

Leena Putkonen

PRELIMINARY DATA ON THE CONTENT OF FERMENTABLE OLIGO-, DI- AND MONOSACCHARIDES AND POLYOLS (FODMAPS) IN TYPICAL FINNISH PRODUCE The Nordic application of the low FODMAP diet

Faculty of Social Sciences A monograph thesis March 2021



Putkonen, Leena: Preliminary data on the content of fermentable oligo-, di- and monosaccharides, and polyols (FODMAPs) in typical Finnish produce. A monogprah thesis Tampere University Master's Programme in Public and Global Health March 2021

Irritable bowel syndrome (IBS) is a disease involving the dysfunction of the the brain-gut-gut microbiota – axis, causing symptoms such as altered bowel habits, abdominal pain, bloating, fatigue and anxiety. Its prevalence globally is 10 percent. There is no cure, but symptoms can be managed with pharmacological, psychological and lifestyle and dietary measures. The most used dietary treatment is a diet that limits the intake of poorly absorbed carbohydrates that are easily fermented in the gut, hence, alleviating typical gut symptoms of IBS. This low FODMAP diet has been shown in clinical trials to alleviate symptoms in up to 70 percent of IBS patients. FODMAP stands for *Fermentable Oligo-, Di- and Monosaccharides And Polyols*.

The low FODMAP diet has been implemented in various cuisines around the world, but data on the FODMAP content of typical Nordic foods is limited. The aim of this study was to analyse the FODMAP content of some typical Finnish foods (per 100g and per portion) and evaluate whether they passed the cutoff values for the low FODMAP diet. Products analysed were lingonberry, bilberry, wild cranberry, oat bread, wheat bread, rye bread and crispbread, various spelt products and some snacks and sweets. Products analysed were lingonberry, bilberry, wild cranberry, oat bread, various spelt products and some snacks and sweets.

Samples were collected in Finland and taken to Australia, where they were processed and analysed using high-performance liquid chromatography and fructan assay at Monash University in Melbourne, Australia. The data were then further processed into tables and figures indicating the FODMAP content of products per 100 g and per portions. It was further evaluated, if the foods per 100 g or per portion passed the low FODMAP criteria that is used to evaluate whether foods are suitable on the low FODMAP diet.

Blackcurrants contained large amounts of sorbitol per 12.5 g and per 25 g portions (0.44 g/100 g and 0.88 g/100 g, respectively). A small portion (12,5 g) and a larger portion (25 g) of sea buckthorn contained excess fructose (0.28 g and 0.55 g, respectively), but only traces of other FODMAPs. Lingonberry and bilberry portions did not contain FODMAP compounds in significant amounts. The main FODMAP type in grain products was fructan. An oat bread slice contained only 0.06 g, whereas wheat breads contained 0.11-0.21 g per slice. Gluten-free, wheat-starch breads fructans content was 0.14-0.20 g. Spelt crispbreads contained 0.10-0.15 g of fructans a piece, being less than in rye crispbread (0.48 g) and sourdough rye crackers (0.22-0.34 g). Fructan content in fresh rye bread varied from 0.31 g to 0.54 g. Of the snacks tested, oat biscuits proved to contain very little FODMAP compounds.

As the sampling procedure could not be adhered to in detail, the findings of this study should be regarded as preliminary and generalisations should be done with caution. Based on the results of this study, people on the low FODMAP diet can add lingonberry, bilberry and some oat bread, and biscuits and spelt porridge to their diet. Some foods, like sea buckthorn and wild cranberries, can also be included in the diet in small amounts. Most grain products were high in FODMAPs, but further studies are needed due to variability of findings.

Keywords: IBS, irritable bowel syndrome, low FODMAP diet, FODMAP, fermentable poorly absorbed carbohydrates.

The originality of this thesis has been checked using the Turnitin OriginalityCheck service.



TABLE OF CONTENT

1.	INTRODUCTION					
2.	REVI	EW OF LITERATURE	3			
	2.1.	Prevalence of IBS	3			
	2.2.	Etiology and risk factors	4			
		2.2.1. Sex	4			
		2.2.2. Genetics	4			
		2.2.3. Epigenetics and trauma	5			
		2.2.4. Gut microbiota	5			
		2.2.5. Post-infection	.6			
	2.3.	Diagnostics of IBS	6			
	2.4.	Characteristics of IBS symptoms	7			
		2.4.1. Bloating and flatus				
		2.4.2. Pain				
		2.4.3. Fatigue				
		2.4.4. Anxiety and depression				
		2.4.5. Upper GI symptoms1				
	2.5.	Cost of IBS1				
	2.6.	Established treatment	1			
		2.6.1. Plasebo and nocebo1				
		2.6.2. Lifestyle management	2			
		2.6.3. Psychological treatment	2			
		2.6.4. Pharmacological treatments				
		2.6.5. Complementary and alternative treatments (CAM)1				
		2.6.6. Dietary treatment				
	2.7.	The low FODMAP diet1	5			
		2.7.1. Mechanisms of action1	5			
		2.7.2. Clinical evidence	7			
		2.7.3. Implementing the diet1	8			
		2.7.4. Critical perspective1	9			
		2.7.5. Cut-off values for the low FODMAP diet2	0			
		2.7.6. FODMAP intake in studies	1			
	2.8. F	ODMAPS IN FINLAND	6			
		2.8.1. Typical features of Finnish cuisine2	:6			
		2.8.2. FODMAP studies in Finland2	:7			
		2.8.3. FODMAP intake in the Finnish diet	1			

		2.8.4. IBS and FODMAPs in short				
3.	AIMS					
4.	MATE	ERIALS AND METHODS				
	4.1.	Sample collection				
	4.2.	Sample preparation	40			
		4.2.1. Fructan assay	41			
		4.2.2. High-performance liquid chromatography (HPLC)	42			
		4.2.3. Evaporative light scattering detector (ELSD)	42			
	4.3.	Sample analysis	43			
		4.3.1. FODMAP content per portion of products	43			
		4.3.2. Analysing the data in relation to the FODMAP criteria	44			
5.	RESU	LTS	45			
	5.1.	The FODMAP content of products per 100 grams	45			
	5.2.	The FODMAP content of a typical portion	46			
	5.3.	Products meeting the low FODMAP criteria				
6.	DISCU	USSION	62			
	6.1.	Main findings	62			
	6.2.	Specific finding by category	62			
		6.2.1. Berries	62			
		6.2.2. Grains	63			
	6.3.	Weaknesses of the study	66			
	6.4.	Strengths of the study	66			
	6.5.	What can be learned	67			
	6.6.	Future perspective	67			
7.	CONCLUSIONS					
8.	ACKNOWLEDGEMENTS					
9.	REFERENCES					



ABBREVIATIONS

- FODMAP = fermentable oligo-, di- and monosaccharides and polyols
- GI = gastrointestinal
- IBD = inflammatory bowel disease
- IBS = irritable bowel syndrome
- IBS-D = irritable bowel syndrome, diarrhea-predominant
- IBS-C = irritable bowel syndrome, constipation-predominant
- IBS-M = irritable bowel syndrome, mixed
- IBS-U = irritable bowel syndrome, unspecified
- LFD = low FODMAP diet
- NICE = National Institute for health and Care Excellence

Irritable bowel syndrome (IBS) is a multifactorial syndrome characterised by altered bowel movements, flatus, bloating, pain and psychological symptoms, such as anxiety and fatigue. Symptoms vary extensively between patients, but also in the same individual over time.

