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Fructose and irritable bowel syndrome

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Abstract

Irritable bowel syndrome (IBS) is a chronic disorder characterised by recurrent abdominal pain or discomfort and transit disturbances with heterogeneous pathophysiological mechanisms. The link between food and gastrointestinal (GI) symptoms is often reported by patients with IBS and the role of fructose has recently been highlighted. Fructose malabsorption can easily be assessed by hydrogen and/or methane breath test in response to 25 g fructose; and its prevalence is about 22 % in patients with IBS. The mechanism of fructose-related symptoms is incompletely understood. Osmotic load, fermentation and visceral hypersensitivity are likely to participate in GI symptoms in the IBS population and may be triggered or worsened by fructose. A low-fructose diet could be integrated in the overall treatment strategy, but its role and implication in the improvement of IBS symptoms should be evaluated. In the present review, we discuss fructose malabsorption in adult patients with IBS and the interest of a low-fructose diet in order to underline the important role of fructose in IBS.

Key words: **Fructose: Irritable bowel syndrome: Fructose intake: Fructose malabsorption: Low-fructose diet**

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Introduction

Irritable bowel syndrome (IBS) is the most frequent functional bowel disorder. IBS is defined according to Rome IV criteria[1] as chronic abdominal pain associated with transit disorders that last for at least 3 months. It is divided into three predominant subtypes according to the gastrointestinal (GI) symptoms experienced by patients: (1) IBS with constipation; (2) IBS with diarrhoea; and (3) mixed IBS. The prevalence of IBS is about 5 to 20 % in Western European and North American populations according to Rome IV diagnostic criteria[2]. In 2000, the direct and indirect costs of IBS in the USA were estimated at 1·7 billion dollars[3]. While in Europe the direct annual cost per patient ranged from 1421 up to 2487 euros and the indirect annual cost per patient ranged from 339 up to 11 248 euros[4].

Food intake has been identified as a trigger of IBS symptoms by patients[5] and meal tests have been used to study symptom response in IBS[6]. Patients with increased digestive postprandial symptoms tend to have higher levels of depression and somatisation disorder[7]. The occurrence or the exacerbation of IBS symptoms as a result of food intake has been associated with more severe symptoms and reduced quality of life[8,9]. The deleterious and symptomatic role of poorly absorbable and rapidly fermentable carbohydrates (fermentable oligo-, di-, monosaccharides and polyols (FODMAP)) in IBS was first proposed by Gibson & Shepherd[10]. The mechanisms underlying the effects of unabsorbed carbohydrates on IBS symptoms may involve osmotic load, alteration of GI tract functions (for example, permeability and intestinal immunity) or modification of gut microbiota composition and functions (for example, fermentation and production of gas)[11]. Among FODMAP, fructose is of particular interest. Consumption of high-fructose corn syrup (HFCS) and sucrose has increased dramatically during the recent decades, resulting in a current average fructose daily intake of 50 g per individual in the USA and most Western countries[12]. Fructose intake challenges the absorption capacity of the small intestine and leads to fructose malabsorption even in patients without hereditary fructose intolerance[13]. Unabsorbed fructose may be fermented by the intestinal microbiome and can lead to gas production such as hydrogen which is known to participate in IBS symptoms. Fructose has also been shown to trigger or worsen symptoms in IBS patients[14]. All these mechanisms suggest that a low-fructose diet may be of potential interest in the management of IBS.

Objectives

The main objective of the present narrative review is to define the prevalence of fructose malabsorption in patients with IBS.

Abbreviations: ChREBP, carbohydrate responsive element-binding protein; FODMAP, fermentable oligo-, di-, mono-saccharides and polyols; GI, gastrointestinal; HFCS, high-fructose corn syrup; IBS, irritable bowel syndrome; KHK, ketohexokinase; KO, knockout.

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Secondary objectives are: (1) to provide an overview of the potential mechanisms underlying fructose-related IBS symptoms; (2) to determine the role of a low-fructose diet in the overall management of patients with IBS; and (3) to identify those patients who could benefit from a low-fructose diet.

Methods

All published studies related to the subject were retrieved from the PubMed database. For the main objective, we used the key words: fructose, fructose malabsorption, fructose breath test, with IBS. Only papers written in English were eligible. Papers about IBS in children, case reports, case–control-led studies and reviews were excluded (Fig. 1). Studies were selected by two independent reviewers.

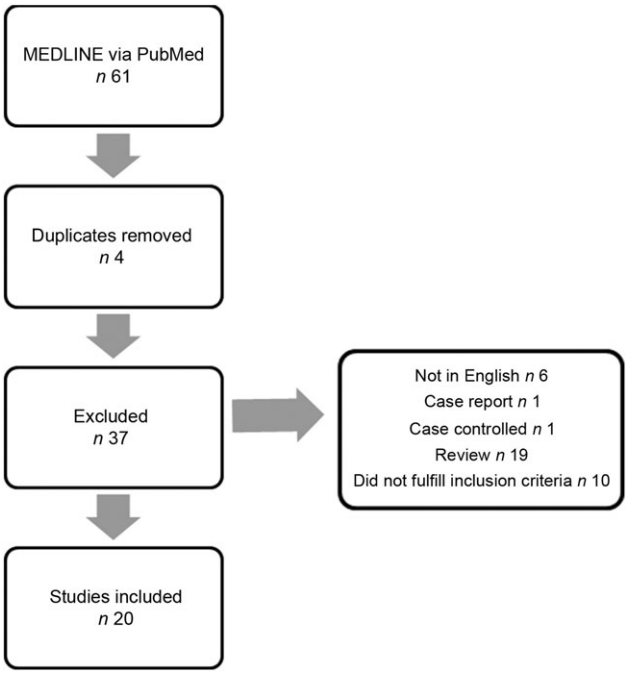


Fig. 1. Systematic review search strategy.

FODMAP and irritable bowel syndrome

The link between food intake and GI dysfunctions in IBS has been confirmed in a prospective study[15]. The majority of patients with IBS consider their symptoms to be related to specific food items; therefore they often change their diet by limiting the food they perceive as problematic[16]. Nevertheless, daily nutrient intake in patients with IBS is similar to the diet of the general population and meets national nutrient recommendations[17]. Reporting by IBS patients of specific foods as IBS symptom triggers has led to focusing attention on some dietary factors such as FODMAP and, more specifically, fructose[18].

