

# Module 2 Summary Factsheet

# 1. Suspected dietary triggers in IBS

People with IBS often associate food intake with the development of gastrointestinal symptoms[1] and dietary restriction is common in this population. Foods commonly implicated with the onset of IBS symptoms include:

- dairy products
- wheat products
- caffeine
- cabbage
- onion
- peas
- beans
- spicy / fatty / smoked foods[2-5].

However, limited evidence supports dietary approaches that restrict any one of these components.

#### 1.1 Role of fat

Observational data suggest that dietary fat intake may trigger IBS symptoms in some patients. However, no high quality, RCTs have measured the effect of fat-restricted diets in the management of IBS. Therefore, we do not know if fat causes IBS symptoms, or whether fat restriction improves IBS symptom control.

### 1.2 Protein

Various proteins have been implicated in onset of IBS symptoms, including  $\beta$ -casein (from milk); rubisco (from spinach); wheat-germ lectin;  $\alpha$ -amylase/trypsin inhibitors, and gluten. However, limited evidence suggests that any one of these proteins triggers IBS symptoms.

Although considerable research has looked at gluten, and the diagnosis of non-coeliac gluten sensitivity (NCGS) has been coined, improvements observed with gluten restriction may be attributed to nocebo responses and/or a reduced intake of fructans (from wheat).

# 1.3 Carbohydrates

#### 1.3.1 Prebiotics

A prebiotics is defined as a substrate that is selectively utilised by host microorganisms conferring a health benefit[6]. Carbohydrates with prebiotic actions include fructooligsaccharides (FOS), galactooligsaccharides (GOS), xylooligosaccharides (XOS), isomaltose (IMO) and inulin.

Although a few trials have assessed the effect of prebiotic supplements in IBS, most have been plagued by design issues (e.g. failing to control background, prebiotic intake from food), poor compliance and high drop-out rates (possibly due to the high doses used and consequent poor tolerability). Very little is known about the effect of natural prebiotics (from food) on IBS symptom control.

## 1.3.2 Short-chain carbohydrates

#### Lactose

- Lactose is a disaccharide made up of two sugar units, glucose and galactose.
- Rich sources include cows' milk, soft cheeses, custard, sweetened condensed milk, evaporated milk, and ice cream.
- In individuals who lack sufficient lactase to complete the breakdown of lactose, malabsorbed lactose attracts water into the small intestine and passes undigested into the large intestine, where it is fermented by gut bacteria. In some people (those with lactose intolerance), fermentation of malabsorbed lactose causes unpleasant symptoms, including bloating, wind, stomach cramps and diarrhoea.
- Reasons for lactase enzyme insufficiency include:
  - > Non-persistence of the lactase gene expression dependent on ethnicity
  - > Congenital abnormality due to genetic makeup rare
  - > Illnesses (e.g. gastroenteritis, untreated coeliac disease) transient

#### Polvols

- Polyols are sugar alcohols that include sorbitol, mannitol, xylitol, and maltitol.
- Natural food sources of sorbitol and/or mannitol, include sweet corn, pears, apples, blackberries, stone fruit, cauliflower, mushroom, snowpeas, sugar free chewing gum, lollies and mints.
- Malabsorption of sorbitol and mannitol is relatively common, so sorbitol and/or mannitol malabsorption are not considered diagnoses per se.
- Excess polyol molecules move slowly through the small intestine, attracting water.
  This increases luminal water content and results in distension. Malabsorbed
  polyols enter the large intestine where they are fermented by colonic bacteria,
  resulting in gas production and bloating.

#### Fructose

- Foods rich in excess fructose include apple, pear, mango, dried fruit, asparagus, sugar snap peas, honey, high fructose corn syrup and fruit juice
- Fructose absorption is dependent on the dose consumed and the luminal glucose concentration. If a sufficiently large dose of fructose is consumed, malabsorption is universal. However, approximately one third of the population exhibits very limited ability to absorb free fructose and is considered to have 'fructose malabsorption'.

#### **Fructans**

- All humans (healthy and unhealthy) malabsorb fructans in the small intestine, facilitating their delivery to the large intestine where they are rapidly fermented by resident bacteria. This leads to the expansion of beneficial bacteria such as bifidobacteria and lactobacilli[7, 8].
- While smaller doses of fructans are generally well tolerated by healthy people, higher doses can cause symptoms of gastroesophageal reflux, flatulence, bloating and abdominal pain. These symptoms are experienced with lower doses of fructans in people with IBS, compared to those without IBS.

