μg/g*	31 ± 9.1	33 ± 7.8	26 ± 7.7

NOTE. Data shown as mean ± SEM (% elevated) unless otherwise indicated. There were no significant differences for diet difference on any measure (compared by repeated measures analysis of variance or Friedman test as appropriate). Healthy reference ranges: human β-defensin-2 (<46.4 ng/mL), eosinophil cationic protein (2.45–14.12 ng/mL), radioallergosorbent test (<50.01–100 kU/L), fecal calprotectin (<50 μg/g). Reference ranges for celiac antibody assays: negative <20 U/mL; weak positive 20–30 U/mL; strong positive >30 U/mL.

Biesiekierski *et al. Gastroenterology* 2013;145:320-8

What about Lactose and Others?

Food	Recommendation	Level of Evidence
Dairy products	Trial of low lactose if triggers symptoms or positive breath test	D
Spicy foods	Restrict if related to symptoms	C
Alcohol	Moderation	C
Fat	Moderation	C
Fiber	Do not increase wheat bran above usual intake	C

- No recommendation for gluten, caffeine, fluids

Non-specific elimination diets are not recommended

McKenzie *et al. J Hum Nutr Diet* 2016;29:549-75

Mediterranean Diet

- Prospective study of 50 children with IBS on Mediterranean diet and 50 continuing regular diet for 6 months

Variables		Group I (Mediterranean diet) (*n* = 50)			Group II (*n* = 50)			*P* value[1]
		Start	End	*P* value	Start	End	*P* value	
IBS scores	IBS-SSS	237.20 ± 65	163.20 ± 33.80	0.001[1]	248.3 ± 71.1	228.50 ± 54.30	0.29	< 0.001[1]
	IBS-QoL	57.30 ± 12.9	72.40 ± 11.2	<0.001[1]	59.1 ± 11.7	59.20 ± 12.70	0.77	< 0.001[1]

- Retrospective study of 106 adults with IBS

	aMED Scores			MEDAS Scores		
	Estimate	Standard error	*P* value	Estimate	Standard error	*P* value
Overall **s**ymptoms	-0.08	0.24	.74	-0.12	0.32	.71
Abdominal **p**ain	-0.03	0.25	.92	-0.39	0.33	.24
Bloating	0.37	0.28	.19	0.61	0.37	.10
VSI **s**core	1.49	0.83	.08	1.17	1.05	.29
IBS-SSS	2.70	4.70	.57	3.06	6.17	.62

Al-Biltagi *et al. World J Clin Pediatr* 2022;11:330-40
Chen *et al. Clin Gastroenterol Hepatol* 2024;22:164-72

Summary of Diets for IBS

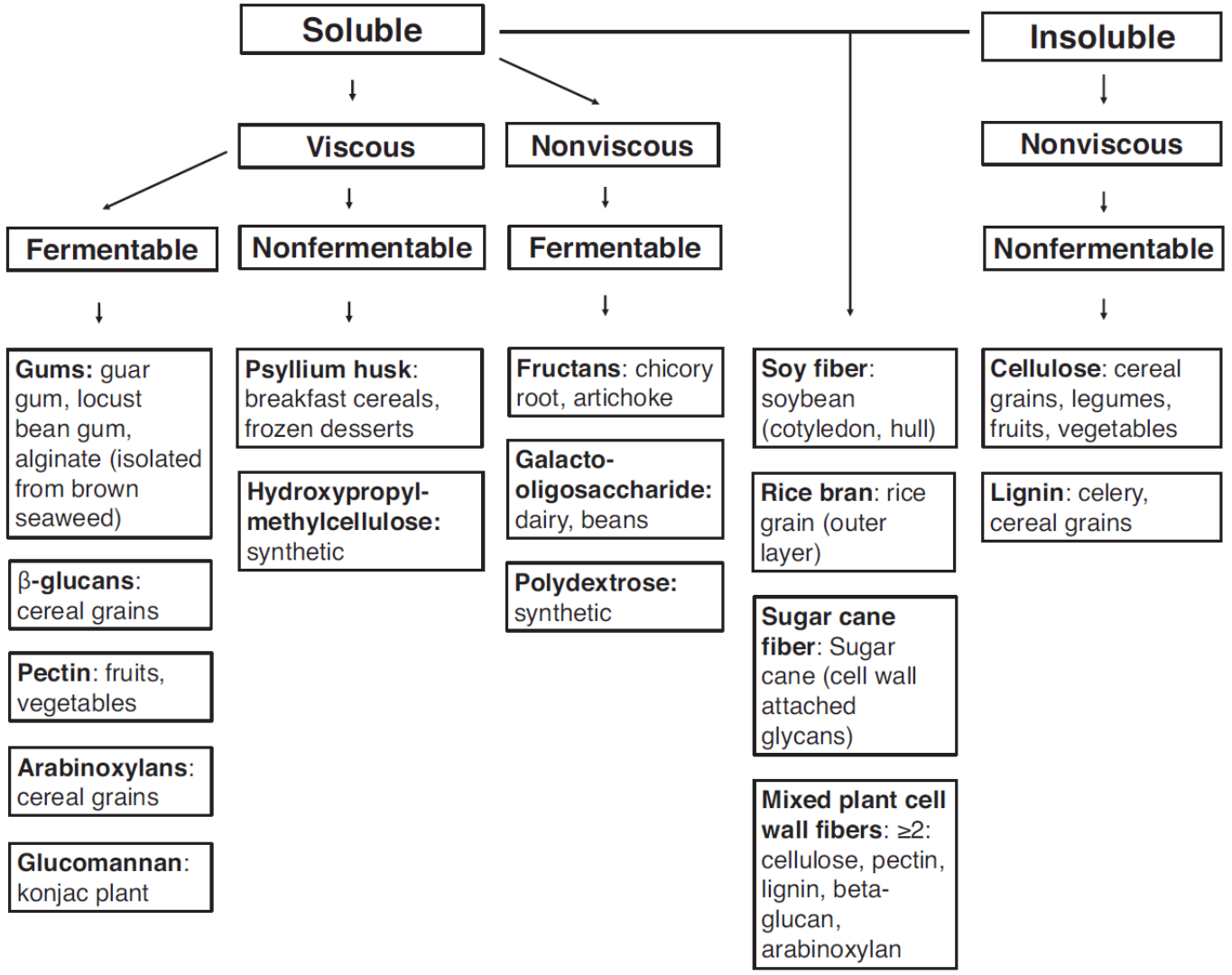
- Low FODMAP diet is most studied and effective diet for treatment of IBS
- No clear evidence for traditional dietary advice or Mediterranean diet
- No clear evidence for necessary gluten or dairy avoidance
- Food exclusions based on relationship with symptoms
- Non-specific elimination diets are not recommended

What About Dietary Supplements?