FODMAP

Ultra-processed foods of the Western diet are of particular interest as their consumption has increased and they are associated with IBS[19,20]. One of the features of ultra-processed foods is the high amount of sugar they contain[21]. A recent study revealed a correlation between carbohydrate intake and IBS severity[22]. Moreover, the majority of patients with IBS are intolerant to incompletely absorbed carbohydrates (70 %)[8] and malabsorbed carbohydrates, i.e. carbohydrates that are not absorbed in the upper GI tract (fructose, fructans, sorbitol, etc.), have been linked to IBS symptoms[23]. The poorly absorbed carbohydrates have been collectively grouped under the FODMAP concept. They are frequently associated with and even trigger GI symptoms[24,25] even if some of them participate in the maintenance of the normal microbial community. Furthermore, diets low in FODMAP improved symptoms in patients with IBS in more than ten controlled randomised trials[24,25], reducing overall symptoms, abdominal pain, bloating and quality of life in comparison with a traditional diet, Western diet or diet recommendation for IBS[26,27]. Even short-term exposure to an enriched-FODMAP diet (diet enriched in fermentable oligo-, di-, monosaccharides and polyols) favoured gut symptoms in patients with IBS when compared with a low-FODMAP diet[28]. However, the unique role of fermentable oligosaccharides in IBS is more controversial. Indeed, some of them such as inulin, fructans or galacto-oligosaccharides have prebiotic actions and their elevated quantity in a high-FODMAP diet may increase the abundance of beneficial bacteria. Consumption of up to 7 g of *trans*-galacto-oligosaccharide per d as a prebiotic supplementation was associated with a beneficial increase in faecal *Bifidobacterium* abundance and a decrease in IBS symptoms and anxiety scores in IBS patients[29]. However, larger doses of prebiotics, for example, 19 g of fructans in children or 40 g of inulin in adults, have a negative impact on IBS symptoms[30,31]. In contrast, dietary restriction of fermentable carbohydrates has shown efficacy in improving IBS symptoms[11,25,32-35]. However, the mechanisms by which FODMAP exacerbate IBS symptoms remain unclear. FODMAP could contribute to GI symptoms by increasing the luminal water volume or by promoting bacterial fermentation and subsequent gas production, mainly hydrogen and methane. These two effects may explain GI symptoms in patients with visceral hypersensitivity. The involvement of microbial composition and metabolism[36], the increase in faecal pH[37] and changes in intestinal permeability[36] are also suspected but need further investigation.

Fructose

Fructose is a monosaccharide belonging to FODMAP. Its intake worsens symptoms in patients with IBS[38]. It is found in many fruits and in honey and is present as added sugars in many industrial foods containing sucrose or HFCS[39]. In these foods, fructose is either free or is part of the sucrose disaccharide while HFCS is composed of a mix of non-bonded glucose and fructose in approximately 1:1 ratio.

Fructose consumption pattern

For thousands of years, man consumed < 5 g of fructose per d from fruit and honey[40]. Since the 1970s, fructose has been

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increasingly consumed in developed countries due to the increase in total sugar consumption and the advent of HFCS. In the USA, this raised the per capita fructose daily intake to a staggering 50–80 g[40]. Despite scarcity of available data for other countries, the consumption of total sugar (including fructose) has increased in most continents over the past 20 years[40-44]. In Europe, the Netherlands is one of the few countries for which recent data on fructose intake are available, revealing a fructose intake of 35–60 g/d in the population aged 7–69 years[41]. In the UK, the daily mean fructose intake has reached 15–18 g for individuals over 4 years old but it can reach 37–43 g/d for the top 2·5th percentile of the same age group[45]. Normal fructose absorption should be considered alongside fructose intake. Indeed, one out of two adults cannot fully absorb a 35 g load of fructose[13]. Fructose absorption is also highly age dependent[46]. Infants display the highest predisposition for fructose malabsorption[47], while they are the age group which consumes the most fructose. Thus, changes in food intake patterns have probably created a prevalent condition of fructose malabsorption leading to its overspill in distal GI tract regions[39].

Intestinal fructose absorption and its regulation

Fructose is mainly absorbed in the proximal small intestine. Since only monosaccharides can be absorbed, sucrose is cleaved into glucose and fructose at the brush border by sucrase–isomaltase. Recently, functional variants in the sucrase–isomaltase gene which result in reduced or defective enzymic activity were identified in IBS patients[48-52], supporting the potential link between sugar absorption defects and IBS. Fructose is mainly passively transported across the apical brush-border membrane of the small intestine via the GLUT5 transporter[53-56] and subsequently exits enterocytes to enter the blood via a different transporter, GLUT2, present at the basolateral membrane. GLUT5 is the only fructose-specific transporter unable to transport glucose or galactose at physiological concentrations[57,58], whereas GLUT2 can transport the three monosaccharides (glucose, fructose and galactose)[59]. GLUT2 can also be recruited transiently at the apical membrane of enterocytes in response to high luminal glucose concentrations (> 1 mM) in order to support glucose transport across this membrane[60-64].

Luminal fructose exerts a rapid, strong and specific up-regulation of GLUT5 mRNA expression above the basal level, leading to an increase in GLUT5 protein and activity levels[65,66]. In enterocytes, the first step of the main pathway of fructose metabolism involves ketohexokinase (KHK or fructokinase), a specific enzyme of fructose metabolism converting fructose into fructose-1-P[67]. Recently, the use of a KHK knockout (KO) ($KHK^{-/-}$) mouse model demonstrated that the suppression of intracellular fructose metabolism prevents fructose-induced up-regulation of GLUT5 in the small intestine and leads to major fructose malabsorption[68-70]. While aldolase B is a known marker of hereditary fructose intolerance[71], the role of other enzymes specific to the fructose metabolic pathway in fructose malabsorption in humans remains unknown.