IBS is amongst the most frequently diagnosed gastrointestinal conditions. Its prevalence varies in populations, being typically 10-14 %, but ranging from as low as 1,1 % to 45 % (Lovell & Ford, 2012). IBS is reported more in females than in males. Due to excessive use of health care services and work-absenteeism, the costs to the society have been estimated to be substantial.

The treatment options for IBS have been limited for decades, but the situation has changed in the recent years, as better understanding of symptom mechanisms and the role of the diet has unravelled. It has been established that certain poorly absorbed carbohydrates are responsible for some of the typical symptoms in IBS. The diet that eliminates and restricts the intake of these trigger compounds, is called the low FODMAP diet. The acronym FODMAP stands for *fermentable oligo-, di- and monosaccharides and polyols*, which indicates the chemical structure of these short-chain carbohydrate compounds. The FODMAP oligosaccharides include fructans and galacto-oligosaccharides, the disaccharide sugar is lactose, monosaccharide sugar is fructose and polyols include compounds such as sorbitol, mannitol, xylitol and maltitol.

These poorly absorbed compounds are in everyday foods and the intake is not restricted to a certain cuisine or diet. The main FODMAP sources in the diet for fructans are wheat, rye, barley and onions and garlic, for galacto-oligosaccharides beans and lentils, and for lactose milk products. Foods high in fructose are fruit juices and, in some cuisines, high fructose corn syrup sweetened soft drinks and other products. Polyols in the diet come from polyol-sweetened chewing gum and drops, and some fruits and vegetables, such as apples, pears, cauliflower and button mushrooms.

There are no low FODMAP diet patient studies conducted in Finland, but a few studies exist looking at the FODMAP content of fermented wheat and rye bread (Laatikainen et al., 2017, 2016). Rye bread is an iconic staple in the Finnish cuisine, but may be problematic for many with gastrointestinal (GI) issues, because as several studies have been published, showing rye to be high

1

in especially FODMAPs fructan and mannitol (Biesiekierski et al., 2011; Karppinen et al., 2003; Laatikainen et al., 2017, 2016).

In addition, the Finnish foods from soups to casseroles typically contain onion and garlic. The Nordic and country-specific nutrition recommendations emphasis the intake of berries (Nordic Nutrition Recommendations, 2012) as they are known to have specific health benefits to metabolic health (Kolehmainen et al., 2015) and are a typical part of the Finnish cuisine. The FODMAP content of local berry produce is unclear, although some previous data exists on their polyol content. The Finns have a special local polyol in their diet that can play a role in GI symptoms, namely birch sugar xylitol, which is known to have anti-cariogenic properties. Xylitol is used as a sweetener in chewing gum, drops and vitamins. Its daily consumption is promoted as a part of dental health routine, starting from child health care centres at an early age. Since both berry-picking and mushroom-picking are accessible to all by a national everyman's right, also mushrooms sometimes pose a challenge for individuals.

This Master's thesis fills in the gaps of previous knowledge on the FODMAP content of some typical Finnish foods. The FODMAP content of samples of Finnish products were analysed by Monash University in Melbourne, Australia. These findings are then used to discuss the implementation of the low FODMAP diet in the Finnish cuisine.

2. REVIEW OF LITERATURE

2.1.Prevalence of IBS

Estimates on the prevalence of irritable bowel syndrome vary to a large extend. This is may be due to used diagnostic criteria, cultural differences in reporting and lifestyle factors. Global mean prevalence of IBS is thought to be around 11%, ranging from 7 % in southeast Asia to 20 % in South America (Lovell & Ford, 2012).

The prevalence data is very polarized, since most of the studies looking at the prevalence of IBS are conducted in Northern Europe or Southeast Asia. Studies from elsewhere, such as Central America, South America, South Asia, Africa and Australasia, are either non-existing or a few in number. This is visualised in Figure 1. On the other hand, IBS is not linked to socioeconomic status (Canavan et al., 2014b, Lovell & Ford, 2012).

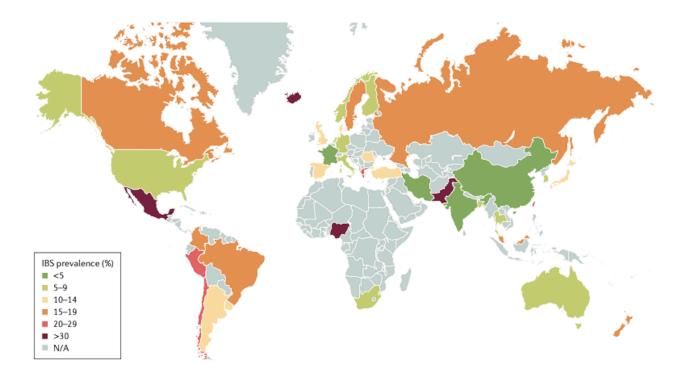


Figure 1. The global prevalence of IBS according to population studies. N/A indicated no prevalence data exists for these countries. (Enck et al., 2016, *with persmission from the author*).

2.2. Etiology and risk factors

Etiological factors of IBS are numerous. Genetic, microbiological, hormonal, neurotransmitterrelated, psychological, and lifestyle factors have been linked to the onset of irritable bowel syndrome (Marynowski et al., 2015). Healthy individuals and people with irritable bowel syndrome show differences among other things in e.g. gut microbiota (Dior et al., 2016; Tana et al., 2010), prevalence of gut hormones along the intestinal tract (El-Salhy et al., 2014a, 2014b, 2015), visceral hypersensitivity (Balemans et al., 2019; Zhou et al., 2010), pain regulation (Tillisch et al., 2011), low-grade mucosal inflammation in the gut (Hod et al., 2011; Gonsalkorale et al., 2003; Liebregts et al., 2007) and altered bile acid profiles (Dior et al., 2016).

2.2.1. <u>Sex</u>

It is estimated that globally women are more likely to report of having IBS, but whether this is due to sex-related physiological etiology or cultural differences in reporting, is unclear. In South Asia, South America and in Africa men report the same or even slightly more often than women of having IBS (Canavan et al., 2014a). There are some physiological, sex-hormone related factors that could explain why women are more likely to have IBS (Heitkemper et al., 2003). Hormones can influence e.g. gut motility, transit time and visceral hypersensitivity.