UCLA Health

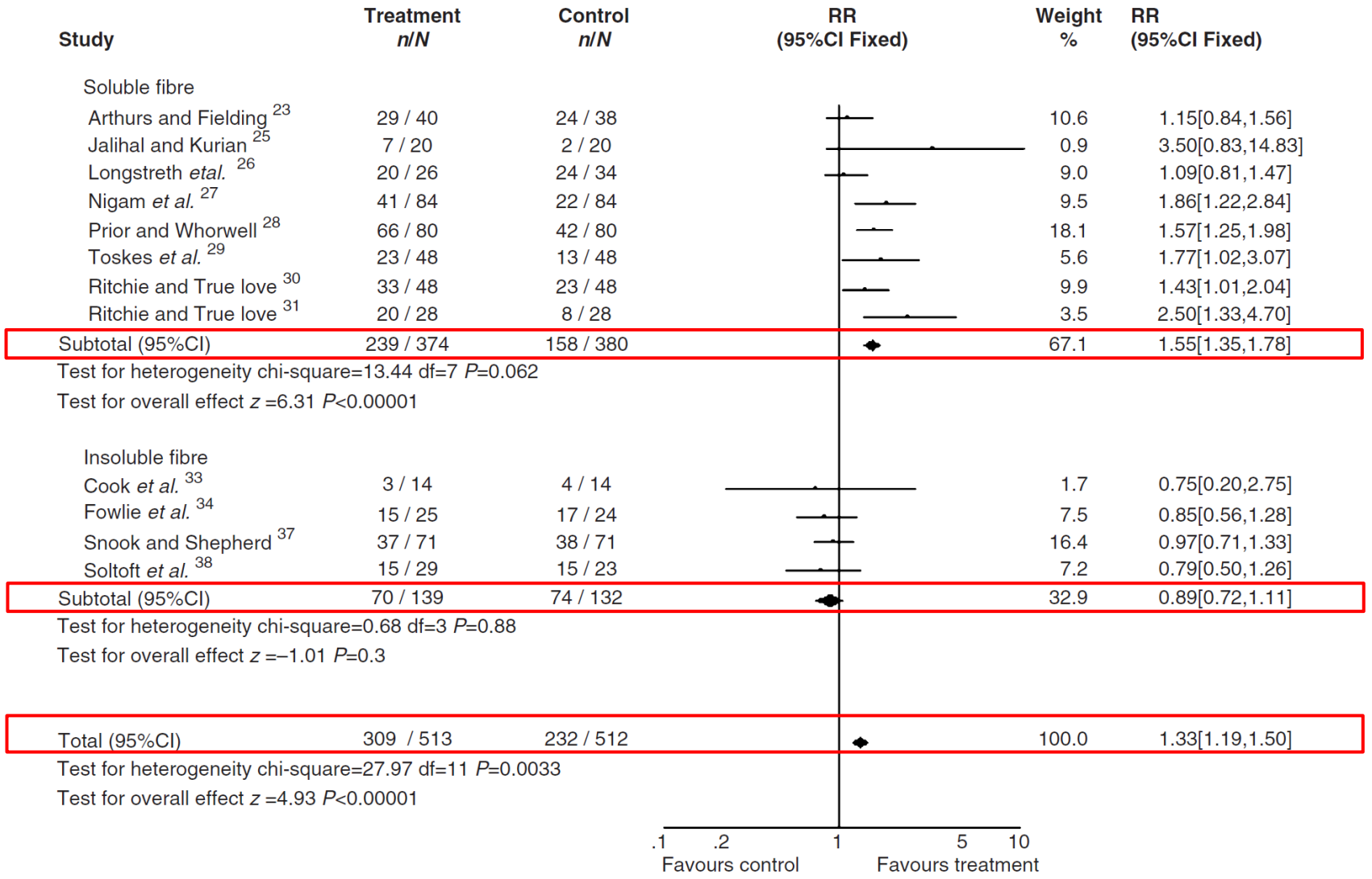
Fiber for IBS

- Fiber provides symptom relief in IBS (RR 0.68; 95% CI 0.80-0.94; NNT 10)
- Psyllium, but not bran, provides symptom relief in IBS (RR 0.83; 95% CI 0.73-0.94; NNT 7)



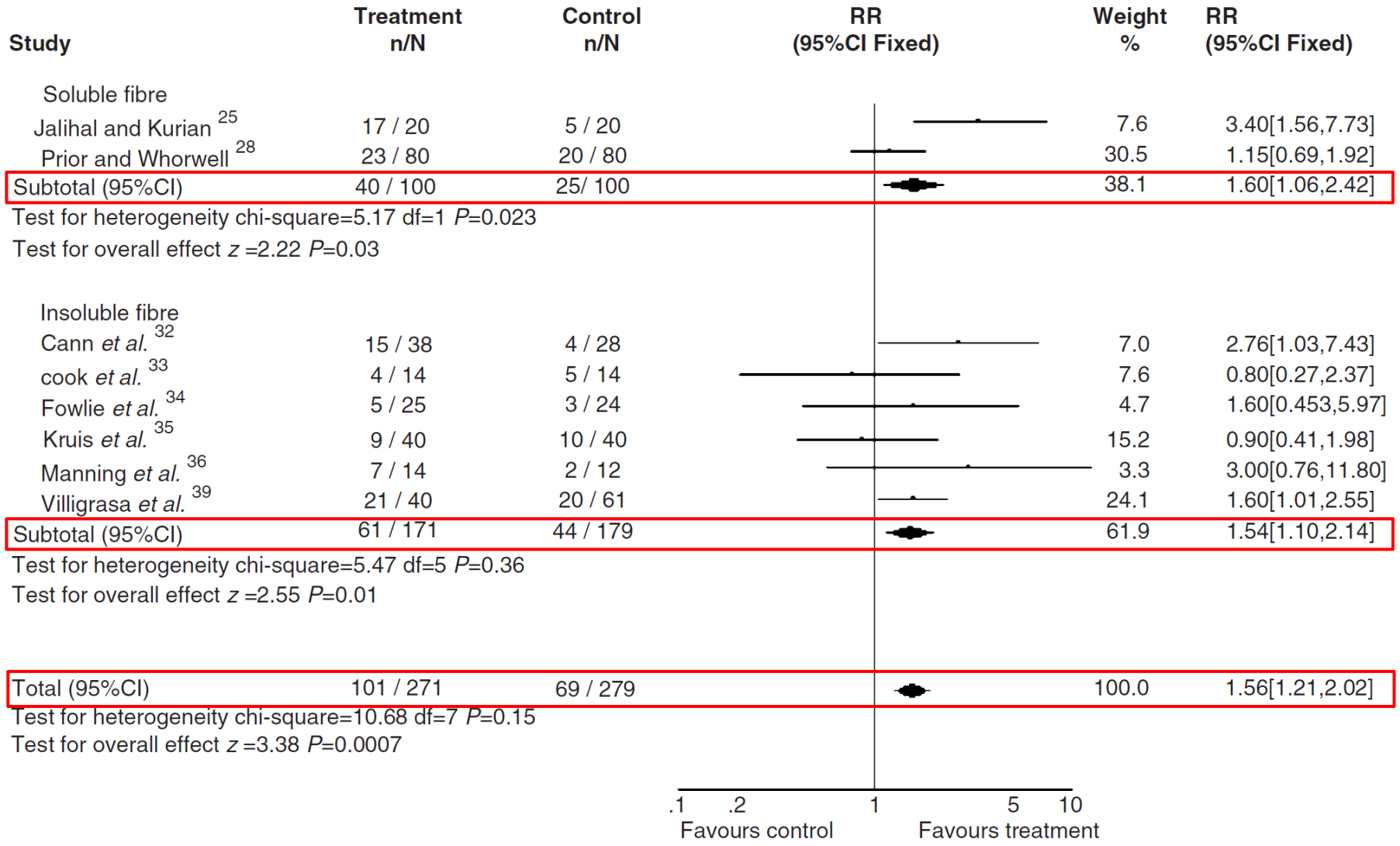
Mysonhimer *et al. Adv Nutr* 2022;13:2237-76
Ford *et al. Am J Gastroenterol* 2014;109 Suppl 1:S2-26
Bijkerk *et al. Aliment Pharmacol Ther* 2004;19:245-51