Fructose breath test

Breath tests estimate amounts of unabsorbed ingested carbohydrates by measuring hydrogen or methane generated by fermentation of the unabsorbed sugar by the intestinal bacteria. These tests can be used for the diagnosis of various carbohydrate malabsorption syndromes and small-intestinal bacterial overgrowth. Breath testing remains a useful, inexpensive, simple and safe diagnostic tool in gastroenterology and is performed with several substrates (for example, glucose, lactulose, fructose, sorbitol, sucrose and inulin) and at various doses. A positive breath test following fructose ingestion, defined as a rise ≥ 20 parts per million[72], indicates that bacteria are able to ferment fructose before its absorption. This may be due to all or any of the following scenarios – inefficient fructose absorptive mechanisms, rapidity of small bowel transit leaving insufficient time for absorption, or small-intestinal bacterial overgrowth. Small-intestinal bacterial overgrowth is a condition characterised by an abnormally high level of bacterial population in the small intestine where fructose is normally absorbed. This condition may produce false-positive sugar breath test results which could be ruled out with a glucose breath test[73]. Fructose malabsorption in humans increases with fructose intake concentration and in healthy adults, there is a significant positive relationship between fructose dose and the breath test result[13]. In healthy volunteers, after 15, 25, 35 and 50 g fructose loads, breath tests were positive in 0, 10, 52 and 65 % of the individuals tested, respectively (Table 1)[74,75]. In healthy subjects the absorption of 15 to 25 g of fructose was not associated with malabsorption signs, suggesting that the intestinal absorptive capacity for fructose is about 25 g per food intake[75]. Conversely, increasing fructose doses (>50 g) were associated with more positive breath tests. Therefore doses > 50 g are not helpful to detect true malabsorbers[75]. Thus, a 25 g load seems to be the most specific dose to diagnose fructose malabsorption which has been accepted as the optimal dose by the North American Consensus[72].

Fructose malabsorption

According to the North American Consensus[72], the prevalence of fructose malabsorption in IBS patients is 22 %[76], which is higher than in healthy individuals[75]. Indeed, after 15, 25, 35 and 50 g fructose loads, breath tests were positive in 20, 22, 45 and 64 % of IBS patients, respectively (Table 1)[76-79]. Surprisingly, fructose malabsorption prevalence is independent of the IBS subtype (diarrhoea, constipation or mixed)[76]. As mentioned above, current fructose intake per food intake probably exceeds the capacity of human absorption[12]. As an example, one can of Pepsi® or Coca-Cola® (33 cl) contains up to 24·6 g of fructose[80]. Fructose absorption is also dependent on the presence of glucose in the lumen[13]; simultaneous consumption of glucose and fructose increases fructose absorption[81]. However, the mechanisms underlying the limited capacity of the intestine to absorb fructose remains unclear. In a randomised controlled study, a 40 g fructose test meal was associated with increased fructose malabsorption in healthy individuals after

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Table 1. Studies assessing fructose malabsorption in health and in irritable bowel syndrome according to fructose load

References	Subjects (*n*)	Fructose load (g)	Prevalence of fructose malabsorption (%)
Health			
Jung *et al.*[79]	35	15	5·7
		25	22·9
Sharma *et al.*[124]	41	25	2·4
Corlew-Roath & Di Palma[125]	55	25	16
Batt *et al.*[74]	100	35	25
Skoog *et al.*[126]	20	40	65
Rao *et al.*[75]	20	15	0
		25	10
		50	80
Irritable bowel syndrome			
Jung *et al.*[79]	35	15	20
		25	15·7
Sharma *et al.*[124]	97	25	14·4
Corlew-Roath & Di Palma[125]	66	25	3
Melchior *et al.*[76]	90	25	22
Wilder-Smith *et al.*[78]	1372	35	45
Skoog *et al.*[126]	30	40	70
Goebel-Stengel[77]	2390	50	76

injection of corticotrophin-releasing hormone (a peptide hormone involved in the stress response) in comparison with placebo[82]. In rat, GLUT2 translocation is inhibited by stress[83]. Interestingly, IBS patients often report that the onset of IBS is associated with stress[15] and the stress scores of patients also correlated with the medical impact of IBS[18]. Therefore, one possible mechanism of fructose malabsorption in IBS could be the inhibition of GLUT2 translocation in response to stress. However, so far GLUT2 has not been identified as a major player in fructose malabsorption[84,85] or as an IBS marker. Carbohydrate responsive element-binding protein (ChREBP) is a transcription factor regulated by sugar intake. ChREBP-KO mice fed with a high-fructose diet developed fructose malabsorption with diarrhoea and caecum distension in association with decrease in expression of genes involved in fructose transport and metabolism[85,86]. More specifically, ChREBP-KO mice were associated with insufficient induction of GLUT5 in response to fructose, which could potentially explain fructose malabsorption[87]. However, GLUT5 mRNA expression and protein level are not affected in patients with fructose intolerance[83]. The mechanism underlying fructose malabsorption in humans is largely unknown and may depend on the transport capacity of GLUT5 or on fructose transporter regulation. However, the reason for a higher prevalence of fructose malabsorption in IBS patients requires further investigation.

Mechanisms underlying fructose-related symptoms in irritable bowel syndrome

The deleterious role of fructose in IBS was emphasised 10 years ago when uncontrolled studies using a low-fructose diet reported an improvement in IBS symptoms[88], while 25 and 50 g intake of fructose was found to promote IBS-like GI symptoms in healthy individuals[12,89]. Fructose is also able to cause GI symptoms (abdominal pain, diarrhoea) in IBS patients but at a dose as low as 14 g/d[90,91].

Unabsorbed fructose may play a role in osmotic load. Fructose is osmotically active in the intestine when poorly absorbed and in healthy humans, unabsorbed fructose increases water volume in the small bowel[89]. Similar results were found in IBS patients in which fructose-induced small bowel water content was associated with increasing symptoms[89].

Furthermore, induction of GI symptoms after a fructose load is linked to intestinal fermentation and gas production (hydrogen, carbon dioxide and methane)[92]. In non-IBS and IBS individuals fructose intake increased colonic luminal volume, gas production and breath hydrogen levels, but only IBS patients experienced increased abdominal symptoms[31]. This suggests that colonic hypersensitivity to distension produces fructose-related symptoms only in patients with IBS[31] even if the role of visceral hypersensitivity in carbohydrate-related symptoms is still debated[93].

The role of barrier function and inflammation has also been proposed. In animal models, there is an association between fructose intake, increased intestinal permeability and inflammation[94-97]. However, in humans, fructose malabsorption in IBS patients does not seem to be linked to low-grade inflammation or to increased intestinal permeability[98,99].

The importance of the microbiota in IBS has been suggested by the transplantation of microbiota from IBS patients into mice and rats which leads the recipient animals to develop IBS-like symptoms[100,101]. In a context of fructose malabsorption, unabsorbed fructose spills over into the distal small intestine and the colon, where it is fermented by anaerobic bacteria. Lactic acid and SCFA, predominantly propionate and butyrate, are some of the potential by-products of this fermentation[70,102,103]. Differences in the ability of intestinal microbiota to metabolise carbohydrates exist and are related to microbiome composition[104]. Fructose can be metabolised by several groups of bacteria[105,106] and in humans it is mainly fermented by lactic acid bacteria (mainly *Lactobacillus* species), and also by *Clostridium* cluster IV genus *Faecalibacterium*[107]. IBS patients with functional variants of the sucrase–isomaltase gene displayed a specific faecal microbiota composition including higher *Blautia* abundance[108]. In a rodent fructose malabsorption model (KHK$^{-/-}$ mice) fructose intake alters microbiota composition and metabolism, including a drastic increase in Coriobacteriaceae, Corynebacteriaceae and Lactobacillaceae as well as higher levels of propionate and lactate in the caecal content[70]. In rodent models of IBS, butyrate was suggested to sensitise the colon, through acid-sensing ion channel 3 (ASIC3) and transient receptor potential vanilloide 1 (TRPV1)[109-111], while lactate production favours luminal acidity which has been associated with an increase in visceral hypersensitivity[112].