2.2.2. Genetics

Genetic background of IBS is poorly understood, but mutations play a part in IBS etiology (Henström et al., 2016). The role of the genetical component seems to be fairly moderate as was demonstrated e.g. by Beyder et al. (2014). They discovered a genetic mutation in genes coding for ion channels involved in gut motility and visceral pain in 2,2 % of IBS patients. It is not uncommon to hear patients refer to family members or even distant relatives with gastrointestinal conditions. This was supported by evidence from a large case-cohort study based on combining health care registers done in the Swedish population (Waehrens et al., 2013). They found that IBS risk is increased in first-, second- and even third-degree relatives of patients. Hence, shared living conditions (e.g. diet, exercise habits, psychological life events) do not explain the increased odds of having IBS. Better diagnostics at an early stage could prevent misdiagnosis with other genetic

conditions manifesting in a similar way, such as sucrose-isomaltase deficiency (Garcia-Etxebarria et al., 2018).

2.2.3. Epigenetics and trauma

Epidemiological research shows that traumatic events, such as physical punishment, emotional and sexual abuse, are more common in people with IBS than in the rest of the population (Bradford et al., 2012; Drossman et al, 1995). Traumatic psychological events occuring especially in early life or in utero can cause epigenetic changes especially in the stress system (Dinan et al., 2010). Epigenetic changes refer to the alteration in gene functioning (i.e. how the DNA is intrepreted by the cell) that can be influenced by external factors. For example, Holocaust victims show an increased prevalence of IBS compared to people not having lived under the Nazi regime (Stermer et al., 1991). These epigenetic changes can be transferred over generations, as is seen with Holocaust survivor women and their children, who also suffer more than the general population of IBS and post-traumatic stress disorder, which both share an element of malfunctioning stress system.

However, connecting the dots between maltreatment and IBS is difficult, as most people do not confide in their GI physicians about their past abuse. A survey by Drossman et al. (1995) revealed that a third of patients with gastrointestinal problems had never told anyone about their abuse and only 17 % had told their GI physicians (Drossman et al., 1995). Abuse history worsens the outcome as it is linked to poorer coping mechanisms, worse symptoms and greater number of health care visits (Drossman et al., 1995).

2.2.4. Gut microbiota

The gut microbiota of people with IBS differs from that of the healthy controls (Dior et al., 2016; Tana et al., 2010). Profiling gut microbiota is already being used as a way to investigate gut microbiota dysbiosis, which refers to the imbalance of bacteria believed to be either beneficial or detrimental to health. This practise is somewhat problematic, as the reference consistency of normal gut microbiota profile is still unclear (Biesiekierski et al., 2019). However, research in altering gut microbiota in the treatment of IBS through probiotics (Sanders et al., 2019; Sniffen at al., 2018), prebiotics (Sanders et al., 2019), and faecal transplants (Lahtinen et al., 2020; Myneedu et al. 2019) is actively on-going, but with mixed results.

2.2.5. Post-infection

The best-known etiological factor is the history of gastroenteritis prior to the onset of IBS. Postinfectious IBS (PI-IBS) is well reported (Mearin, 2012; Porter et al., 2011). In some, IBS symptoms are alleviated in within 10 years (Youn et al., 2016) and in some in 6 years (Neal et al., 2002), but those susceptible to anxiety and depression were less unlikely to recover (Wouters et al., 2016; Neal et al., 2002).

2.3. Diagnostics of IBS

Often in research settings Rome criteria is used. These are crafted by The Rome Foundation, a nonprofit organisation aimed at supporting the scientific and educational work of people working with functional gastrointestinal disorders (The Rome Foundation, 2020). The latest version, the Rome IV criteria, was released in 2016 and is shown in Table 1 (Lacy & Patel, 2017).

Table 1. The Rome IV criteria for irritable bowel syndrome. Modified source: IrritableBowelSyndrome.net, 2016.

Rome IV	Recurrent abdominal pain, on average, at least 1 day/week in the last 3 months,					
Criteria	associated with two or more of the following criteria:					
	 Related to defecation Associated with a change in frequency of stool Associated with a change in form (appearance) of stool. 					
	Criteria fulfilled for the last 3 months with symptom onset at least 6 months					
	before diagnosis.					

In addition to the general diagnostic criteria, the Rome IV criteria also include advice on how to divide the patients into the four subtypes (Lacy & Patel, 2017). These are namely, 1) predominantly constipated (IBS-C), 2) predominantly diarrhea (IBS-D), 3) with mixed bowel habits (IBS-M), and 4) unclassified symptoms (IBS-U). Bristol Stool Scale is used to categorize stool consistency (Lewis & Heaton, 1997). The scale includes pictures and descriptions of stool types.

- Type 1: Separate hard lumps, like nuts (hard to pass)
- Type 2: Sausage-shaped, but lumpy
- Type 3: Like a sausage but with cracks on its surface
- Type 4: Like a sausage or snake, smooth and soft
- Type 5: Soft blobs with clear cut edges (passed easily)
- Type 6: Fluffy pieces with ragged edges, a mushy stool
- Type 7: Watery, no solid pieces, entirely liquid

The new criteria acknowledge that patients may have fluctuating bowel habits and therefore, have included clarifications that e.g. in constipation subtype, over 25 % of stool produced is of type 1-2 (i.e. hard stool, difficult to pass). Types 3 and 4 are generally considered as "normal" stool consistency.

In the clinical settings, practitioners often choose in addition to verify the diagnosis by exclusion, ruling out organic illnesses such as celiac and inflammatory bowel diseases. The problem of using exclusion diagnostics is inaccuracy and distinguishing IBS from overlapping conditions, such as anxiety, chronic fatigue syndrome, depression, fibromyalgia, migraine (Cole at al., 2006; Lau et al., 2014). Developing a positive diagnostic tool is difficult, since the underlying mechanisms of the different subtypes of irritable bowel are still partially unknown.

2.4. Characteristics of IBS symptoms

Bowel habits and stool consistency are somewhat straight-forward to analyse, especially with the Rome Foundation tools provided for practitioners. What is much more difficult to characterise are the numerous other symptoms associated with irritable bowel syndrome.

It is known that health-related quality of life in IBS patients is low. The survey study by Drossman et al. (2009) found out that IBS patients would be willing to shorten their remaining life by 25 % (average 15 years), if they could achieve symptom control (Drossman et al., 2009). In the same survey, the patients reported restricting their activities for 73 days a year on average. Adequate symptom control could have a dramatic positive impact on patients' lives.