Types of Fiber: Global Symptoms



Bijkerk *et al. Aliment Pharmacol Ther* 2004;19:245-51

Types of Fiber: Constipation

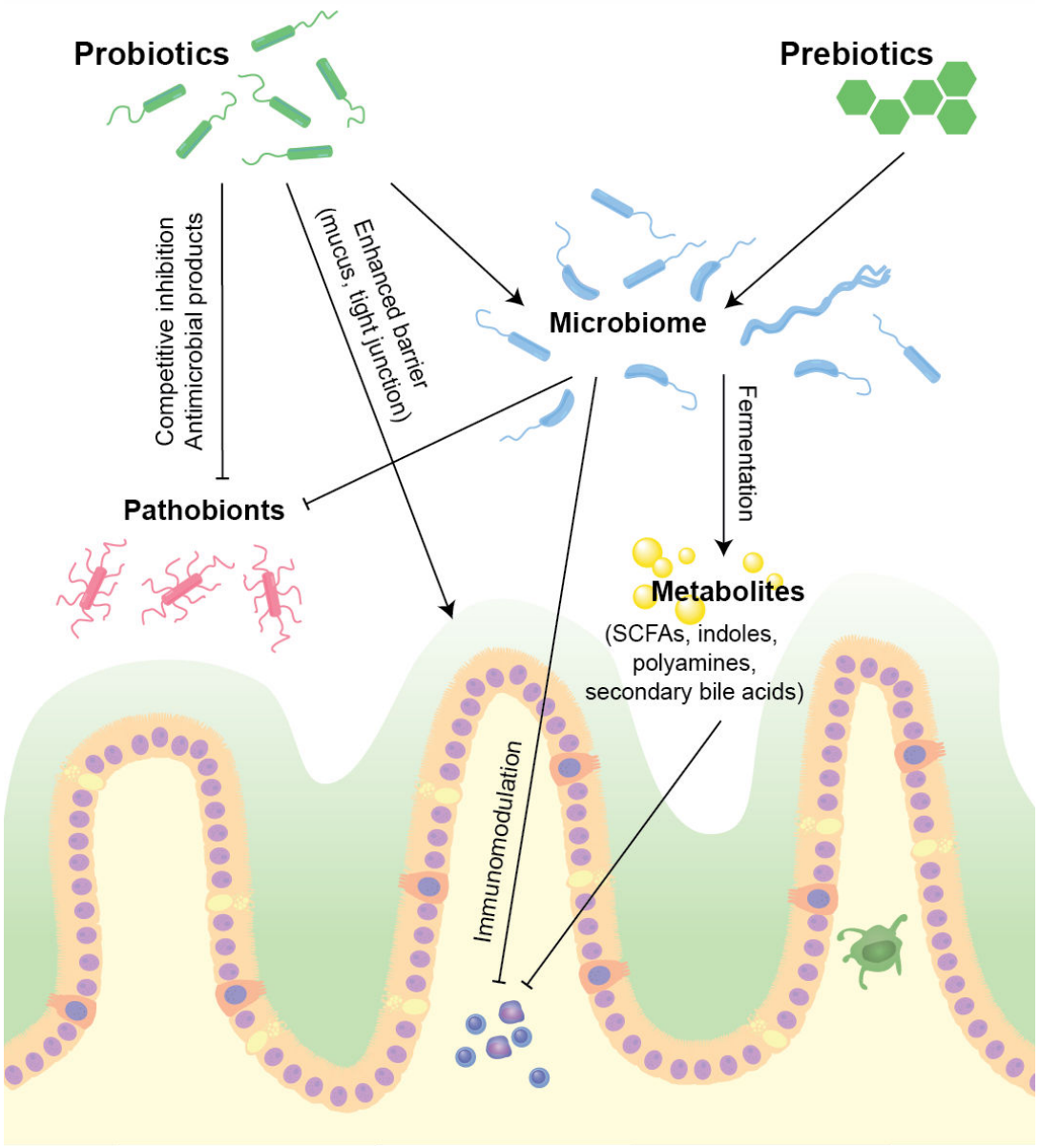


Bijkerk *et al. Aliment Pharmacol Ther* 2004;19:245-51

Probiotics for IBS

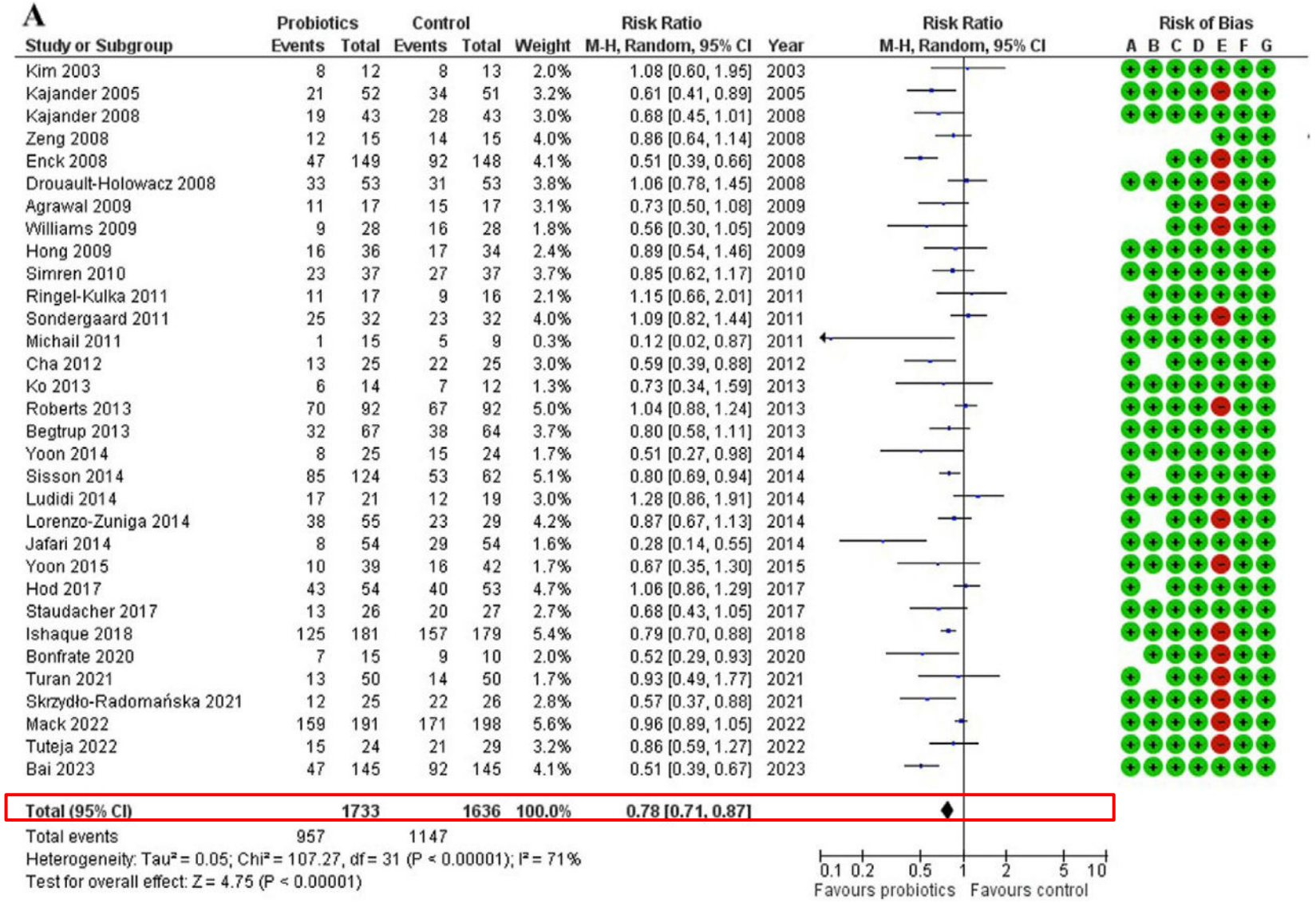
- Probiotics are “live microorganisms which when administered in adequate amounts confer a health benefit on the host” (WHO/FAO)