Low-fructose diet in irritable bowel syndrome

A low-fructose diet consists in reducing daily fructose intake; the most frequently allowed dose is under 6 g/d. The efficacy of a low-fructose diet has been suggested in several studies (Table 2). However, the dose for fructose restriction in low-fructose diet has not yet been established. In a study which

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Table 2. Studies assessing low-fructose diet in irritable bowel syndrome (IBS)

References	Subjects (*n*)	Population	Methods	Efficacy (%)
Berg *et al.*[113]	88	IBS patients	Open controlled study	55–65
Choi *et al.*[90]	26	IBS with fructose malabsorption	Retrospective	46
Fernandez-Banares *et al.*[114]	26	IBS with sugar malabsorption	Open labelled	81
Shepherd & Gibson[115]	62	IBS with fructose malabsorption	Retrospective	74
Melchior *et al.*[117]	88	IBS with *v.* without fructose malabsorption	Prospective	62·5

included twenty-six patients with IBS, patients compliant with a low-fructose diet had improvement in their GI symptoms (abdominal pain and diarrhoea), with a moderate impact on their quality of life[90]. A larger study, with 182 IBS patients, found that a low-fructose diet improved symptom scores (abdominal pain) but had a modest effect on stool frequency[113]. In patients with IBS with fructose and sorbitol malabsorption, 81 % reported improvement after 1 month of a low-fructose and -sorbitol diet and 67 % at 12 months[114]. On the other hand, after 22 weeks of a low-fructose diet, 70 % of IBS patients challenged with fructose and fructans reported symptoms in a dose-dependent manner compared with only 14 % in the placebo group with glucose[38]. To summarise, in open-label studies, the efficacy of a low-fructose diet achieves adequate symptom relief in 46 to 81 % of IBS patients (Table 2)[90,113,115]. These large fluctuations could be explained by the different endpoints used in the studies (abdominal pain, transit, quality of life, etc.). Unfortunately, most of the studies provided a low level of evidence with retrospective analysis and were done without control or placebo groups. Moreover, it is still unclear which patients could benefit from a low-fructose diet. In several open studies, the fructose breath tests were not predictive of the efficacy of a low-fructose diet on IBS symptoms[113,116,117]. Different doses of fructose for breath testing may have to be used to better select the candidates for this diet. Moreover, in IBS patients, certain factors appear to be involved in the efficacy of low-FODMAP or low-fructose diets. For instance, sucrase–isomaltase variants in IBS patients were associated with a lower efficacy to reduce IBS symptoms in response to a low-FODMAP diet[50,118]. In three randomised trials, the efficacy of a low-FODMAP diet in IBS patients was predicted by the amount of volatile organic compounds present in the faeces[119], by the initial faecal bacterial profiles of the patients[120] or the increased peak concentrations of breath methane during the fructose breath test preceding the low-FODMAP intervention[121]. These data suggest a potential role of the gut microbiota composition and metabolism of the patients in their ability to respond to the dietary interventions.

Irritable bowel syndrome patients' management regarding fructose

One of the first steps regarding IBS patients' management regarding fructose would be to avoid high fructose consumption. Indeed, high fructose consumption can lead to GI symptoms without IBS. Adolescents are among the higher fructose consumers[40], their consumption exceeds intestinal ability to absorb fructose. Lowering their fructose to a normal consumption often resolves the GI symptoms they experience.

A second step would be to identify the individuals in whom fructose malabsorption should be tested. Those included in priority the IBS patients refractory to first-line therapies and/or with a clear link between carbohydrate intake and GI symptoms. For instance, young male IBS patients could be at a higher risk for fructose malabsorption and be systematically tested[76].

Diet could be recommended in all IBS patients in second-line therapy. The only validated restrictive diet is the low-FODMAP diet. Initially, a 4-week low-FODMAP diet could be introduced and, if efficient, FODMAP have to be reintroduced progressively to identify foods triggering symptoms, as a low-FODMAP diet could lead to nutritional deficiency such as fibre, Ca, Fe, Zn, folate, vitamins B and D and natural antioxidants[122]. Following this, the patient can follow a less restrictive diet that only excludes their personal FODMAP triggers[123]. The restriction of individual FODMAP (such as lactose, fructose, etc.) could be of interest for long-term management.

Conclusion

Fructose plays an important role in IBS. Fructose malabsorption is frequent in patients with IBS but its mechanisms are not well understood. Exceeding the capacity of intestinal fructose absorption leads to an osmotic effect and fermentation by-products by the microbiome. The roles of visceral hypersensitivity and specific microbiota profiles in fructose-induced symptoms require better understanding. Further controlled studies are needed to identify predictive factors of the efficacy of a low-fructose diet on IBS symptoms.

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There are no conflicts of interest.