2.4.1. Bloating and flatus

Dietary fibre is fermented by the gut microbiota in the colon, producing beneficial compounds called short-chain fatty acids (butyrate, propionate and acetate). Certain gases are also produced, namely hydrogen (H₂), carbon dioxide (CO₂), and in some people, methane (CH₄). This phenomenon is part of normal human physiology, but in patients with IBS can cause distention of the gut, causing pain (Serra et al., 2001). People with IBS may suffer from allodynia or hyperalgenia. Merskey (1994) defines allodynia as a painful sensation to a harmless stimuli, and hyperalgenia as an excessive reaction to a painful simuli (Merskey, 1994). It has been discussed whether people with IBS produce more gas than healthy, but the recent studies show that the amount of gas does not differ between IBS patients and healthy controls (Major et al., 2017). In addition, it has been discussed whether gas is insufficiently evacuated from the gut (Serra et al., 2001).

2.4.2. Pain

The most common complaint of IBS symptoms alongside bowel problems, bloating and excess flatus is visceral pain (Drossman et al., 2009). Visceral pain differs from somatic pain, as it is by nature alternating and difficult to localize. The severity of pain can vary from mild discomfort to immobilizing pain.

Pain mechanisms in IBS are under active research. It has been established that there are several underlying mechanism, ranging from immune and nervous system activation to enteroendocrine factors (Barbara et al., 2011). Anxiety and other psychological factors amplify pain, but don't alone explain the complex central and peripheral mechanisms involved. In addition, gut microbiota and mucosal barrier integrity are involved in etiology of visceral pain.

2.4.3. Fatigue

Fatigue is more common in patients with irritable bowel syndrome than in healthy controls (Simrén et al., 2008). Little over half of patients with IBS suffer from fatigue (Han & Yang, 2016). In many studies, it predicts low health-related quality of life. Subjective sleeping difficulties and the feeling of not getting enough sleep partially explain these findings (Simrén et al., 2008). Objectively

measured sleep studies confirm that poor sleep worsens IBS symptoms the next day in women (Buchanan et al., 2014).

However, attention has been paid to the possible biochemical mechanisms behind fatigue in IBS, as it overlaps with other functional conditions, such as fibromyalgia and chronic fatigue syndrome. It is postulated that e.g. low-grade inflammation measured by mucosal cell counts, especially that of mast cells, is involved in fatigue mechanisms (Piche et al., 2008). Caecal mucosal mast cell counts in IBS subjects is higher than in healthy controls or in subjects with depression. Other studies show that dysregulation of the autonomic nervous system is linked to both, gastrointestinal symptoms and sleep (Buchanan et al., 2014).

2.4.4. Anxiety and depression

Anxiety and depression are also symptoms of IBS. The gut-brain axis, or better yet, the gut microbiota-gut-brain-axis, is thought to explain this link between gut symptoms and mental health conditions.

Anxiety can be interpreted as the manifestation of emotional stress. Chronic stress can cause a dysregulation of different systems involved in stress, such as the amygdala, hypothalamic-pituitaryadrenal-axis and the autonomic nervous system (Myers & Greenwood-Van Meerveld, 2009). People with IBS show hyper-responsiveness to stress and they also have elevated cortisol levels at baseline. Coinciding gut and brain symptoms are not surprising as the central amygdala is involved in processes that regulate both anxiety and gut functions such as gastric emptying and colonic motility.

In a retrospective cohort study the odds of having depression was 40 % higher in the IBS cohort than in the non-IBS cohort (Cole et al., 2006). It is possible that the dysfunction of the immune and neuroendocrine system in the gut is involved in the pathophysiology of depression (Mudyanadzo et al., 2018). In fact, the systemic chronic inflammation is known to prevail also in the brain, in which case it is referred to as neuroinflammation. Some of the systems involved are the same as in anxiety, e.g. the hypothalamic-pituitary-adrenal-axis (Mudyanadzo et al., 2018). The gut microbiota composition and gut permeability influence the low grade inflammation in the gut, but the

9

management of this system by means of probiotics or bioactive compounds, such as prebiotics, is in its infancy.

2.4.5. Upper GI symptoms

Some people with IBS symptoms may suffer from both lower abdominal gut pain and upper GItrack symptoms, such as acid reflux, dyspepsia and belching. The lower and upper GI-track are interconnected, demonstrated by the fact that the diet low in slowly fermentable carbohydrates is shown to affect the esophageal sphincter relaxation (Masuy et al., 2018). However, not all IBS patients suffer from upper GI symptoms, and hence these symptoms are only occasionally referred to in this thesis.

2.5.Cost of IBS

For a long time, people with chronic pain and functional ailments have been left to deal with the condition on their own or with peer-groups. Unfortunately, the attitude towards them has been at worst hostile within the health care sector. Their needs have been disregarded and behaviour thought to be socially learned (Levy et al., 2001). Nevertheless, belittling is short-sighted, as the cost of IBS to the health care sector, and to the society in general through work absenteeism, is estimated to be substantial.

In the United States the annual direct cost for each IBS patient was \$348-8750, a sum that does not include cost of comorbidities, which are known to be common in IBS (Maxion-Bergemann et al., 2006). The same review stated that days off work due to IBS ranged from 8.5 to 21.6 in a year.

The cost of IBS has been evaluated in a Finnish postal survey, in which the annual cost (direct and indirect) per subject ranged from \notin 286 to \notin 333, depending on diagnostic criteria (Hillilä et al., 2010b). IBS patients' direct costs of GI symptoms and non-GI consultations have been calculated to be as high as 5 % of the total annual outpatient care and medicine expenditure (Hillilä, 2010a). The treatment-seeking behaviour of this patient group, as well as the high prevalence of IBS, explain the extensive economic burden of the disease.

In an observational, retrospective-prospective study in IBS-C patients, the annual mean cost for a Spanish patient was \in 568, but the direct cost to the national health care system were much more, \in 1067 (Mearin et al., 2019). Those 13% of IBS patients that took sick leave, took leave often (mean 6.3 times /year) and for a long period of time (mean duration 52 days). In a review about annual IBS costs, the healthcare cost was around 2000 euros or dollars per person per year (18 studies from 8 different countries), altough there is great heterogeneity within and between the studies (Canavan et al. 2014b). The authors of this publication summarise, that overall costs to the healthcare are higher in IBS patients than in patients without IBS.

It is noteworthy to point out that the high costs are related to repeated health care visits and unsatisfactory treatment (Williams et al., 2006) as both diagnostics and treatment of IBS have not been optimal nor efficient. Repeated visits are linked more to the mental burden of the illness than the severity of symptoms (Williams et al., 2006). Finding better diagnostic tools and treatments is essential in keeping the cost of one of the most common health conditions under control.

2.6.Established treatment

Treatment options for IBSinclude dietary experiments, psychological and pharmacological interventions and lifestyle counselling. Many of these treatments require dedication and time, and often the benefit diminishes over time when treatment is stopped. However, this is not a sign of inefficient treatment, but shows the complexity and ever-presence of the syndrome.

2.6.1. Plasebo and nocebo

It is noteworthy to point out that anticipation and expectation play a part in the treatment of IBS. Placebo effect refers to the psychological phenomenon of believing a given treatment to be healing. The opposite of this is nosebo effect, in which case an individual anticipates worsening of symptoms or a condition due to the belief that a substance or a treatment will do harm.