- General Criteria
  - Human origin
  - Resistant to gastric acid and bile
  - Adherence to mucosa
  - Antimicrobial activity
  - Clinically demonstrated benefit
  - Safe



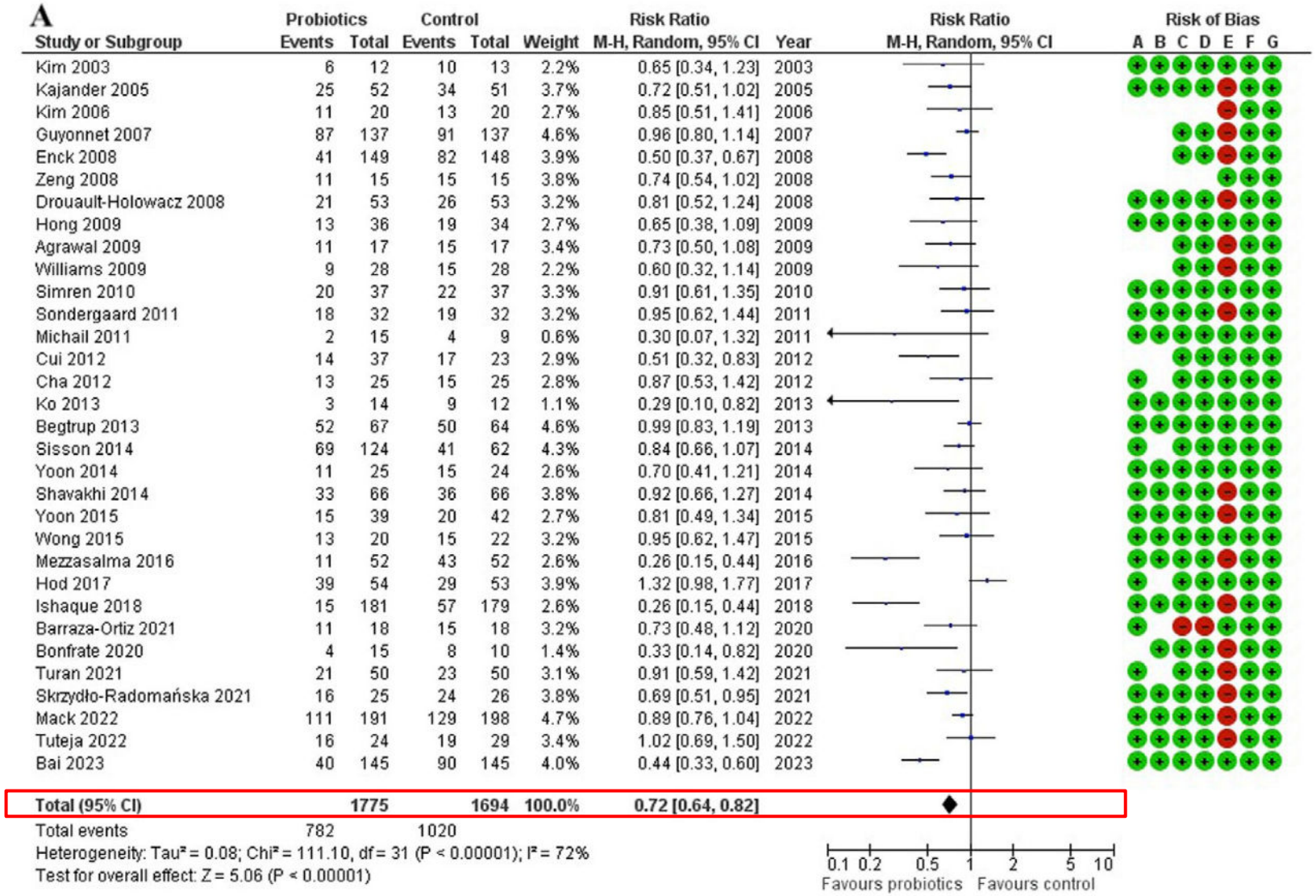
Rau *et al. Nutrients* 2024;16:778

Probiotics for Global IBS Symptoms



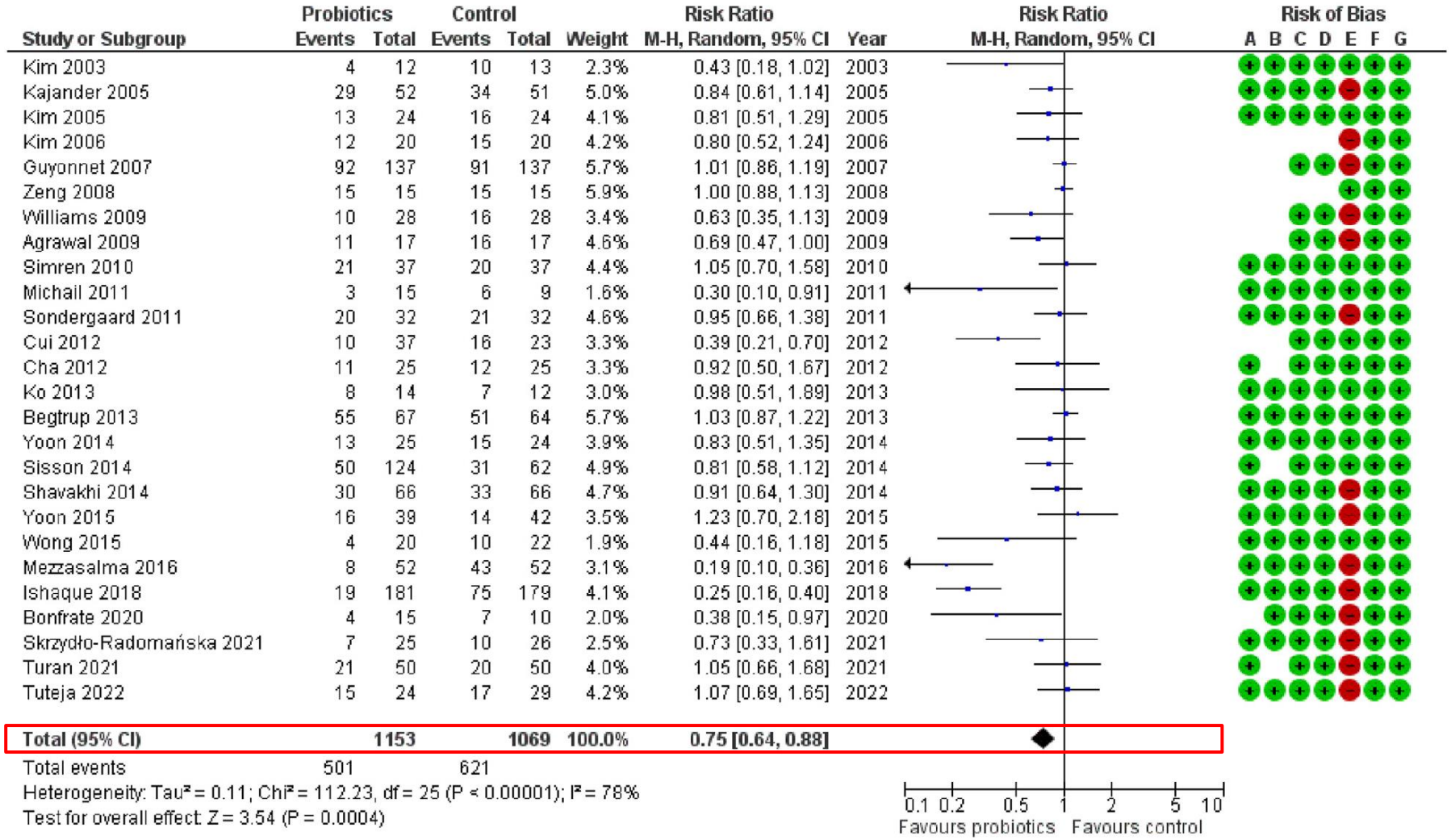
Goodoory *et al. Gastroenterology* 2023;165:1206-18