#### GOS

- Galactooligosaccharides (GOS) are oligosaccharides present in foods primarily as raffinose and stacchyose. GOS are universally malabsorbed because humans lack the enzyme (α-galactosidase) needed to hydrolyse the galactosidic linkages of stachyose and raffinose into their simple sugar units.
- Malabsorbed GOS travels to the large intestine where it is rapidly fermented by gut bacteria. In particular, GOS consumption promotes the growth of beneficial groups of bacteria (bifidobacteria and lactobacilli)[7, 8].
- Rich sources of GOS include vegetables (e.g. green peas, beetroot), nuts (e.g. cashews and pistachios), pulses (e.g. red kidney beans, baked beans)

Fructans and GOS are considered prebiotics as they selectively stimulate the growth and activity of beneficial gut bacteria, in particular bifidobacteria and lactobacillus.

# 2. Diet therapies for IBS

## 2.1 Low lactose diet

- Lactose is found predominantly in dairy foods, although as shown in Table 1,
  the lactose content of dairy foods varies widely. This is important because most
  people who malabsorb lactose can tolerate 12–15g of lactose per day (equivalent
  to ~250ml of regular milk), and possibly more if lactose intake is spread out over
  the day[9, 10].
- Dietary restriction of lactose is necessary to control symptoms in people with IBS and lactose intolerance. However, lactose restriction in isolation is considered an ineffective therapy for IBS.
- Lactase enzyme preparations are available over-the-counter, allowing people to consume larger lactose loads. However these vary in their efficacy and do not help all people with lactose intolerance[11].

Table 1 - Lactose content of common dairy products.

DAIRY PRODUCT	<b>LACTOSE</b> (grams per serve)	SERVING SIZE (grams or millilitres)	LACTOSE classification / serve (low / moderate high)	
Full cream milk	16g	257ml	High	
Low-fat milk	16g	257ml	High	
Skim milk	13g	257ml	High	
Natural yoghurt	10g	200g	High	
Flavoured yoghurt	7g	200g	High	
Thickened cream	2g	40g	Moderate	
Ice cream	3g	88g	Moderate	
Sour cream	1g	40g	Low	
Cream cheese	1g	40g	Low	
Ricotta cheese	< 1g	40g	Low	
Cottage cheese	< 1g	40g	Low	
Feta cheese	< 1g	40g	Low	
Cheddar cheese	< 1g	40g	Low	
Camembert cheese	< 1g	40g	Low	
Brie cheese	< 1g	40g	Low	

### 2.2 Fructose and sorbitol restricted diet

While a small number of studies have investigated the benefit of fructose and sorbitol restricted diets to treat IBS, these studies were uncontrolled, with methods poorly described and as such, these diets never gained traction in clinical practice.

## 2.3 Fructose malabsorption diet

Numerous studies have measured the efficacy of fructose restricted diets in IBS[12-15]. While some of these showed improvements in gastrointestinal symptoms, symptom improvements were greater when other FODMAPs were restricted at the same time (e.g. fructose + fructans)[16].

#### 3. FODMAPs

FODMAP is an acronym which stands for Fermentable Oligo- Di- Mono-saccharides And Polyols.

## 3.1 Mechanism of action

The sensations of pain and discomfort experienced by people with IBS are exaggerated due to disturbances in gut motility and/or heightened gut sensitivity. When the gut is distended by the movement of gas and water, this causes pain and bloating. Distension of the gut may also cause changes in gut motility and bowel habits, including diarrhoea, constipation or a mixture of both.

Short-chain carbohydrates behave similarly in the intestine.

- Due to their small size and because they are either poorly absorbed or not absorbed at all, they drag water into the intestine via osmosis[17, 18].
- They are also readily fermented by colonic bacteria, so upon malabsorption in the small intestine they enter the large intestine where they are fermented, generating gases, including hydrogen, carbon dioxide and methane[19].

These actions cause an expansion in volume of intestinal contents, stretching the intestinal wall and stimulating nerves in the gut. It is the 'stretching' of the intestinal wall that triggers the sensations of pain and discomfort that are commonly experienced by IBS sufferers[19-21].

The different FODMAP subgroups are known to have different actions in the gut — see Box 1.

## Box 1 - Effects of different FODMAP subgroups

## Oligosaccharides [fructans and galacto-oligosaccharides (GOS)]

Not absorbed in the small intestine because humans lack the enzymes needed to break the bonds between these chains of sugars. Fermented by gut bacteria in the large intestine producing gas. This causes wind in healthy people, which is a normal part of digestion, but in people with IBS, the accumulation of gas causes symptoms of bloating, abdominal discomfort and altered motility.