According to a meta-analysis covering 73 randomized controlled trials (RCTs) and including 8364 subjects, nearly 40 % of treatment effect is due to placebo in IBS patients (Ford & Moayyedi, 2010). Nosebo effect is known to e.g. worsen visceral pain even in healthy women (Elsenbruch et al., 2012). Care should be taken to use this knowledge wisely, not to deceive patients, but to

11

understand the power of taking the patient seriously and attending to their needs, as this alone can mean significant improvements in patients.

2.6.2. Lifestyle management

IBS symptoms can have a devastating impact on the quality of life and social relationships. In a situation like this, discussing ways to exercise, sleep and relax can seem degrading. However, there is evidence suggesting this conversation should not be missed.

Exercise is known to positively effect IBS symptom control (Johannesson et al., 2015). Some of the mechanisms are: 1) beneficial influences of gut microbiota (Munukka et al., 2018), especially its diversity, as shown by animal studies (Lambert et al., 2018), 2) downplaying low-grade inflammation, measured by inflammatory markers of the gut lumen (Hajizadeh Maleki et al., 2018) and 3), increasing the antioxidant levels in the body (Hajizadeh Maleki et al., 2018). Poor sleep, as mentioned in the previous chapter, Characteristics of IBS symptoms, can worsen IBS symptoms.

The role of stress management is being emphasized, as the role of the gut-brain-axis is becoming clearer. Stress mechanisms can downright be the root cause of IBS, as it influences gut permeability, gut microbiota composition and the regulation of the central and enteral nervous system (Konturek et al., 2011). It is no wonder, that psychological treatments show a promise in the treatment of IBS.

2.6.3. Psychological treatment

Evidence shows that IBS patients may benefit from several psychological treatments, namely meditation and mindfulness practise (Ballou & Keefer, 2017), cognitive-behavioural therapy (Zomorodi et al., 2014), acceptance and commitment therapy (Sebastián Sánchez et al., 2017) and hypnotherapy (Peters et al., 2016). They can be a first-line treatment, and certainly a second-line treatment, if lifestyle, diet or pharmacological treatments are to no avail.

2.6.4. Pharmacological treatments

Most common drug therapies are focused in relieving pain, bloating and stabilising bowel motility (Nee et al., 2015). No curing medication exists for IBS, but drugs like antispasmodics, antidepressants, laxatives and even antibiotics (namely rifamixin) have been used for individual symptoms. Proton-pump inhibitors are commonly used for upper-GI problems. They are commonly used long-term, although this is not recommended due to the negative effects a long-term usage can have, ranging from malabsorption of vitamins to small bacterial overgrowth (Arkkila, 2015).

2.6.5. Complementary and alternative treatments (CAM)

The use of complementary and alternative therapies in the treatment of IBS is common. 37 % of recipient of an international survey answered 'yes' to using CAM (Drossman et al., 2009). The definition of CAM varies from established alternative treatments, such as acupuncture and osteopathy, to less studied herbal remedies, of which some are over-the-counter products (Yoon et al., 2011). There is good evidence of the use of peppermint oil for IBS, at least for a short-term treatment (Khanna et al., 2014). However, comparing the efficacy of CAM on a larger scale is problematic, as unified study protocols do not exist and the studies have been small in number of study participants.

2.6.6. Dietary treatment

Exclusion diets were recommended long before etiology of IBS was even known. Most patients report that food is a culprit of their symptoms (Böhn et al., 2013). However, for many, it is difficult to name the food items they find problematic, as many do not take into account the transit time nor the location of the part of the gut that seems to be the source of discomfort. Excluding entire food groups has been common, such as avoiding dairy, grains, wheat or gluten or trying to restrict certain nutrients, such as carbohydrates or fat.

Some of the dietary treatments have focused on eating behavior and some simple advice on foods to avoid. Even though conservative dietary treatment varies slightly from country to country and from one health care facility to another, the British National Institute for health and Care Excellence (NICE) guidelines for IBS (table 2.) summarize the general instructions given to patients. No

13

official guidelines for IBS exist in Finland, although, general recommendations are similar to the NICE guidelines.

Table 2. NICE guidelines recommendation for first-line treatment of IBS (National Institute for Health and Care Excellence, 2015).

Diet and nutrition should be assessed for people with IBS and the following general advice given.

- Have regular meals and take time to eat.
- Avoid missing meals or leaving long gaps between eating.
- Drink at least 8 cups of fluid per day, especially water or other non-caffeinated drinks, for example herbal teas.
- Restrict tea and coffee to 3 cups per day.
- Reduce intake of alcohol and fizzy drinks.
- It may be helpful to limit intake of high-fibre food (such as wholemeal or high-fibre flour and breads, cereals high in bran, and whole grains such as brown rice).
- Reduce intake of 'resistant starch' (starch that resists digestion in the small intestine and reaches the colon intact), which is often found in processed or re-cooked foods.
- Limit fresh fruit to 3 portions per day (a portion should be approximately 80 g).
- People with diarrhoea should avoid sorbitol, an artificial sweetener found in sugar-free sweets (including chewing gum) and drinks, and in some diabetic and slimming products.
- People with wind and bloating may find it helpful to eat oats (such as oat-based breakfast cereal or porridge) and linseeds (up to 1 tablespoon per day). [2008]

For some of the patients, these recommendations are not sufficient to alleviate symptoms, even though, as such they form a healthy basis for diet and eating habits. This is why specialized dietary therapy is called for.

2.7. The low FODMAP diet

Due to the low FODMAP diet, the dietary treatment of IBS has taken a major leap in the past decade. The low FODMAP diet has become popular among the IBS population, mostly due to individual success stories and enthusiasm online. This success is backed up by research, which show that up to 70 % of irritable bowel sufferers benefit from the low FODMAP diet (Marum et al., 2017).

2.7.1. Mechanisms of action

The FODMAP is an acronym that stands for *Fermentable Oligo-, Di- and Monosaccharides And Polyols*, entailing both the action and the compounds that are involved. FODMAPs are a group of poorly absorbed carbohydrates, both fibres and sugars.

These compounds are not broken down and absorbed in the small intestine, but end up in the large intestine, where the gut microbiota utilizes them as sustenance (Ong et al., 2010; Staudacher et al., 2014). Gas, mostly carbon dioxide and hydrogen, but also methane in some people, is produced. Fructans and galacto-oligosaccharides have been shown to ferment actively and explain most of the gas production. This explains, why people with IBS suffer from bloating, flatus and visceral pain.