Probiotics for Abdominal Pain



Goodoory *et al. Gastroenterology* 2023;165:1206-18

Probiotics for Bloating/Distention



Study or Subgroup	Probiotics Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kim 2003	4	12	10	13	2.3%	0.43 [0.18, 1.02]	2003
Kajander 2005	29	52	34	51	5.0%	0.84 [0.61, 1.14]	2005
Kim 2005	13	24	16	24	4.1%	0.81 [0.51, 1.29]	2005
Kim 2006	12	20	15	20	4.2%	0.80 [0.52, 1.24]	2006
Guyonnet 2007	92	137	91	137	5.7%	1.01 [0.86, 1.19]	2007
Zeng 2008	15	15	15	15	5.9%	1.00 [0.88, 1.13]	2008
Williams 2009	10	28	16	28	3.4%	0.63 [0.35, 1.13]	2009
Agrawal 2009	11	17	16	17	4.6%	0.69 [0.47, 1.00]	2009
Simren 2010	21	37	20	37	4.4%	1.05 [0.70, 1.58]	2010
Michail 2011	3	15	6	9	1.6%	0.30 [0.10, 0.91]	2011
Sondergaard 2011	20	32	21	32	4.6%	0.95 [0.66, 1.38]	2011
Cui 2012	10	37	16	23	3.3%	0.39 [0.21, 0.70]	2012
Cha 2012	11	25	12	25	3.3%	0.92 [0.50, 1.67]	2012
Ko 2013	8	14	7	12	3.0%	0.98 [0.51, 1.89]	2013
Begtrup 2013	55	67	51	64	5.7%	1.03 [0.87, 1.22]	2013
Yoon 2014	13	25	15	24	3.9%	0.83 [0.51, 1.35]	2014
Sisson 2014	50	124	31	62	4.9%	0.81 [0.58, 1.12]	2014
Shavakhi 2014	30	66	33	66	4.7%	0.91 [0.64, 1.30]	2014
Yoon 2015	16	39	14	42	3.5%	1.23 [0.70, 2.18]	2015
Wong 2015	4	20	10	22	1.9%	0.44 [0.16, 1.18]	2015
Mezzasalma 2016	8	52	43	52	3.1%	0.19 [0.10, 0.36]	2016
Ishaque 2018	19	181	75	179	4.1%	0.25 [0.16, 0.40]	2018
Bonfrate 2020	4	15	7	10	2.0%	0.38 [0.15, 0.97]	2020
Skrzydło-Radomańska 2021	7	25	10	26	2.5%	0.73 [0.33, 1.61]	2021
Turan 2021	21	50	20	50	4.0%	1.05 [0.66, 1.68]	2021
Tuteja 2022	15	24	17	29	4.2%	1.07 [0.69, 1.65]	2022
Total (95% CI)		**1153**		**1069**	**100.0%**	**0.75 [0.64, 0.88]**	
Total events	501		621				

Heterogeneity: Tau² = 0.11; Chi² = 112.23, df = 25 (P < 0.00001); I² = 78%

Test for overall effect: Z = 3.54 (P = 0.0004)

Goodoory *et al. Gastroenterology* 2023;165:1206-18

Probiotics for Global IBS Symptoms

- Overall
  - Multi-strain probiotics
  - *Lactobacillus*
  - *Escherichia*
  - *Clostridium*
  - *Streptococcus*
- IBS-D
  - Multi-strain probiotics
  - *Lactobacillus*
  - *Clostridium*
- IBS-C
  - None

	Number of trials	Number of patients	RR of persistence of global symptoms (95% CI)	*P* value for the difference	I^2 (*P* value for χ^2)
All patients					
All combination probiotics	32	3369	0.78 (0.71–0.87)	<.001	71% (<.001)
VSL#3	4	155	0.78 (0.53–1.16)	.23	47% (.13)
Lactobacillus paracasei ssp paracasei F19, Lactobacillus acidophilus La5, and *Bifidobacterium lactis Bb12*	3	269	0.92 (0.76–1.11)	.38	14% (.31)
Enterococcus faecalis DSM16440 and *Escherichia coli DSM17252*	2	686	0.71 (0.33–1.51)	.37	97% (<.001)
LacClean Gold S	2	130	0.59 (0.37–0.93)	.02	0% (.56)
Duolac 7s	2	76	0.62 (0.43–0.89)	.009	0% (.62)
All *Lactobacillus* strains	16	1498	0.84 (0.72–0.98)	.03	69% (<.001)
Lactobacillus plantarum 299V	5	453	0.73 (0.59–0.92)	.007	59% (.04)
All *Bifidobacterium* strains	5	1161	0.82 (0.67–1.02)	.07	74% (.004)
Bifidobacterium bifidum MIMBb75	2	565	0.69 (0.46–1.04)	.07	83% (.01)
All *Bacillus* strains	3	216	0.44 (0.34–0.57)	<.001	0% (.48)
All *Saccharomyces* strains	2	469	0.94 (0.80–1.11)	.49	0% (.86)
All *Escherichia* strains	2	418	0.86 (0.79–0.93)	<.001	0% (.78)
All *Blautia* strains	1	366	0.93 (0.84–1.03)	.15	N/A
All *Clostridium* strains	1	200	0.80 (0.64–0.99)	.04	N/A
All *Streptococcus* strains	1	54	0.72 (0.53–0.99)	.04	N/A
Patients with IBS-D					
All combination probiotics	13	1272	0.78 (0.67–0.92)	.002	69% (<.001)
VSL#3	2	49	0.42 (0.04–4.85)	.49	82% (.02)
Duolac 7s	2	76	0.62 (0.43–0.89)	.009	0% (.62)
All *Lactobacillus* strains	4	157	0.57 (0.36–0.89)	.01	27% (.25)
All *Saccharomyces* strains	2	169	0.99 (0.76–1.28)	.92	0% (.81)
All *Clostridium* strains	1	200	0.80 (0.64–0.99)	.04	N/A
All *Blautia* strains	1	202	0.94 (0.82–1.08)	.36	N/A
All *Escherichia* strains	1	54	1.00 (0.57–1.74)	1.00	N/A
All *Bifidobacterium* strains	1	44	0.64 (0.36–1.16)	.14	N/A
All *Bacillus* strains	1	40	0.57 (0.31–1.05)	.07	N/A
Patients with IBS-C					
All combination probiotics	4	295	1.01 (0.89–1.14)	.87	8% (.35)
All *Saccharomyces* strains	1	180	0.82 (0.62–1.08)	.16	N/A
All *Blautia* strains	1	164	0.92 (0.78–1.07)	.26	N/A
All *Escherichia* strains	1	35	0.84 (0.41–1.73)	.64	N/A