### Fructose and polyols (sorbitol and mannitol)

Slowly absorbed in the small intestine, resulting in water movement into the small intestine. If these sugars reach the large intestine, they are fermented by bacteria creating gas. These effects contribute to symptoms of pain, bloating and altered bowel habit.

#### Lactose

Normally absorbed in the small intestine, but in people who lack the enzyme needed to break this disaccharide into individual sugars (glucose and galactose), lactose reaches the large intestine intact. Lactose attracts water into the small and large intestine (osmotic effect) and is fermented by gut bacteria, resulting in symptoms of bloating, wind, pain and diarrhoea (depending upon the dose of lactose consumed).

### 4. Low FODMAP diet

FODMAPs are found in a wide range of foods including fruit, vegetables, breads, cereals, grains, nuts, seeds, dairy products, processed foods and beverages (Table 2).

Table 2 - Foods rich in different FODMAP subgroups

	FRUCTANS	GOS	SORBITOL	MANNITOL	FRUCTOSE IN EXCESS OF GLUCOSE	LACTOSE
FRUIT	Grapefruit Persimmon Dates Dried fig Dried pineapple Dried mango		Apple Pear Avocado Apricot Nectarine Plum Yellow peach Blackberries Lychee Fresh coconut		Apple Pear Mango Boysenberry Fig (fresh) Grapes Watermelon	
VEGETABLES	Onion Garlic Leek (bulb only) Artichoke (globe) Artichoke (Jerusalem) Spring onion Bitter melon	Green peas		Mushrooms Cauliflower Celery Sweet potato Snow peas	Asparagus Sugar snap peas	
BREADS AND CEREALS	Breakfast cereal (wheat/rye barley based) Bread (wheat/ rye based) Pasta Pumperkickle bread Barley flakes Cous cous (wheat) Gnocchi Semolina					
PULSES / VEGETARIAN	Falafels	Black beans Borlotti beans Haricot beans Navy beans Red kidney beans Split peas Baked beans				
NUTS AND SEEDS		Cashews Pistachios				
DAIRY / ALTERNATIVES		Soy milk (from soy beans)	Coconut milk			Cows' milk Yoghurt Custard Sweetened condensed milk
SUGARS / SWEETENERS			Sugar-free confectionery		Honey, high fructose corn syrup	
OTHER	Garlic / onion based marinades and sauces Vegetarian mince	Vegetarian mince			Fruit juice	

# 5.1 Efficacy

Numerous studies have shown that a low FODMAP diet improves overall functional symptoms, symptom severity and quality of life in people with IBS, when compared to a normal Western diet[22-46]. These studies have included observational studies, comparative studies, and RCTs. These studies are summarised in the following table:

Table 3 - Evidence supporting the efficacy of a low FODMAP diet (continued on next page)

REFERENCE	STUDY DESIGN	SUBJECTS	FINDINGS RELATED TO SYMPTOM CONTROL	
STUDIES INVESTIGATING PRECURSORS OF THE LOW FODMAP DIET				
Ledochowski et al., 2000; Austria [22]	Consecutive patients educated to restrict fructose and sorbitol for 4-weeks	Patients with gastrointestinal complaints and fructose malabsorption (n=53)	27% reduction in meteorism (p<0.0001)	
Bohmer et al., 2001; The Netherlands [23]	Consecutive patients educated to restrict lactose for 6-weeks	Patients with IBS and lactose malabsorption (n=17)	17% reduction in cumulative symptom score (p<0.001)	
Shepherd et al., 2006; Australia [24]	Retrospective telephone questionnaire after restriction of fructose and fructan	Patients with IBS previously educated in a fructose and fructan restricted diet (n=62)	74% of all patients responded positively in all abdominal symptoms	
Shepherd et al., 2008; Australia [25]	Randomised, placebo- controlled re-challenge of fructose and fructans	Patients with IBS and fructose malabsorption who previously responded to diet that restricted fructose and fructans (n=25)	70% of patients receiving fructose, 77% receiving fructans, and 79% receiving a mixture reported symptoms were not adequately controlled, compared with 14% receiving glucose (p<0.002)	
	STUDIES UTILISING THE CO	MPLETE LOW FODMAP DIET		
Barrett et al., 2010; Australia [26]	Randomized, cross-over, single-blinded intervention study – low vs high FODMAP	Ileostomates without evidence of small intestinal disease (n=12)	Water content of daily output decreased by 20% on the low FODMAP diet and patients felt effluent consistency was thicker (p=0.006)	
Ong et al., 2010; Australia [27]	Single-blind, crossover intervention, feeding trial — low vs high FODMAP	Healthy subjects (n=15) and patients with IBS (n=15)	Gastrointestinal symptoms and lethargy were significantly induced by the high FODMAP diet in patients with IBS (p=0.002)	
Staudacher et al., 2011; United Kingdom [28]	Non-randomised comparative study – low FODMAP vs standard (NICEa) diet	IBS patients who received standard (n = 39) or low FODMAP dietary advice (n = 43)	76% of patients in the low FODMAP group reported satisfaction compared to the standard group (p=0.038)	