On the other hand, the loose stool and urgency to empty the bowel can be explained by the osmotic effect exerted by maldigestion of the FODMAP sugars in the small intestine (Barrett et al., 2010). Fructose is absorbed actively when combined with glucose, but when alone, it is taken up through a passive uptake, making it likely to be maldigested. People with lactose-intolerance lack the enzyme lactose, which breaks down milk sugar lactose into galactose and glucose. If enzymatic activity is poor or lacking, gut symptoms, such as diarrhea, cramps and bloating occur. People with IBS are often lactose-intolerant. Polyols, such as sorbitol, mannitol and xylitol, are absorbed at different efficacy in different people. Large quantities are generally known to have an laxative effect even in healthy people. The main dietary sources of FODMAPs are shown in Table 3.

Table 3. The FODMAP acronym groups under it several different fibres and sugars that are poorly absorbed and hence fermented in the large intestine.

Compound	Main dietary sources
Fructans	Wheat, rye, barley, onion, leek, garlic
Galacto-oligosaccharides	Beans, lentils, peas
Fructose (in excess)	Fruit juices, fructose-sweetened beverages,
	high-fructose corn syrup
Lactose	Dairy products
Polyols, such as sorbitol, mannitol and xylitol	Apples, pears, peaches, plums, nectarines
	(sorbitol)
	Mushroom, cauliflower (mannitol)
	Sugar-free chewing gum and drops (sorbitol,
	xylitol)

It should be noted that there are compounds other than FODMAPs that can exerts similar effects in the gut, e.g. trehalose in mushrooms, resistant starch in certain grains and bananas and certain added fibres, such as xylo-oligosaccharides (Halmos & Gibson, 2019). Should they be forgotten in the clinical setting, symptom alleviation may not be achieved.

The gas production of fibres and osmotic effect were amongst the first mechanisms explaining why restricting FODMAP compounds relieved many IBS symptoms (Barrett et al., 2010; Ong et al., 2010; Staudacher et al., 2014). Later, other research findings have provided additional explanations.

Histamine activation is known to be involved in IBS pathophysiology, especially in regards to gut motility, visceral hypersensitivity and immune activation, although, mechanisms are not fully understood (Fabisiak et al., 2017). Histamine is also an inflammatory marker. The low FODMAP diet has been shown to lower urinary histamine secretion eightfold compared to a high FODMAP

diet (McIntosh et al., 2015), which may explain part of the effectiveness of the diet. The diet has been shown to lower other inflammatory markers besides histamine, namely cytokines interleukin-6 and interleukin-8 (Hustoft et al, 2017). The effects of the diet are not limited to the lower gastrointestinal track, as e.g. fructans are shown to cause higher upper postprandial gastric pressure (Masuy et al., 2018). One cannot also undermine the finding that the low FODMAP diet increases health-related quality of life (Staudacher et al., 2017). However, the diet is not a cure for IBS. It only manages the mechanisms behind the symptoms, and without the diet, the symptoms return.

2.7.2. Clinical evidence

Studies have been conducted in several countries, and the results are not limited to the Australia (Halmos et al., 2015; Ong et al., 2010), where the diet originates. Research participants in e.g. New Zealand (de Roest et al., 2013), Mexico (Pérez y López et al., 2015), the United States (Eswaran et al., 2016) and Switzerland (Wilder-Smith et al., 2017) have benefitted from the dietary treatment. Adequate relief and satisfaction have varied from 50 % (Eswaran et al., 2016) to over 70 % (Marum et al., 2017). The low FODMAP diet has become part of some national guidelines regarding the treatment and management of IBS. It was first mentioned in the United Kingdom National Institute for Health and Care Excellence (NICE) guideline in 2015 as a second-line symptom-management alternative (NICE, 2015).

The diet has been shown to alleviate gut symptoms in different patient groups, although most evidence is from the IBS patient group. There are studies showing effect 1) in gut symptom management in IBD (Cox et al., 2020; Gearry et al., 2009), 2) in controlling gut symptoms during athletic performances (Lis et al., 2018; Wiffin et al., 2019), 3) in reducing crying-fussing in colicy babies whose mothers were on a low FODMAP diet (Iacovou et al., 2018), and 4) in fibromyalgia (Marum et al., 2017). In addition, the diet has been beneficial in managing gut symptoms in children (Chumpitazi et al, 2015).

No additional health benefits have been achieved in the low FODMAP diet research in healthy controls (Halmos et al., 2014). Therefore, it should be noted that the diet should be applied only in patients with GI problems.

2.7.3. Implementing the diet

Dietary management utilising the low FODMAP diet has three phases: 1) elimination of foods high in FODMAPs, 2) re-introduction of previously eliminated foods high in FODMAPs and 3) personalisation according to individual FODMAP sensitivities (Whelan et al., 2018).

The paradox of the low FODMAP diet is that most of the foods that cause symptoms are in fact nutritionally healthy, because they are rich in vitamins, minerals and a variety of fibre compounds. It is, hence, recommended that high FODMAP foods are removed from the diet for only a short period of time (Whelan et al., 2018). In clinical work four to six weeks is usually recommended (Whelan et al., 2018). After this period a reintroduction phase follows, allowing to examine, which of the FODMAP compounds are responsible for the individual symptoms. The goal is that the intake of FODMAPs is restricted to an individual level, where the diet is flexible and varied, but symptoms are under control. It should be noted that these novel findings do not undermine the former IBS counselling principles of e.g. eating small portions regularly, chewing properly and eating a balanced diet. Rather they add to it as the advice is incorporated to the low FODMAP diet counselling.

The strongest evidence of diet efficacy comes from studies where the dietary counselling is given by dietitians (O'Keeffe & Lomer, 2017). Implementation of the diet can lead to nutritional deficiencies without sufficient counselling from a dietitian. The nutrient deficiencies due to the low FODMAP diet have been limited to only a few nutrients, namely calcium (Staudacher et al., 2012), which can be speculated to be due the use of specialised dietitians in the studies. In the longest follow-up study done (6-18 months), at least 95 % of patients following an adpated FODMAP diet met intake needs for energy and most nutrients (O'Keeffe et al., 2018). Intake of folate and vitamin A was in fact higher than in the patients, who were following a habitual diet.

Quality of general online material, often recommended by physicians to their patients, varies and cannot be be used as a reliable and trustworthy way to counsel IBS patients (Alfaro-Cruz et al., 2019; Trott et al., 2019). The patients themselves feel the counselling given by a non-dietitian is too simplistic and they are sceptical about the suggest online sources, rightfully so (Alfaro-Cruz et al., 2019). Especially worrysome is that the non-dietitian counselling may only provide advice for the first, elimination phase, and not the essential re-introduction phase (Trott et al., 2019).

2.7.4. Critical perspective

Fermentation of fibre by gut microbiota produces short-chain fatty acids, such as butyrate, acetate and propionic acid (Cummings & Macfarlane, 1997). The fatty acids provide important nutrition for the epithelial cells, keeping the gut barrier intact.