Goodoory *et al. Gastroenterology* 2023;165:1206-18

Probiotics for Abdominal Pain

- Overall
  - Multi-strain probiotics
  - *Lactobacillus*
  - *Saccharomyces*
  - *Bifidobacterium*
  - *Bacillus*
  - *Escherichia*

	Number of trials	Number of patients	RR of persistence of abdominal pain (95% CI)	*P* value for the difference	I^2 (*P* value for χ^2)
All combination probiotics	32	3469	0.72 (0.64–0.82)	<.001	72% (<.001)
VSL#3	4	144	0.87 (0.64–1.18)	.36	19% (.29)
Lactobacillus paracasei ssp paracasei F19, Lactobacillus acidophilus La5, and *Bifidobacterium lactis Bb12*	3	269	0.97 (0.83–1.14)	.74	0% (.91)
Enterococcus faecalis DSM16440 and *Escherichia coli DSM17252*	2	686	0.67 (0.37–1.22)	.19	92% (<.001)
Bifidobacterium animalis DN173 010, *Streptococcus thermophilus*, and *Lactobacillus bulgaricus*	2	308	0.89 (0.70–1.12)	.32	33% (.22)
LacClean Gold S	2	130	0.76 (0.52–1.10)	.14	0% (.72)
Duolac 7s	2	76	0.55 (0.18–1.65)	.28	73% (.05)
All *Lactobacillus* strains	11	1183	0.59 (0.45–0.76)	<.001	73% (<.001)
Lactobacillus plantarum 299V	3	220	0.45 (0.15–1.35)	.16	78% (.010)
All *Saccharomyces* strains	9	1744	0.75 (0.57–0.99)	.04	89% (<.001)
Saccharomyces cerevisiae I-3856	5	1482	0.64 (0.45–0.90)	.01	93% (<.001)
Saccharomyces boulardii	3	232	1.21 (0.87–1.67)	.26	44% (.17)
All *Bifidobacterium* strains	3	389	0.78 (0.64–0.95)	.02	37% (.20)
All *Bacillus* strains	3	212	0.33 (0.23–0.47)	<.001	10% (.33)
All *Blautia* strains	1	366	0.92 (0.79–1.06)	.25	N/A
All *Escherichia* strains	1	298	0.87 (0.79–0.95)	.002	N/A
All *Clostridium* strains	1	200	0.93 (0.76–1.14)	.49	N/A

Goodoory *et al. Gastroenterology* 2023;165:1206-18

Probiotics for Bloating/Distention

- Overall
  - Multi-strain probiotics
  - *Bacillus*
  - *Bifidobacterium*

	Number of trials	Number of patients	RR of persistence of abdominal bloating or distension (95% CI)	*P* value for the difference	I^2 (*P* value for χ^2)
All combination probiotics	26	2222	0.75 (0.64–0.88)	<.001	78% (<.001)
VSL#3	5	192	0.65 (0.42–1.02)	.06	52% (.08)
Lactobacillus paracasei ssp paracasei F19, Lactobacillus acidophilus La5, and *Bifidobacterium lactis Bb12*	3	269	1.02 (0.89–1.18)	.78	0% (.92)
Bifidobacterium animalis DN173 010, Streptococcus thermophilus, and *Lactobacillus bulgaricus*	2	308	0.86 (0.60–1.26)	.45	71% (.06)
LacClean Gold S	2	130	0.98 (0.67–1.45)	.94	8% (.30)
Duolac 7s	2	76	0.94 (0.61–1.47)	.80	0% (.88)
All *Lactobacillus* strains	5	723	0.67 (0.43–1.04)	.07	88% (<.001)
All *Saccharomyces* strains	5	641	0.87 (0.64–1.17)	.34	60% (.04)
Saccharomyces boulardii	3	232	0.97 (0.77–1.23)	.80	0% (.79)
All *Bacillus* strains	3	212	0.41 (0.31–0.56)	<.001	0% (.83)
All *Clostridium* strains	1	200	0.97 (0.81–1.16)	.75	N/A
All *Bifidobacterium* strains	1	122	0.66 (0.49–0.88)	.005	N/A

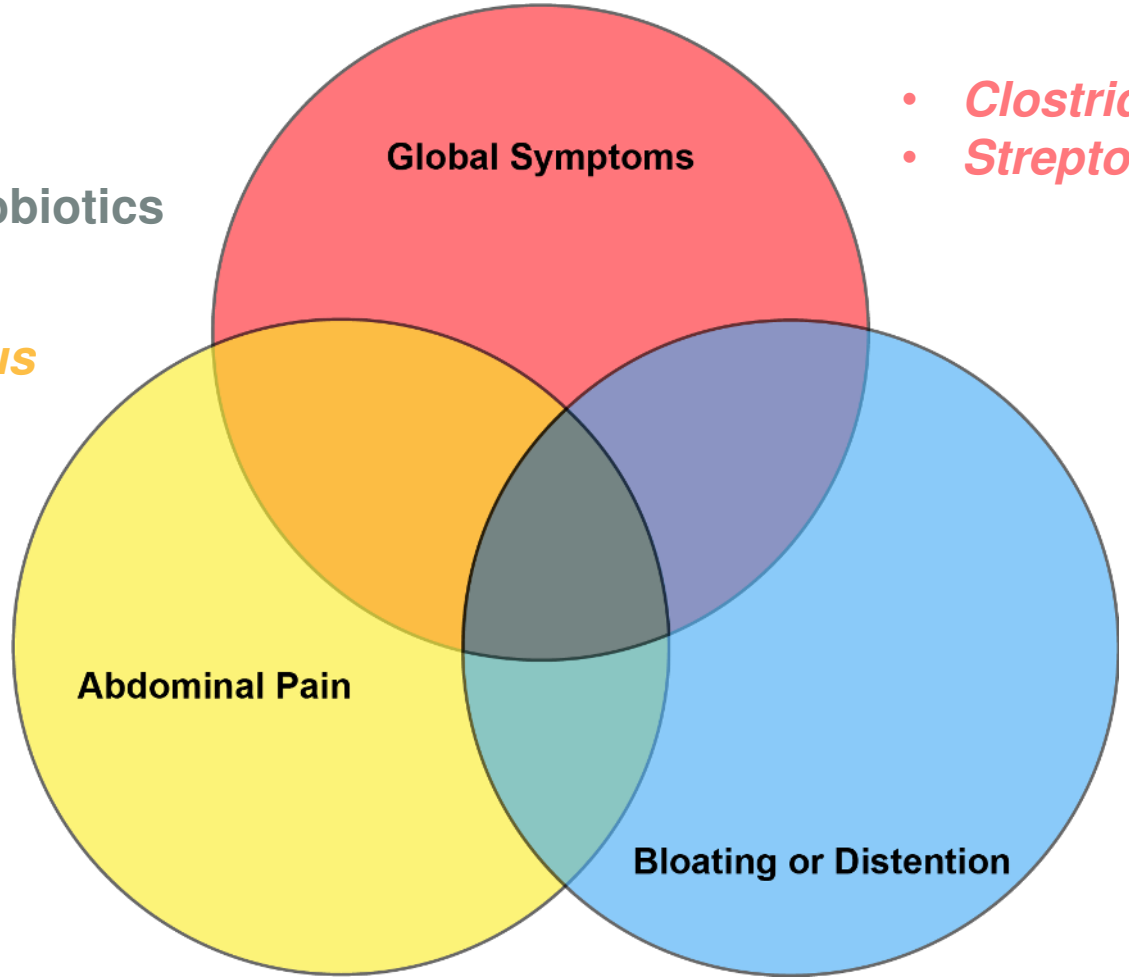
Goodoory *et al. Gastroenterology* 2023;165:1206-18