Table 3 - Evidence supporting the efficacy of a low FODMAP diet (continued on next page)

REFERENCE	STUDY DESIGN	SUBJECTS	FINDINGS RELATED TO SYMPTOM CONTROL	
STUDIES UTILISING THE COMPLETE LOW FODMAP DIET				
Staudacher et al., 2012; United Kingdom [29]	Randomized, controlled trial  – low FODMAP vs habitual diet	Patients with IBS randomised to low FODMAP diet (n=19) or habitual diet (n=22)	More patients in the intervention group reported adequate control of symptoms (13/19, 68%) compared with controls (5/22, 23%; p=0.005)	
De Roest et al., 2013; New Zealand [30]	Prospective symptom questionnaire following low FODMAP diet education	Patients with IBS patients taught the low FODMAP diet (n=90)	72% were satisfied with symptom response	
Halmos et al., 2014; Australia [31]	Randomized, controlled, single-blind, cross-over, feeding trial – low FODMAP vs typical Australian diet	Patients with IBS (n=30) and healthy subjects (n=8) – all low FODMAP diet-naïve	Subjects with IBS had significantly lower overall symptoms on the low FODMAP diet compared to the Australian diet (p<0.001). Improvements were also seen in bloating, pain and flatulence	
Pedersen et al., 2014; Denmark [32]	Randomised, unblinded controlled trial – low FODMAP diet vs probiotic vs normal diet	Patients with IBS randomised to low FODMAP diet (n=42), probiotics (n=41) and normal diet (n=40)	Significant reduction in symptom score with low FODMAP diet and probiotic groups compared to the normal diet (p<0.01)	
Bohn et al., 2015; Sweden [33]	Multi-centre, randomised, parallel, single-blind study – low FODMAP vs traditional (NICE) advice	IBS patients received low FODMAP diet (n=33) vs traditional advice (n=34) for 4-weeks	IBS symptom severity was reduced in both groups during the intervention (p<.0001), with no difference between the groups (p=0.62)	
Chumpitazi et al., 2015; USA [34]	Double-blind, crossover trial  – low FODMAP vs typical  American diet	2-day interventions in children (aged 7-17 years) with IBS (n=33)	Less abdominal pain occurred with the low FODMAP diet (p<0.05)	
Wingham et al., 2015; United Kingdom [35]	Non-randomised comparative study – group vs one-to-one FODMAP education	Patients with IBS received either group education (n=263) or one-to-one education (n=101) on the low FODMAP diet	Group education was as clinically effective as one-to-one education. In addition, group education was found to be more cost-effective	
Eswaran et al., 2016; United States of America [36]	Randomised controlled trial – low FODMAP diet vs modified traditional (NICE) advice	Patients with IBS-D randomised to either low FODMAP diet (n=45) or modified NICE diet (n=39) for 4-weeks	Adequate relief reported in 52% on low FODMAP diet vs 41% on the modified NICE diet (p=0.31). Higher proportion had improved abdominal pain with low FODMAP diet (p=0.008)	

Table 3 - Evidence supporting the efficacy of a low FODMAP diet (continued)