The low FODMAP diet has influenced the gut microbiota composition in several studies (Bennet et al., 2018; Hustoft et al., 2016; Halmos et al., 2015; MacIntosh et al., 2015; Staudacher et al., 2012). Especially the decrease in bifidobacteria has caused worries, as these bacteria are known to have beneficial, immunomodulatory health effects (Staudacher et al., 2017, 2012). However, successful strategies to overcome this unfortunate effect of the diet has been trialled. Supplementing with a multi-strain probiotic resulted in a greater bifidobacteria count in stool, compared to the non-supplemented arm of the study (Staudacher et al., 2012), indicating that a probiotic could be used in addition to the diet to neutralize the effect on gut microbiota.

It should be noted, that in some studies, the gut microbiota composition changed, but the diversity did not (Halmos et al., 2015). A diverse gut microbiota is regarded as a general marker for good gut health. Production of short-chain fatty acids have decreased (Hustoft et al., 2016) or remained the same or been non-significant (Halmos et al, 2015; Staudacher et al., 2012). These controversial findings indicate that the complex interactions of dietary components and gut microbiota need further elucidation. Little is known of the gut microbiota ability to adapt to the diet, especially as the strict phase of the diet is intended to be only for some weeks.

FODMAPs are considered to be prebiotic and healthy compounds, but this assumption is challenged by new findings by Zhou et al. (Zhou et al., 2018). Rats fed on a high FODMAP diet showed increased gut permeability and inflammatory markers as well as heightened visceral hypersensitivity. However, the number of animals used in the study was few, and the results on rats cannot be extrapolated to humans. Were this finding true in humans, the effects of the re-introduction phase of the low FODMAP diet would be put into question, at least in a subgroup of IBS patients.

As important as the physiological effects are the toll the diet takes on mental health. People need plenty of support and advice on how to accustom the diet to their everyday life (Trott et al., 2019).

19

Especially as this patient group is susceptible to anxiety, food fears and orthorexic (the need to constantly eat "right" and "healthy") thoughts may worsen the treatment outcome (Halmos & Gibson, 2019). Higher costs due to the diet have also been mentioned by study participants as a negative consequence of following the low FODMAP diet (O'Keeffe et al., 2017).

2.7.5. Cut-off values for the low FODMAP diet

Even the most comprehensive nutrient databases do not list different FODMAPs and their content is practically impossible to deduct from existing nutrient content. The Department of Gastroenterology at Monash University in Melbourne, Australia, have alongside clinical low FODMAP diet studies, compiled a database on FODMAPs. This information is available to consumers and professionals in a form of a mobile application. Some data have been published in academic journals (Biesiekierski et al., 2011; Muir et al., 2009; Varney et al., 2017). The analysis procedure is explained in detail in Methods.

The cutoff values defined by the Monash University for low FODMAP food groups are shown in Table 4. A well-tolerated intake of FODMAPs per sitting has been set to less than 0.5 g, excluding lactose (Barrett et al., 2010; Halmos et al., 2014; Ong et al., 2010; Varney et al., 2017).

FODMAP cutoff categories	Grams per serving
Grain, legume, nut and seed oligosaccharides	< 0.3 g
(fructan and α -galacto-oligosaccharides)	
Vegetable, fruit and other food	< 0.2 g
oligosaccharides	
Fructose in excess to glucose when the only	$< 0.4 { m g}$
FODMAP present	
Fructose in excess to glucose when other	< 0.15 g
FODMAP present	
Sorbitol or mannitol individually	$< 0.2 { m g}$
Total polyol if several polyol present	$< 0.4 { m g}$
Lactose	< 1.0 g

Table 4. The cutoff values for the low FODMAP diet (Varney et al., 2017, modified).

2.7.6. FODMAP intake in studies

Varied levels of daily FODMAP intake have been used or achieved in studies. In Table 5., the per day intake of FODMAPs is given in studies showing efficacy of the low FODMAP diet in alleviating symptoms and the study designs and number of participants. Patients studied have mostly been IBS patients, excluding the Ong et al. study that had both IBS patients and healthy controls, as did Halmos et al. (healthy data not shown). Marum et al. (2017) study was done in a fibromyalgia cohort (Halmos et al., 2015, 2014; Marum et al., 2017; Ong et al., 2010).

Ong et al. (2010) was one of the early LFD studies, evaluating mechanisms of symptom aggrevation). This study was only two days long, as the intention was to measure by breath hydrogen throughout the day and collect data on symptoms. The differences between intake were stark as this was a feeding study, in which the participants received the food consumed, making it easier to control the FODMAP intake. There was a great and statistically significant difference in FODMAP intake between the groups (p=0.0001), which is unsurprising as the diets were designed as high (48.1 g/day) and low FODMAP intake (8.3 g/day).

Staudacher et al. investigated both the efficacy of LFD in symptom alleviation and its effect on gut microbiota (Staudacher et al., 2012). The participants were randomized into either the control or the intervention group for four weeks. Participants in the intervention group reported better symptom control compared to the control group. This is the first LFD studies to show alterations in the gut microbiota composition. Whilst the total luminal bacteria did not differ between the groups, there were significantly lower concentrations (p=0.001) and proportions (p=0.001) of bifidobacteria in the intervention group. There was a statistically significant difference between the FODMAP intake between the groups (p=0.001), although the level of FODMAPs in the intervention group was much higher than in studies where the participants received the food during the study period (Halmos et al., 2015; Ong et al., 2010).

Later, the same author and the team designed a 2x2 study, in which they created a sham diet as a plasebo treatment and also looked at the effects of probiotics (Staudacher et al., 2017). The sham diet advice was similar in difficulty as the LFD advice, and also similar number of foods were restricted on both diets. The sham diet was designed so that the FODMAP intake did not alter during the study. Probiotics part of the study was also placebo-controlled. Due to the study design,

the participants were randomized into one of four treatment groups: 1) sham diet/placebo, 2) sham diet/probiotic, 3) LFD/placebo and 4) LFD/probiotic. This study supported the role of LFD in the symptom control of patients with IBS, but also showed that the probiotic supplement helped to maintain the level of bifidobacteria on the LFD. The FODMAP intake differed significantly (p<0.001) in the sham diet group (9.9 g/day) compared to LFD group (17.4 g/day).

Böhn et al. investigated the difference in efficacy of the LFD and that of so-called traditional IBS dietary advice in a randomized, multi-centre, parallel, single-blind study (Böhn et al., 2015). The tradional IBS dietary advice was based on the NICE guidelines (presented in Table 2. of this publication). These guidelines focus on dietary habits as much as they do on individual food items or groups. Both diets were deemed equally effective in managing IBS symtoms. The FODMAP intake differed significantly (p=0.05) being 3.8 g/day in the LFD group and 13.5 g/day in the traditional IBS dietary advice group.

Halmos et al. conducted a randomized, controlled, single-blind, cross-over trial that looked at the effects of the LFD and the typical Australian diet (Halmos et al., 2015, 2014). In a cross-over setting the particiants are randomised to different treatments (in this case diets) in the same study. In the Halmos et al. study the participants were allocated either to the LFD or the typical Australian diet group. After the given time, the treatments are swapped, typically with a wash-out period in between treatments. All participants go throught the same treatments, but in a randomized order.