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References

1. Lacy BE, Mearin F, Chang L, *et al.* (2016) Bowel disorders. *Gastroenterology* **150**, 1393–1407.e5.
2. Whitehead WE, Palsson OS & Simren M (2017) Irritable bowel syndrome: what do the new Rome IV diagnostic guidelines mean for patient management? *Expert Rev Gastroenterol Hepatol* **11**, 281–283.
3. Sandler RS, Everhart JE, Donowitz M, *et al.* (2002) The burden of selected digestive diseases in the United States. *Gastroenterology* **122**, 1500–1511.
4. Tack J, Stanghellini V, Mearin F, *et al.* (2019) Economic burden of moderate to severe irritable bowel syndrome with constipation in six European countries. *BMC Gastroenterol* **19**, 69.
5. Simren M, Mansson A, Langkilde AM, *et al.* (2001) Food-related gastrointestinal symptoms in the irritable bowel syndrome. *Digestion* **63**, 108–115.
6. Posserud I, Strid H, Storsrud S, *et al.* (2013) Symptom pattern following a meal challenge test in patients with irritable bowel syndrome and healthy controls. *United European Gastroenterol J* **1**, 358–367.
7. Van Oudenhove L, Tornblom H, Storsrud S, *et al.* (2016) Depression and somatization are associated with increased postprandial symptoms in patients with irritable bowel syndrome. *Gastroenterology* **150**, 866–874.
8. Bohn L, Storsrud S, Tornblom H, *et al.* (2013) Self-reported food-related gastrointestinal symptoms in IBS are common and associated with more severe symptoms and reduced quality of life. *Am J Gastroenterol* **108**, 634–641.
9. Chey WD (2013) The role of food in the functional gastrointestinal disorders: introduction to a manuscript series. *Am J Gastroenterol* **108**, 694–697.
10. Gibson PR & Shepherd SJ (2010) Evidence-based dietary management of functional gastrointestinal symptoms: the FODMAP approach. *J Gastroenterol Hepatol* **25**, 252–258.
11. Eswaran S (2017) Low FODMAP in 2017: lessons learned from clinical trials and mechanistic studies. *Neurogastroenterol Motil* **29**, e13055.
12. Beyer PL, Caviar EM & McCallum RW (2005) Fructose intake at current levels in the United States may cause gastrointestinal distress in normal adults. *J Am Diet Assoc* **105**, 1559–1566.
13. Jones HF, Butler RN & Brooks DA (2011) Intestinal fructose transport and malabsorption in humans. *Am J Physiol Gastrointest Liver Physiol* **300**, G202–G206.
14. Hammer HF & Hammer J (2012) Diarrhea caused by carbohydrate malabsorption. *Gastroenterol Clin North Am* **41**, 611–627.
15. Ragnarsson G & Bodemar G (1998) Pain is temporally related to eating but not to defaecation in the irritable bowel syndrome (IBS). Patients' description of diarrhea, constipation and symptom variation during a prospective 6-week study. *Eur J Gastroenterol Hepatol* **10**, 415–421.
16. Hayes P, Corish C, O'Mahony E, *et al.* (2013) A dietary survey of patients with irritable bowel syndrome. *J Hum Nutr Diet* **27**, Suppl. 2, 36–47.
17. Bohn L, Storsrud S & Simren M (2013) Nutrient intake in patients with irritable bowel syndrome compared with the general population. *Neurogastroenterol Motil* **25**, 23–30.e1.
18. Boeckxstaens GE, Drug V, Dumitrascu D, *et al.* (2016) Phenotyping of subjects for large scale studies on patients with IBS. *Neurogastroenterol Motil* **28**, 1134–1147.
19. Schnabel L, Buscail C, Sabate JM, *et al.* (2018) Association between ultra-processed food consumption and functional gastrointestinal disorders: results from the French NutriNet-Santé cohort. *Am J Gastroenterol* **113**, 1217–1228.
20. Buscail C, Sabate JM, Bouchoucha M, *et al.* (2017) Western dietary pattern is associated with irritable bowel syndrome in the French NutriNet cohort. *Nutrients* **9**, E986.
21. Poti JM, Mendez MA, Ng SW, *et al.* (2015) Is the degree of food processing and convenience linked with the nutritional quality of foods purchased by US households? *Am J Clin Nutr* **101**, 1251–1262.
22. Solar I, Santos LAO, Yamashita LM, *et al.* (2018) Irritable bowel syndrome: associations between FODMAPS intake, problematic foods, adiposity, and gastrointestinal symptoms. *Eur J Clin Nutr* **73**, 637–641.
23. Rumessen JJ (1992) Fructose and related food carbohydrates. Sources, intake, absorption, and clinical implications. *Scand J Gastroenterol* **27**, 819–828.
24. Shepherd SJ, Lomer MC & Gibson PR (2013) Short-chain carbohydrates and functional gastrointestinal disorders. *Am J Gastroenterol* **108**, 707–717.
25. Staudacher HM & Whelan K (2017) The low FODMAP diet: recent advances in understanding its mechanisms and efficacy in IBS. *Gut* **66**, 1517–1527.
26. Altobelli E, Del Negro V, Angeletti PM, *et al.* (2017) Low-FODMAP diet improves irritable bowel syndrome symptoms: a meta-analysis. *Nutrients* **9**, E940.
27. Schumann D, Klose P, Lauche R, *et al.* (2018) Low fermentable, oligo-, di-, mono-saccharides and polyol diet in the treatment of irritable bowel syndrome: a systematic review and meta-analysis. *Nutrition* **45**, 24–31.
28. Ong DK, Mitchell SB, Barrett JS, *et al.* (2010) Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. *J Gastroenterol Hepatol* **25**, 1366–1373.
29. Silk DB, Davis A, Vulevic J, *et al.* (2009) Clinical trial: the effects of a *trans*-galactooligosaccharide prebiotic on faecal microbiota and symptoms in irritable bowel syndrome. *Aliment Pharmacol Ther* **29**, 508–518.
30. Chumpitazi BP, McMeans AR, Vaughan A, *et al.* (2018) Fructans exacerbate symptoms in a subset of children with irritable bowel syndrome. *Clin Gastroenterol Hepatol* **16**, 219–225.e1.
31. Major G, Pritchard S, Murray K, *et al.* (2017) Colon hypersensitivity to distension, rather than excessive gas production, produces carbohydrate-related symptoms in individuals with irritable bowel syndrome. *Gastroenterology* **152**, 124–133.e2.
32. Bohn L, Storsrud S, Liljebo T, *et al.* (2015) Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: a randomized controlled trial. *Gastroenterology* **149**, 1399–1407.e2.
33. Halmos EP, Power VA, Shepherd SJ, *et al.* (2014) A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology* **146**, 67–75.e5.
34. Laatikainen R, Koskenpato J, Hongisto SM, *et al.* (2016) Randomised clinical trial: low-FODMAP rye bread vs. regular rye bread to relieve the symptoms of irritable bowel syndrome. *Aliment Pharmacol Ther* **44**, 460–470.
35. McIntosh K, Reed DE, Schneider T, *et al.* (2017) FODMAPs alter symptoms and the metabolome of patients with IBS: a randomised controlled trial. *Gut* **66**, 1241–1251.
36. Zhou SY, Gillilland M 3rd, Wu X, *et al.* (2018) FODMAP diet modulates visceral nociception by lipopolysaccharide-mediated intestinal inflammation and barrier dysfunction. *J Clin Invest* **128**, 267–280.
37. Halmos EP, Christophersen CT, Bird AR, *et al.* (2015) Diets that differ in their FODMAP content alter the colonic luminal microenvironment. *Gut* **64**, 93–100.