REFERENCE	STUDY DESIGN	SUBJECTS	FINDINGS RELATED TO SYMPTOM CONTROL	
STUDIES UTILISING THE COMPLETE LOW FODMAP DIET				
Peters et al., 2016; Australia [37]	Randomised clinical trial  – low FODMAP diet vs gut- directed hypnotherapy vs combined treatment	Patients with IBS randomised to either low FODMAP diet (n=24), hypnotherapy (n=25) or combination therapy (n=25) for 6-weeks	Improvements in overall symptoms were observed from baseline to week 6 for hypnotherapy (72%), diet (71%), and combination therapy (72%) with no difference across groups (p=0.67)	
Maagaard et al., 2016; Denmark [38]	Retrospective, cross- sectional study following low FODMAP diet education	Questionnaire sent to IBS (n=131) and IBD (n=49) patients previously educated on a low FODMAP diet	Eighty-six percent reported either partial (54%) or full (32%) efficacy with greatest improvement of bloating (82%) and abdominal pain (71%)	
McIntosh et al., 2016; Canada [39]	Prospective, randomised, single blind parallel study – low vs high FODMAP	IBS FODMAP diet-naïve patients (n=40) who received dietary advice on either low or high FODMAP diet	72% had reduced symptoms on the low FODMAP diet compared to 21% on the high FODMAP diet (p=0.01)	
O'Keeffe et al., 2018; UK [40]	Prospective, uncontrolled, unblinded intervention study that measured short and long term symptom response to dietitian delivered education re FODMAP restriction and reintroduction.	Patients with IBS (n=103) who all completed 2 education sessions with a specialised gastroenterology dietitian about 1) FODMAP restriction and 2) FODMAP reintroduction	Satisfactory relief of IBS symptoms reported by 12% at baseline, 61% following FODMAP restriction (6-weeks post baseline) and 57% following FODMAP reintroduction (6-18 months post baseline). 82% followed an 'adapted FODMAP diet' at 6-18 months post baseline [M., 2018 #1966].	
Schumann, D., et al; Germany [41]	Single blinded RCT that compared a 12 week yoga intervention to dietitian delivered education about a low FODMAP diet	Patients with IBS (n=59) randomised to yoga (2 sessions per week for 12 weeks) or low FODMAP diet education (3 sessions over 12 weeks)	No difference in symptom severity between yoga and low FODMAP diet interventions. At 12 weeks, 82% of patients reported adequate relief of their IBS symptoms.	
Schumann, D., et al; Germany [42]	Meta-analysis and review that looked at the efficacy of a low FODMAP diet	Nine RCTs that included 596 subjects and compared a low FODMAP diet to another dietary intervention.	A low FODMAP diet led to significant improvements in gastrointestinal symptoms, abdominal pain, and QOL compared to other diets. A low FODMAP diet also reduced luminal bifidobacteria in 3 studies. No adverse events were reported.	

Table 3 - Evidence supporting the efficacy of a low FODMAP diet (continued on next page)

REFERENCE	STUDY DESIGN	SUBJECTS	FINDINGS RELATED TO SYMPTOM CONTROL	
STUDIES UTILISING THE COMPLETE LOW FODMAP DIET				
Zahedi, et. al; 2018; Iran [43]	Randomised controlled trial. Patients educated by GI dietitian to follow a 6 week low FODMAP diet vs 'general dietary advice (GDA). GDA was consistent with British Dietetic Association guidelines to limit caffeine, alcohol, spicy food, fatty food, carbonated drinks; chewing gum and polyol sweeteners.	Patients with IBS-D (n=110)	Both diets improved over IBS symptoms, but this improvement was greater in the LFD group.	
Staudacher, et. al; 2017; UK [44]	Randomised controlled trial. Subjects counselled to follow a sham or low FODMAP diet, along with a placebo or multistrain probiotic (4 group study).	Subjects with IBS (n=104)	Adequate symptom relief experienced by more patients following the low FODMAP diet than the sham diet.	
Paduano, et. al; 2019; Italy [45]	Non-randomised intervention study. Participants educated by a dietitian to follow 3 different diets in succession and each for 4 weeks: low FODMAP diet, gluten free diet and balanced Mediterranean diet.	Subjects with IBS (n=42)	All the diets reduced symptom severity, bloating and QOL, but patients expressed a strong preference for the balanced diet.	
Marsh, et. al; 2015; Australia [46]	Systematic review and meta-analysis.	Six RCTs and 16 non- randomized interventions in people with IBS or IBD.	LFD reduced IBS symptom severity, improved IBS QOL and improved abdominal pain, bloating and overall symptoms.	