Probiotics for IBS: Stratified by Strain and Outcome

- Multi-strain probiotics

- *Lactobacillus*
- *Escherichia*

- *Saccharomyces*

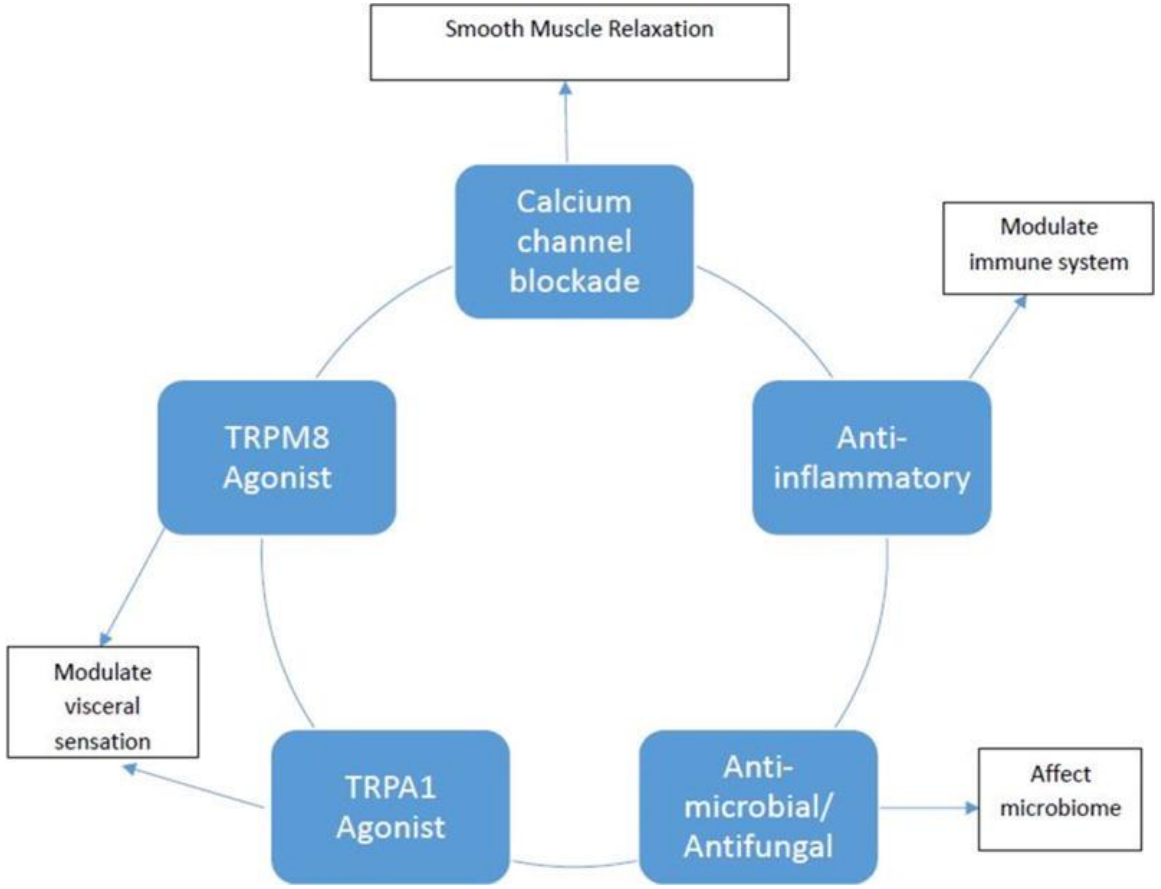


- *Clostridium*
- *Streptococcus*

- *Bifidobacterium*
- *Bacillus*

Peppermint Oil

- Peppermint (*Mentha x piperita*), a source of menthol and menthone
- Among oldest herbs used for culinary and medicinal purposes
- Peppermint oil and leaves used topically for muscle pain, nerve pain, itching, fragrance

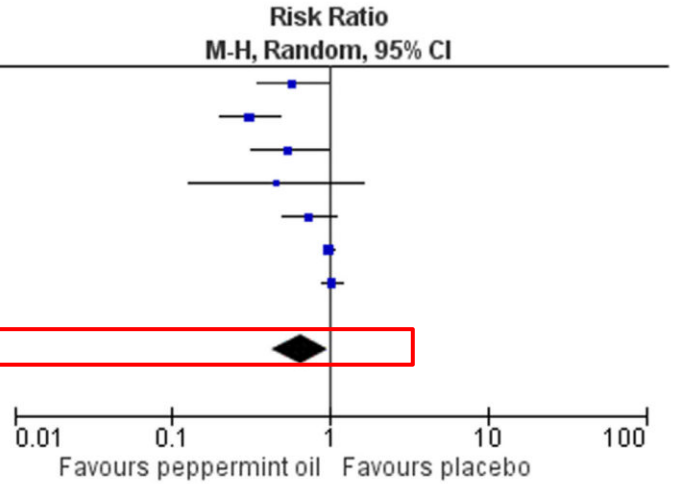


Chumpitazi *et al. Aliment Pharmacol Ther* 2018;47:738-52
Image Source: Wikipedia