https://doi.org/10.1017/S0954422420000025 Published online by Cambridge University Press

38. Shepherd SJ, Parker FC, Muir JG, *et al.* (2008) Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. *Clin Gastroenterol Hepatol* **6**, 765–771.
39. Muir JG, Rose R, Rosella O, *et al.* (2009) Measurement of short-chain carbohydrates in common Australian vegetables and fruits by high-performance liquid chromatography (HPLC). *J Agric Food Chem* **57**, 554–565.
40. Douard V & Ferraris RP (2013) The role of fructose transporters in diseases linked to excessive fructose intake. *J Physiol* **591**, 401–414.
41. Sluik D, Engelen AI & Feskens EJ (2015) Fructose consumption in the Netherlands: the Dutch National Food Consumption Survey 2007–2010. *Eur J Clin Nutr* **69**, 475–481.
42. Stuckler D, Reeves A, Loopstra R, *et al.* (2016) Textual analysis of sugar industry influence on the World Health Organization's 2015 sugars intake guideline. *Bull World Health Organ* **94**, 566–573.
43. Svensson A, Larsson C, Eiben G, *et al.* (2014) European children's sugar intake on weekdays versus weekends: the IDEFICS study. *Eur J Clin Nutr* **68**, 822–828.
44. Tappy L, Le KA, Tran C, *et al.* (2010) Fructose and metabolic diseases: new findings, new questions. *Nutrition* **26**, 1044–1049.
45. Scientific Advisory Committee on Nutrition (2015) *Carbohydrates and Health*. London: The Stationery Office.
46. Douard V, Cui XL, Soteropoulos P, *et al.* (2008) Dexamethasone sensitizes the neonatal intestine to fructose induction of intestinal fructose transporter (Slc2A5) function. *Endocrinology* **149**, 409–423.
47. Jones HF, Butler RN, Moore DJ, *et al.* (2013) Developmental changes and fructose absorption in children: effect on malabsorption testing and dietary management. *Nutr Rev* **71**, 300–309.
48. Garcia-Etxebarria K, Zheng T, Bonfiglio F, *et al.* (2018) Increased prevalence of rare sucrase–isomaltase pathogenic variants in irritable bowel syndrome patients. *Clin Gastroenterol Hepatol* **16**, 1673–1676.
49. Henstrom M, Diekmann L, Bonfiglio F, *et al.* (2018) Functional variants in the sucrase–isomaltase gene associate with increased risk of irritable bowel syndrome. *Gut* **67**, 263–270.
50. Husein DM & Naim HY (2019) Impaired cell surface expression and digestive function of sucrase–isomaltase gene variants are associated with reduced efficacy of low FODMAPs diet in patients with IBS-D. *Gut* (epublication ahead of print version 22 July 2019).
51. Husein DM, Wanes D, Marten LM, *et al.* (2019) Heterozygotes are a potential new entity among homozygotes and compound heterozygotes in congenital sucrase–isomaltase deficiency. *Nutrients* **11**, 2290.
52. Kim SB, Calmet FH, Garrido J, *et al.* (2020) Sucrase–isomaltase deficiency as a potential masquerader in irritable bowel syndrome. *Dig Dis Sci* **65**, 534–540.
53. Burant CF & Saxena M (1994) Rapid reversible substrate regulation of fructose transporter expression in rat small intestine and kidney. *Am J Physiol* **267**, G71–G79.
54. Burant CF, Takeda J, Brot-Laroche E, *et al.* (1992) Fructose transporter in human spermatozoa and small intestine is GLUT5. *J Biol Chem* **267**, 14523–14526.
55. Cura AJ & Carruthers A (2012) Role of monosaccharide transport proteins in carbohydrate assimilation, distribution, metabolism, and homeostasis. *Compr Physiol* **2**, 863–914.
56. Douard V & Ferraris RP (2008) Regulation of the fructose transporter GLUT5 in health and disease. *Am J Physiol Endocrinol Metab* **295**, E227–E237.
57. Kane S, Seatter MJ & Gould GW (1997) Functional studies of human GLUT5: effect of pH on substrate selection and an analysis of substrate interactions. *Biochem Biophys Res Commun* **238**, 503–505.
58. Manolescu A, Salas-Burgos AM, Fischbarg J, *et al.* (2005) Identification of a hydrophobic residue as a key determinant of fructose transport by the facilitative hexose transporter SLC2A7 (GLUT7). *J Biol Chem* **280**, 42978–42983.
59. Uldry M & Thorens B (2004) The SLC2 family of facilitated hexose and polyol transporters. *Pflugers Arch* **447**, 480–489.
60. Gouyon F, Caillaud L, Carriere V, *et al.* (2003) Simple-sugar meals target GLUT2 at enterocyte apical membranes to improve sugar absorption: a study in GLUT2-null mice. *J Physiol* **552**, 823–832.
61. Caccia S, Casartelli M, Grimaldi A, *et al.* (2007) Unexpected similarity of intestinal sugar absorption by SGLT1 and apical GLUT2 in an insect (*Aphidius ervi*, Hymenoptera) and mammals. *Am J Physiol Regul Integr Comp Physiol* **292**, R2284–R2291.
62. Cottrell JJ, Stoll B, Buddington RK, *et al.* (2006) Glucagon-like peptide-2 protects against TPN-induced intestinal hexose malabsorption in enterally refed piglets. *Am J Physiol Gastrointest Liver Physiol* **290**, G293–G300.
63. Ait-Omar A, Monteiro-Sepulveda M, Poitou C, *et al.* (2011) GLUT2 accumulation in enterocyte apical and intracellular membranes: a study in morbidly obese human subjects and ob/ob and high fat-fed mice. *Diabetes* **60**, 2598–2607.
64. Barone S, Fussell SL, Singh AK, *et al.* (2009) Slc2a5 (Glut5) is essential for the absorption of fructose in the intestine and generation of fructose-induced hypertension. *J Biol Chem* **284**, 5056–5066.
65. Ferraris RP (2001) Dietary and developmental regulation of intestinal sugar transport. *Biochem J* **360**, 265–276.
66. Ferraris RP & Diamond J (1997) Regulation of intestinal sugar transport. *Physiol Rev* **77**, 257–302.
67. Diggle CP, Shires M, Leitch D, *et al.* (2009) Ketohexokinase: expression and localization of the principal fructose-metabolizing enzyme. *J Histochem Cytochem* **57**, 763–774.
68. Patel C, Douard V, Yu S, Gao N, *et al.* (2015) Transport, metabolism, and endosomal trafficking-dependent regulation of intestinal fructose absorption. *FASEB J* **29**, 4046–4058.
69. Patel C, Douard V, Yu S, *et al.* (2015) Fructose-induced increases in expression of intestinal fructolytic and gluconeogenic genes are regulated by GLUT5 and KHK. *Am J Physiol Regul Integr Comp Physiol* **309**, R499–R509.
70. Zhang X, Grosfeld A, Williams E, *et al.* (2019) Fructose malabsorption induces cholecystokinin expression in the ileum and cecum by changing microbiota composition and metabolism. *FASEB J* **33**, 7126–7142.
71. Oppelt SA, Sennott EM & Tolan DR (2015) Aldolase-B knockout in mice phenocopies hereditary fructose intolerance in humans. *Mol Genet Metab* **114**, 445–450.
72. Rezaie A, Buresi M, Lembo A, *et al.* (2017) Hydrogen and methane-based breath testing in gastrointestinal disorders: the North American consensus. *Am J Gastroenterol* **112**, 775–784.
73. Nucera G, Gabrielli M, Lupascu A, *et al.* (2005) Abnormal breath tests to lactose, fructose and sorbitol in irritable bowel syndrome may be explained by small intestinal bacterial overgrowth. *Aliment Pharmacol Ther* **21**, 1391–1395.
74. Batt C, Fanning N, Drake J, *et al.* (2017) Fructose malabsorption in people with and without gout: a case–control study. *Semin Arthritis Rheum* **47**, 257–263.
75. Rao SS, Attaluri A, Anderson L, *et al.* (2007) Ability of the normal human small intestine to absorb fructose: evaluation by breath testing. *Clin Gastroenterol Hepatol* **5**, 959–963.