Table 4 - Guideline recommendations for the FODMAP diet

GUIDELINE	RECOMMENDATION
British Society of Gastroenterology 2021[47]	A low FODMAP diet is an effective second line therapy, but implementation should be supervised by a dietitian and FODMAPs should be reintroduced to tolerance.
American College of Gastroenterology[48]	A limited trial of a low FODMAP diet is recommended to improve global symptoms. The 3 step FODMAP diet should be followed under the guidance of a GI trained dietitian.
Japanese Society of Gastroenterology 2020[49]	Patients with IBS should initially be treated with behavioral modification (including exercise) and diet therapy (such as the low FODMAP diet).
Korean Society of Neurogastroenterology and Motility 2017[50]	A low FODMAP is effective and recommended as a first line therapy alongside medical treatment in patients with medically diagnosed IBS and alarm symptoms excluded.
Spanish clinical practice guideline for the management of IBS and functional constipation[51]	The low FODMAP diet improves abdominal pain and distension, but not constipation in IBS. Current evidence does not support the routine use of this diet in IBS.
British Dietetic Association 2016[52]	A low FODMAP diet is recommended as a second-line therapy, after dietetic assessment of lifestyle and eating habits (focussing on alcohol, fat, fibre, milk, spicy foods and use of probiotics). A low FODMAP diet should be delivered by a dietitian with expertise in FODMAP education.
NICE Guidelines 2015[53]	A low FODMAP diet is recommended as a second-line therapy if symptoms persist after general lifestyle and dietary advice. See NICE Guidelines diet in Module 9. A low FODMAP diet should be delivered by a healthcare professional with expertise in dietary management.

## References

- 1. Monsbakken, K.W., P.O. Vandvik, and P.G. Farup, Perceived food intolerance in subjects with irritable bowel syndrome-- etiology, prevalence and consequences. Eur J Clin Nutr, 2006. 60(5): p. 667-72.
- 2. Ostgaard, H., et al., Diet and effects of diet management on quality of life and symptoms in patients with irritable bowel syndrome. Mol Med Rep, 2012. 5(6): p. 1382-90.
- 3. Bohn, L., et al., Self-reported food-related gastrointestinal symptoms in IBS are common and associated with more severe symptoms and reduced quality of life. Am J Gastroenterol, 2013. 108(5): p. 634-41.
- 4. Nanda, R., et al., Food intolerance and the irritable bowel syndrome. Gut, 1989. 30(8): p. 1099- 104.
- 5. Simren, M., et al., Food-related gastrointestinal symptoms in the irritable bowel syndrome. Digestion, 2001. 63(2): p. 108-15.
- 6. Gibson, G.R., Scott, K.P., Rastall, R.A. et. al., Dietary prebiotics: current status and new definition. Food Science and Technology Bulletin: Functional Foods 2017. 7(1): p. 1.
- 7. Roberfroid, M.B., J.A. Van Loo, and G.R. Gibson, The bifidogenic nature of chicory inulin and its hydrolysis products. J Nutr, 1998. 128(1): p. 11-9.
- 8. Gibson, G.R., A.L. McCartney, and R.A. Rastall, Prebiotics and resistance to gastrointestinal infections. Br J Nutr, 2005. 93 Suppl 1: p. S31-4.
- 9. Shaukat, A., et al., Systematic review: effective management strategies for lactose intolerance. Ann Intern Med, 2010. 152(12): p. 797-803.
- 10. Suarez, F.L., et al., Tolerance to the daily ingestion of two cups of milk by individuals claiming lactose intolerance. Am J Clin Nutr, 1997. 65(5): p. 1502-6.
- 11. Vesa, T.H., P. Marteau, and R. Korpela, Lactose intolerance. J Am Coll Nutr, 2000. 19(2 Suppl): p. 165S-175S.
- 12. Berg, L.K., et al., Effect of fructose-reduced diet in patients with irritable bowel syndrome, and its correlation to a standard fructose breath test. Scand J Gastroenterol, 2013. 48(8): p. 936-43.
- 13. Goldstein, R., D. Braverman, and H. Stankiewicz, Carbohydrate malabsorption and the effect of dietary restriction on symptoms of irritable bowel syndrome and functional bowel complaints. Isr Med Assoc J, 2000. 2(8): p. 583-7.
- 14. Fernandez-Banares, F., et al., Sugar malabsorption in functional bowel disease: clinical implications. Am J Gastroenterol, 1993. 88(12): p. 2044-50.
- 15. Choi, Y.K., et al., Fructose intolerance in IBS and utility of fructose-restricted diet. J Clin Gastroenterol, 2008. 42(3): p. 233-8.
- 16. Shepherd, S.J., et al., Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. Clin Gastroenterol Hepatol, 2008. 6(7): p. 765-71.