Peppermint Oil: Global Symptoms and Abdominal Pain

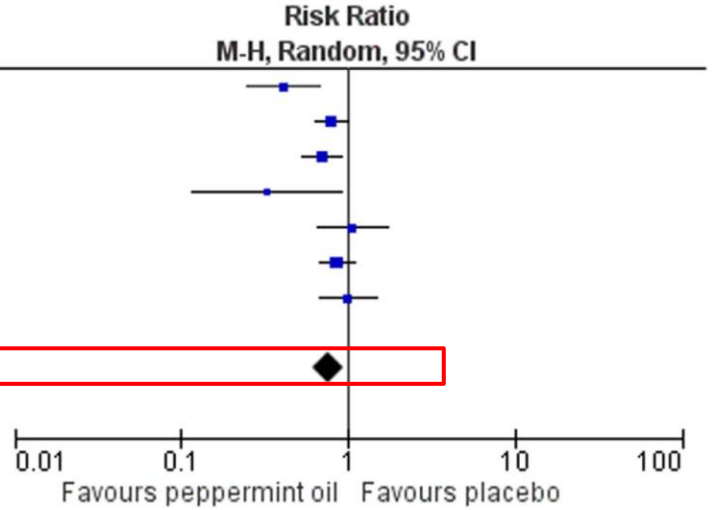
Study or Subgroup	Favours peppermint oil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Lech 1988	10	23	18	24	14.0%	0.58 [0.34, 0.98]	1988
Capanni 2005	18	91	56	87	14.9%	0.31 [0.20, 0.48]	2005
Cappello 2007	10	28	19	29	13.5%	0.55 [0.31, 0.96]	2007
Cash 2016	3	35	7	37	6.6%	0.45 [0.13, 1.62]	2016
Mosaffa-Jahromi 2016	19	40	26	40	15.4%	0.73 [0.49, 1.09]	2016
Weerts 2020	118	125	61	64	17.9%	0.99 [0.92, 1.06]	2020
Nee 2021	39	46	72	87	17.6%	1.02 [0.88, 1.20]	2021
Total (95% CI)		**388**		**368**	**100.0%**	**0.65 [0.43, 0.98]**	
Total events	217		259				

Heterogeneity: Tau² = 0.24; Chi² = 100.32, df = 6 (P < 0.00001); I² = 94%
Test for overall effect: Z = 2.06 (P = 0.04)



Study or Subgroup	Peppermint oil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Liu 1997	14	55	34	55	10.7%	0.41 [0.25, 0.68]	1997
Merat 2010	31	45	39	45	21.2%	0.79 [0.63, 1.00]	2010
Alam 2013	23	37	33	37	18.9%	0.70 [0.53, 0.92]	2013
Cash 2016	4	35	13	37	3.5%	0.33 [0.12, 0.90]	2016
Mosaffa-Jahromi 2016	18	40	17	40	10.7%	1.06 [0.64, 1.74]	2016
Weerts 2020	70	125	42	64	20.8%	0.85 [0.67, 1.08]	2020
Nee 2021	21	46	40	87	14.1%	0.99 [0.67, 1.47]	2021
Total (95% CI)		**383**		**365**	**100.0%**	**0.76 [0.62, 0.93]**	
Total events	181		218				

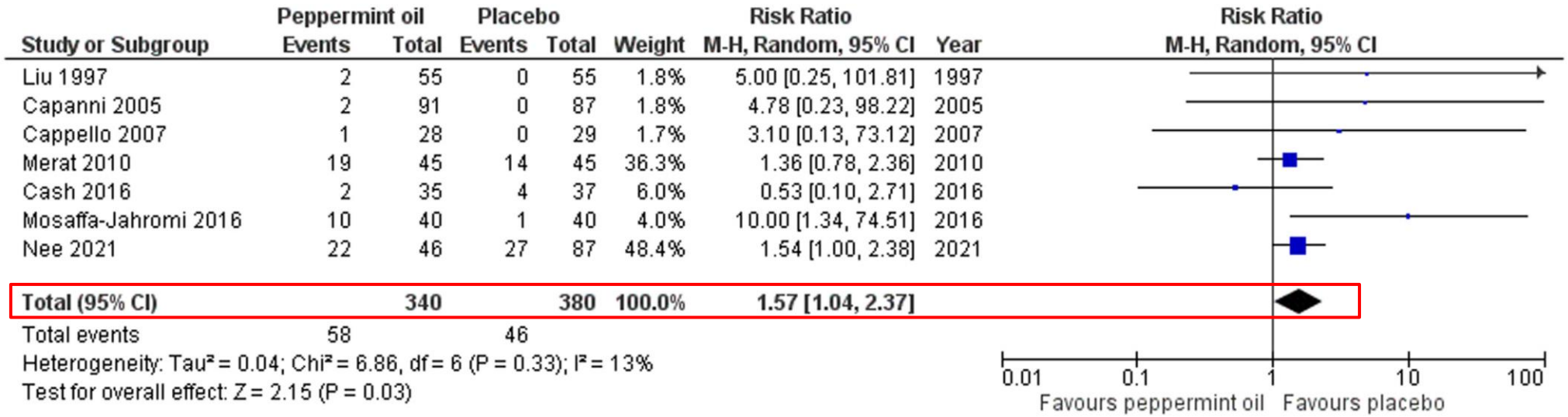
Heterogeneity: Tau² = 0.04; Chi² = 13.58, df = 6 (P = 0.03); I² = 56%
Test for overall effect: Z = 2.67 (P = 0.008)



Ingrosso *et al. Aliment Pharmacol Ther* 2022;56:932-41

Peppermint Oil: Safety

- 17.1% vs. 12.1% (NNH 14.5)
- Reported adverse effects: Heartburn/reflux, dyspepsia, flatulence



Study or Subgroup	Peppermint oil Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Liu 1997	2	55	0	55	1.8%	5.00 [0.25, 101.81]	1997
Capanni 2005	2	91	0	87	1.8%	4.78 [0.23, 98.22]	2005
Cappello 2007	1	28	0	29	1.7%	3.10 [0.13, 73.12]	2007
Merat 2010	19	45	14	45	36.3%	1.36 [0.78, 2.36]	2010
Cash 2016	2	35	4	37	6.0%	0.53 [0.10, 2.71]	2016
Mosaffa-Jahromi 2016	10	40	1	40	4.0%	10.00 [1.34, 74.51]	2016
Nee 2021	22	46	27	87	48.4%	1.54 [1.00, 2.38]	2021
Total (95% CI)		**340**		**380**	**100.0%**	**1.57 [1.04, 2.37]**	
Total events	58		46				

Heterogeneity: Tau² = 0.04; Chi² = 6.86, df = 6 (P = 0.33); I² = 13%

Test for overall effect: Z = 2.15 (P = 0.03)

Ingrosso *et al. Aliment Pharmacol Ther* 2022;56:932-41

Take Home Points: Diets

- Screen patients for eating disorders prior to initiating an exclusion diet
- Low FODMAP diet is effective for treatment of IBS
- Begin with strict elimination for 4-6 weeks
  - If there is benefit, proceed with gradual reintroduction of foods with FODMAPs
  - If there is no benefit, switch to a different dietary strategy
- There is a risk of nutritional deficiency on an exclusion diet, so careful monitoring is crucial

Take Home Points: Diets

- Targeted symptoms-based food exclusion can be considered
- Non-specific food elimination is not recommended
- Data on the Mediterranean diet or others are inconsistent

Take Home Points: Dietary Supplements

- Fiber (preferably soluble fiber) consumption can help with global IBS symptoms
- Fiber (soluble or insoluble) can help with constipation
- Multi-strain probiotics can help with global IBS symptoms, abdominal pain, and bloating and distention
- Peppermint oil can improve global IBS symptoms and abdominal pain
- Reported adverse effects with peppermint oil are heartburn/reflux, dyspepsia, flatulence

Thank You

UCLA Health