https://doi.org/10.1017/S0954422420000025 Published online by Cambridge University Press

76. Melchior C, Gourcerol G, Dechelotte P, *et al.* (2014) Symptomatic fructose malabsorption in irritable bowel syndrome: a prospective study. *United European Gastroenterol J* **2**, 131–137.
77. Goebel-Stengel M, Stengel A, Schmidtmann M, *et al.* (2014) Unclear abdominal discomfort: pivotal role of carbohydrate malabsorption. *J Neurogastroenterol Motil* **20**, 228–235.
78. Wilder-Smith CH, Materna A, Wermelinger C, *et al.* (2013) Fructose and lactose intolerance and malabsorption testing: the relationship with symptoms in functional gastrointestinal disorders. *Aliment Pharmacol Ther* **37**, 1074–1083.
79. Jung KW, Seo M, Cho YH, *et al.* (2018) Prevalence of fructose malabsorption in patients with irritable bowel syndrome after excluding small intestinal bacterial overgrowth. *J Neurogastroenterol Motil* **24**, 307–316.
80. Ventura EE, Davis JN & Goran MI (2011) Sugar content of popular sweetened beverages based on objective laboratory analysis: focus on fructose content. *Obesity (Silver Spring)* **19**, 868–874.
81. Latulippe ME & Skoog SM (2011) Fructose malabsorption and intolerance: effects of fructose with and without simultaneous glucose ingestion. *Crit Rev Food Sci Nutr* **51**, 583–592.
82. Murray KA, Lam C, Rehman S, *et al.* (2016) Corticotropin-releasing factor increases ascending colon volume after a fructose test meal in healthy humans: a randomized controlled trial. *Am J Clin Nutr* **103**, 1318–1326.
83. Shepherd EJ, Helliwell PA, Mace OJ, *et al.* (2004) Stress and glucocorticoid inhibit apical GLUT2-trafficking and intestinal glucose absorption in rat small intestine. *J Physiol* **560**, 281–290.
84. Wilder-Smith CH, Li X, Ho SS, *et al.* (2014) Fructose transporters GLUT5 and GLUT2 expression in adult patients with fructose intolerance. *United European Gastroenterol J* **2**, 14–21.
85. Kato T, Iizuka K, Takao K, *et al.* (2018) ChREBP-knockout mice show sucrose intolerance and fructose malabsorption. *Nutrients* **10**, E340.
86. Kim M, Astapova, II, Flier SN, *et al.* (2017) Intestinal, but not hepatic, ChREBP is required for fructose tolerance. *JCI Insight* **2**, 96703.
87. Oh AR, Sohn S, Lee J, *et al.* (2018) ChREBP deficiency leads to diarrhea-predominant irritable bowel syndrome. *Metabolism* **85**, 286–297.
88. Heizer WD, Southern S & McGovern S (2009) The role of diet in symptoms of irritable bowel syndrome in adults: a narrative review. *J Am Diet Assoc* **109**, 1204–1214.
89. Murray K, Wilkinson-Smith V, Hoad C, *et al.* (2014) 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* **109**, 110–119.
90. Choi YK, Kraft N, Zimmerman B, *et al.* (2008) Fructose intolerance in IBS and utility of fructose-restricted diet. *J Clin Gastroenterol* **42**, 233–238.
91. Gibson PR, Newnham E, Barrett JS, *et al.* (2007) Review article: fructose malabsorption and the bigger picture. *Aliment Pharmacol Ther* **25**, 349–363.
92. Wilder-Smith CH, Olesen SS, Materna A, *et al.* (2018) Fermentable sugar ingestion, gas production, and gastrointestinal and central nervous system symptoms in patients with functional disorders. *Gastroenterology* **155**, 1034–1044.e6.
93. Tuck CJ, McNamara LS & Gibson PR (2017) Editorial: Rethinking predictors of response to the low FODMAP diet – should we retire fructose and lactose breath-hydrogen testing and concentrate on visceral hypersensitivity? *Aliment Pharmacol Ther* **45**, 1281–1282.
94. Do MH, Lee E, Oh MJ, *et al.* (2018) High-glucose or -fructose diet cause changes of the gut microbiota and metabolic disorders in mice without body weight change. *Nutrients* **10**, E761.
95. Haub S, Kanuri G, Volynets V, *et al.* (2010) Serotonin reuptake transporter (SERT) plays a critical role in the onset of fructose-induced hepatic steatosis in mice. *Am J Physiol Gastrointest Liver Physiol* **298**, G335–G344.
96. Spruss A, Kanuri G, Stahl C, *et al.* (2012) Metformin protects against the development of fructose-induced steatosis in mice: role of the intestinal barrier function. *Lab Invest* **92**, 1020–1032.
97. Volynets V, Louis S, Pretz D, *et al.* (2017) Intestinal barrier function and the gut microbiome are differentially affected in mice fed a Western-style diet or drinking water supplemented with fructose. *J Nutr* **147**, 770–780.
98. Melchior C, Aziz M, Aubry T, *et al.* (2014) Does calprotectin level identify a subgroup among patients suffering from irritable bowel syndrome? Results of a prospective study. *United European Gastroenterol J* **5**, 261–269.
99. Kuzma JN, Cromer G, Hagman DK, *et al.* (2016) No differential effect of beverages sweetened with fructose, high-fructose corn syrup, or glucose on systemic or adipose tissue inflammation in normal-weight to obese adults: a randomized controlled trial. *Am J Clin Nutr* **104**, 306–314.
100. De Palma G, Lynch MD, Lu J, *et al.* (2017) Transplantation of fecal microbiota from patients with irritable bowel syndrome alters gut function and behavior in recipient mice. *Sci Transl Med* **9**, eaaf6397.
101. Crouzet L, Gaultier E, Del'Homme C, *et al.* (2013) The hypersensitivity to colonic distension of IBS patients can be transferred to rats through their fecal microbiota. *Neurogastroenterol Motil* **25**, e272–e282.
102. Louis P & Flint HJ (2017) Formation of propionate and butyrate by the human colonic microbiota. *Environ Microbiol* **19**, 29–41.
103. Jang C, Hui S, Lu W, *et al.* (2018) The small intestine converts dietary fructose into glucose and organic acids. *Cell Metab* **27**, 351–361.e3.
104. Chassard C & Lacroix C (2013) Carbohydrates and the human gut microbiota. *Curr Opin Clin Nutr Metab Care* **16**, 453–460.
105. Endo A, Maeno S, Tanizawa Y, *et al.* (2018) Fructophilic lactic acid bacteria, a unique group of fructose-fermenting microbes. *Appl Environ Microbiol* **84**, e01290–18.
106. Endo A, Futagawa-Endo Y & Dicks LM (2009) Isolation and characterization of fructophilic lactic acid bacteria from fructose-rich niches. *Syst Appl Microbiol* **32**, 593–600.
107. Moens F & De Vuyst L (2017) Inulin-type fructan degradation capacity of *Clostridium* cluster IV and XIVa butyrate-producing colon bacteria and their associated metabolic outcomes. *Benef Microbes* **8**, 473–490.
108. Thingholm L, Ruhlemann M, Wang J, *et al.* (2019) Sucrase–isomaltase 15Phe IBS risk variant in relation to dietary carbohydrates and faecal microbiota composition. *Gut* **68**, 177–178.
109. Jones RC 3rd, Otsuka E, Wagstrom E, *et al.* (2007) Short-term sensitization of colon mechanoreceptors is associated with long-term hypersensitivity to colon distention in the mouse. *Gastroenterology* **133**, 184–194.
110. Matricon J, Gelot A, Etienne M, *et al.* (2011) Spinal cord plasticity and acid-sensing ion channels involvement in a rodent model of irritable bowel syndrome. *Eur J Pain* **15**, 335–343.
111. Matricon J, Muller E, Accarie A, *et al.* (2013) Peripheral contribution of NGF and ASIC1a to colonic hypersensitivity in a rat model of irritable bowel syndrome. *Neurogastroenterol Motil* **25**, e740–e754.