- 17. Murray, K., et al., Differential effects of FODMAPs (fermentable oligo-, di-, mono-saccharides and polyols) on small and large intestinal contents in healthy subjects shown by MRI. Am J Gastroenterol, 2014. 109(1): p. 110-9.
- 18. Marciani, L., et al., Postprandial changes in small bowel water content in healthy subjects and patients with irritable bowel syndrome. Gastroenterology, 2010. 138(2): p. 469-77, 477 e1.
- 19. Ong, D.K., et al., Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. J Gastroenterol Hepatol, 2010. 25(8): p. 1366-73.
- 20. Staudacher, H.M., et al., Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. J Hum Nutr Diet, 2011. 24(5): p. 487-95.
- 21. Tuck, C.J., et al., Fermentable oligosaccharides, disaccharides, monosaccharides and polyols: role in irritable bowel syndrome. Expert Rev Gastroenterol Hepatol, 2014. 8(7): p. 819-34. 22.
- 22. Ledochowski M, Widner B, Bair H, Probst T, Fuchs D. Fructose- and sorbitol-reduced diet improves mood and gastrointestinal disturbances in fructose malabsorbers. Scandinavian journal of gastroenterology. 2000;35(10):1048-52.
- 23. Bohmer CJ, Tuynman HA. The effect of a lactose-restricted diet in patients with a positive lactose tolerance test, earlier diagnosed as irritable bowel syndrome: a 5-year follow-up study. Eur J Gastroenterol Hepatol. 2001;13(8):941-4.
- 24. Shepherd SJ, Gibson PR. Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management. Journal of the American Dietetic Association. 2006;106(10):1631-9.
- 25. Shepherd SJ, Parker FC, Muir JG, Gibson PR. Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association. 2008;6(7):765-71.
- 26. Barrett JS, Gearry RB, Muir JG, Irving PM, Rose R, Rosella O, et al. Dietary poorly absorbed, short-chain carbohydrates increase delivery of water and fermentable substrates to the proximal colon. Alimentary pharmacology & therapeutics. 2010;31(8):874-82.
- 27. Ong DK, Mitchell SB, Barrett JS, Shepherd SJ, Irving PM, Biesiekierski JR, et al. Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. Journal of gastroenterology and hepatology. 2010;25(8):1366-73.
- 28. Staudacher HM, Whelan K, Irving PM, Lomer MC. Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. Journal of human nutrition and dietetics: the official journal of the British Dietetic Association. 2011;24(5):487-95. 29. Staudacher HM, Lomer
- 29. MC, Anderson JL, Barrett JS, Muir JG, Irving PM, et al. Fermentable carbohydrate restriction reduces luminal bifidobacteria and gastrointestinal symptoms in patients with irritable bowel syndrome. The Journal of nutrition. 2012;142(8):1510-8.

- 30. de Roest RH, Dobbs BR, Chapman BA, Batman B, O'Brien LA, Leeper JA, et al. The low FODMAP diet improves gastrointestinal symptoms in patients with irritable bowel syndrome: a prospective study. Int J Clin Pract. 2013;67(9):895-903.
- 31. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. Gastroenterology. 2014;146(1):67-75 e5.
- 32. Pedersen N, Andersen NN, Vegh Z, Jensen L, Ankersen DV, Felding M, et al. Ehealth: Low FODMAP diet vs Lactobacillus rhamnosus GG in irritable bowel syndrome. World journal of gastroenterology. 2014;20(43):16215-26.
- 33. Böhn L, Störsrud S, Liljebo T, Collin L, Lindfors P, Törnblom H, et al. Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: a randomized controlled trial. Gastroenterology. 2015;149(6):1399-407.e2.
- 34. Chumpitazi BP, Cope JL, Hollister EB, Tsai CM, McMeans AR, Luna RA, et al. Randomised clinical trial: gut microbiome biomarkers are associated with clinical response to a low FODMAP diet in children with the irritable bowel syndrome. Alimentary pharmacology & therapeutics. 2015;42(4):418-27.
- 35. Whigham L, Joyce T, Harper G, Irving PM, Staudacher HM, Whelan K, et al. Clinical effectiveness and economic costs of group versus one-to-one education for short-chain fermentable carbohydrate restriction (low FODMAP diet) in the management of irritable bowel syndrome. Journal of Human Nutrition and Dietetics. 2015;28(6):687-96.
- 36. Eswaran SL, Chey WD, Han-Markey T, Ball S, Jackson K. A Randomized Controlled Trial Comparing the Low FODMAP Diet vs. Modified NICE Guidelines in US Adults with IBS-D. The American journal of gastroenterology. 2016.
- 37. GW, Muir JG, Gibson PR. Randomised clinical trial: the efficacy of gut-directed hypnotherapy is similar to that of the low FODMAP diet for the treatment of irritable bowel syndrome. Alimentary pharmacology & therapeutics. 2016;44(5):447-59.
- 38. Maagaard L, Ankersen DV, Vegh Z, Burisch J, Jensen L, Pedersen N, et al. Follow-up of patients with functional bowel symptoms treated with a low FODMAP diet. World journal of gastroenterology. 2016;22(15):4009-19.
- 39. McIntosh K, Reed DE, Schneider T, Dang F, Keshteli AH, De Palma G, et al. FODMAPs alter symptoms and the metabolome of patients with IBS: a randomised controlled trial. Gut. 2016.
- 40. O'Keeffe M, Jansen C, Martin L, Williams M, Seamark L, Staudacher HM, et al. Longterm impact of the low-FODMAP diet on gastrointestinal symptoms, dietary intake, patient acceptability, and healthcare utilization in irritable bowel syndrome. Neurogastroenterology and motility: the official journal of the European Gastrointestinal Motility Society. 2018;30(1).
- 41. Schumann D, Langhorst J, Dobos G, Cramer H. Randomised clinical trial: yoga vs a low-FODMAP diet in patients with irritable bowel syndrome. Alimentary pharmacology & therapeutics. 2018;47(2):203-11.
- 42. Schumann D, Klose P, Lauche R, Dobos G, Langhorst J, Cramer H. Low fermentable, oligo-, di-, mono-saccharides and polyol diet in the treatment of irritable bowel syndrome: A systematic review and meta-analysis. Nutrition (Burbank, Los Angeles County, Calif). 2018;45:24-31.