https://doi.org/10.1017/S0954422420000025 Published online by Cambridge University Press

112. Holzer P (2015) Acid-sensing ion channels in gastrointestinal function. *Neuropharmacology* **94**, 72–79.
113. Berg LK, Fagerli E, Martinussen M, *et al.* (2013) Effect of fructose-reduced diet in patients with irritable bowel syndrome, and its correlation to a standard fructose breath test. *Scand J Gastroenterol* **48**, 936–943.
114. Fernandez-Banares F, Rosinach M, Esteve M, *et al.* (2006) Sugar malabsorption in functional abdominal bloating: a pilot study on the long-term effect of dietary treatment. *Clin Nutr* **25**, 824–831.
115. Shepherd SJ & Gibson PR (2006) Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management. *J Am Diet Assoc* **106**, 1631–1639.
116. Helwig U, Koch AK, Koppka N, *et al.* (2018) The predictive value of the hydrogen breath test in the diagnosis of fructose malabsorption. *Digestion* **99**, 140–147.
117. Melchior C, Desprez C, Houivet E, *et al.* (2019) Is abnormal 25 g fructose breath test a predictor of symptomatic response to a low fructose diet in irritable bowel syndrome? *Clin Nutr* (epublication ahead of print version 8 May 2019).
118. Zheng T, Eswaran S, Photenhauer AL, *et al.* (2019) Reduced efficacy of low FODMAPs diet in patients with IBS-D carrying sucrase–isomaltase (SI) hypomorphic variants. *Gut* **69**, 397–398.
119. Rossi M, Aggio R, Staudacher HM, *et al.* (2018) Volatile organic compounds in feces associate with response to dietary intervention in patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol* **16**, 385–391.e1.
120. Bennet SMP, Bohn L, Storsrud S, *et al.* (2017) Multivariate modelling of faecal bacterial profiles of patients with IBS predicts responsiveness to a diet low in FODMAPs. *Gut* **67**, 872–881.
121. Wilder-Smith CH, Olesen SS, Materna A, *et al.* (2017) Predictors of response to a low-FODMAP diet in patients with functional gastrointestinal disorders and lactose or fructose intolerance. *Aliment Pharmacol Ther* **45**, 1094–1106.
122. Catassi G, Lionetti E, Gatti S, *et al.* (2017) The low FODMAP diet: many question marks for a catchy acronym. *Nutrients* **9**, E292.
123. Whelan K, Martin LD, Staudacher HM, *et al.* (2018) The low FODMAP diet in the management of irritable bowel syndrome: an evidence-based review of FODMAP restriction, reintroduction and personalisation in clinical practice. *J Hum Nutr Diet* **31**, 239–255.
124. Sharma A, Srivastava D, Verma A, *et al.* (2014) Fructose malabsorption is not uncommon among patients with irritable bowel syndrome in India: a case–control study. *Indian J Gastroenterol* **33**, 466–470.
125. Corlew-Roath M & Di Palma JA (2009) Clinical impact of identifying lactose maldigestion or fructose malabsorption in irritable bowel syndrome or other conditions. *South Med J* **102**, 1010–1012.
126. Skoog SM, Bharucha AE & Zinsmeister AR (2008) Comparison of breath testing with fructose and high fructose corn syrups in health and IBS. *Neurogastroenterol Motil* **20**, 505–511.

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