- 43. Zahedi MJ, Behrouz V, Azimi M. Low fermentable oligo-di-mono-saccharides and polyols diet versus general dietary advice in patients with diarrhea-predominant irritable bowel syndrome: A randomized controlled trial. Journal of gastroenterology and hepatology. 2018;33(6):1192-9. 44.
- 44. Staudacher HM, Lomer MCE, Farquharson FM, Louis P, Fava F, Franciosi E, et al. A Diet Low in FODMAPs Reduces Symptoms in Patients With Irritable Bowel Syndrome and A Probiotic Restores Bifidobacterium Species: A Randomized Controlled Trial. Gastroenterology. 2017;153(4):936-47.
- 45. Paduano D, Cingolani A, Tanda E, Usai P. Effect of Three Diets (Low-FODMAP, Gluten-free and Balanced) on Irritable Bowel Syndrome Symptoms and Health-Related Quality of Life. Nutrients. 2019;11(7).
- 46. Marsh A, Eslick EM, Eslick GD. Does a diet low in FODMAPs reduce symptoms associated with functional gastrointestinal disorders? A comprehensive systematic review and meta-analysis. European journal of nutrition. 2015.
- 47. Vasant DH, Paine PA, Black CJ, Houghton LA, Everitt HA, Corsetti M, et al. British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. Gut. 2021;70(7):1214.
- 48. Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. Official journal of the American College of Gastroenterology | ACG. 2021;116(1).
- 49. Fukudo S, Okumura T, Inamori M, Okuyama Y, Kanazawa M, Kamiya T, et al. Evidence-based clinical practice guidelines for irritable bowel syndrome 2020. Journal of gastroenterology. 2021;56(3):193-217.
- 50. Song KH, Jung HK, Kim HJ, Koo HS, Kwon YH, Shin HD, et al. Clinical Practice Guidelines for Irritable Bowel Syndrome in Korea, 2017 Revised Edition. Journal of neurogastroenterology and motility. 2018;24(2):197-215.
- 51. Mearin F, Ciriza C, Minguez M, Rey E, Mascort JJ, Pena E, et al. Clinical Practice Guideline: Irritable bowel syndrome with constipation and functional constipation in the adult. Rev Esp Enferm Dig. 2016;108(6):332-63.
- 52. McKenzie YA, Bowyer RK, Leach H, Gulia P, Horobin J, O'Sullivan NA, et al. British Dietetic Association systematic review and evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update). Journal of human nutrition and dietetics: the official journal of the British Dietetic Association. 2016;29(5):549-75.
- 53. Hookway C, Buckner S, Crosland P, Longson D. Irritable bowel syndrome in adults in primary care: summary of updated NICE guidance. BMJ (Clinical research ed). 2015;350:h701.