Participants with IBS had better symptoms control on the LFD. Six of the IBS participants could not complete the typical Australian diet cross-over phase due to severe worsening of symtoms. There was a significant difference between the FODMAP intake (p<0.001) between the LFD diet phase (3.05 g/day) and the typical Australian diet (23.7 d/day). This was a feeding study, meaning the participants got the study food. This study found out that there is no additional health benefits to healthy controls and the LFD should therefore be used only as a terapeutic diet for suitable patient groups. There were gut microbiota changes during the diets. During the LFD phase there was greater diversity, but reduced total bacterial abundance compared to the Australian diet phase.

Marum et al. studied the effect of the LFD in the treatment of fibromyalgia, hence looking at symptoms other than gut specific (Marum et al., 2017). The participants followed the elimination LFD protocol for four weeks, after which they reintroduced FODMAPs back into the diet. The

latter phase lasted for another four weeks. As a result all fibromyalgia symptoms, including somatic pain, was significantly lower after the LFD. Intake of FODMAPs differed significantly (p < 0.01) during the strictest phase (2.6 g/day) and the baseline line (24.4 g/day).

Most of these studies have been short-term, but a few studies have looked at the long-term low FODMAP diet followers and their dietary intake (Harvie et al., 2017; Maagard et al. 2016; O'Keeffe et al, 2018).

In Maagaard et al. (2016) retrospective study IBS (n=131) and IBD (n=29) participants were followed for a median of 16 months after initial low FODMAP diet counselling (Maagard et al. 2016). Majority, 84 % of participants, were living on a modified LFD, in which they had reintroduced some foods back to the diet. Most commonly, wheat, dairy products and onions, were reintroduced. No data on specific FODMAP intake were given. Generaly patients were satisfied with the treatment, since 86 % reported either partial (54 %) or full (32 %) efficacy. Greatest improvements were seen in bloating and abdominal pain. However, as this was a retrospective study, there could have been selection bias, as 48 % of participants who were asked to join the study, did not.

Harvie et al. (2017) studied the effects of FODMAP reintroduction to symptoms, dietary intake, and the gut microbiota (Harvie et al., 2017). In a group that went through elimination and reintroduction, the FODMAP intake fell from baseline 28 g/day (SD 15 g/day) to 12 g/day (SD 8 g/day) at three months follow-up. After this FODMAP foods were reintroduced into the diet. At 6 months the intake of FODMAPs was lower than at baseline, but highter than at 3 months follow-up, being 22 g/day (SD 11 g/day). The diet effected positively quality of life and IBS-SSS was significantly lower at both 3 and 6 month follow-up points.

O'Keeffe et al. (2018) studied 103 participants with IBS, 84 were on the the "adapted FODMAP" diet after 6-18 months follow-up period (O'Keeffe et al, 2018). The adapted version of the diet means that they had reintroduced high FODMAP foods to their diet. The total FODMAP intake mean in this adapted group was 20.6, (SD 14.9 g/day), whilst in the group reporting having gone back to a habitual diet, the intake of total FODMAPs was 29.4 (SD 22.9 g/day).



Table 5. The mean (standard deviation) intake of FODMAPs (g/day) in the low FODMAP group and the comparatory group.

Publication (country)	Study design	Comparison groups	Study participants (number)	Duration	The low FODMAP group of the study (SD)	The comparatory group of the study (SD	p-value
Ong et al., 2010 (Australia)	A randomized, single-blinded, crossover intervention trial	Low FODMAP vs. high FODMAP	IBS (n=15)*	2 days + 7 day wash-out + 2 days	8.3 (0.4)	48.1 (2.2)	<0.0001
Staudacher et al., 2012 (the UK)	A randomized controlled trial	Low FODMAP vs. habitual diet	IBS Intervention (n = 19), habitual diet (n = 22	4 weeks	17.8 (SD data not shown)	29.7 (SD data not shown)	0.001
Böhn et al., 2015 (Sweden)	A randomized, multi-center, parallel, single- blind trial	Low FODMAP vs. traditional IBS diet	IBS Intervention (n=33) Traditional IBS diet (n =34)	4 weeks	3.8 (3.3)	13.5 (8.7)	0.05
Halmos et al., 2015 (Australia)	A randomized, controlled, single-blind, crossover trial	Low FODMAP vs. typical Australian diet	IBS (n = 30)*	21 days + 21 day wash-out + 21 days	3.05 (SD data not shown)	23.7 (SD data not shown)	<0.001



Publication (country)	Study design	Comparison groups	Study participants (number)	Duration	The low FODMAP group of the study (SD)	The comparatory group of the study (SD	p-value
Staudacher et al., 2017 (the UK)	2x2 factorial design, multicenter, randomized, placebo- controlled trial	Low FODMAP vs. sham diet	IBS, (n=104) Sham diet & placebo (n=22), sham diet & probiotic (n=22), low FODMAP & placebo (n=18), low FODMAP & probiotic	4 weeks	9.9 (6.4)	17.4 (10.5)	<0.001
Marum et al., 2017 (Portugal)	A, non- randomized intervention trial	Low FODMAP vs. baseline	(n=25) Fibromyalgia (n=31)	4 weeks of elimination + 4 weeks reintroduction with 3 day wash-outs in between reintroductions	2.6 (SD data not shown)	24.4 (SD data not shown)	< 0.01

*These studies also investigated the effect of LFD in healthy participant without IBS.

2.8. FODMAPS IN FINLAND

2.8.1. Typical features of Finnish cuisine

In addition to FODMAP content data, it is likely that the dietary customs in countries affect the way the low FODMAP diet can be utilised in the treatment of gastrointestinal symptoms. Ideally the Finnish diet can be a a very nutritious and varied entity, rich in wholegrain produce, fish, seasonal vegetables, especially root vegetables, garden and wild berries, canola oil, low fat dairy and lean meat, enriched further with the utilization of wild produce, such as wild herbs, berries, mushroom, wild fish and game. This type of a diet is what is recommended by the national dietarary guidelines and has been referred to as the New Nordic diet and, in Finland, as the Baltic sea diet. The national dietary guidelines are based on the Nordic nutrition recommendations, commonly compiled by Island, Norway, Denmak, Sweden and Finland (Nordic Nutrition Recommendations, 2012). There are country-specific differences, but also shared features in the preferance of produce, dietary patterns and cooking methods. Similar climate and the fact that all countries have a coastline or inland lakes, influence what foods are produced, harvested and consumed. The Nordic dietary habits have also been studied especially in relation to metabolic health (Kolehmainen et al., 2015).

In Finland, the Nordic traditions fuse together with Russian and Slavic food traditions on the plate, as the nation borders Russia to the east. Especially the rich bread and savoury pie making of Eastern Finland originated from Russia. It is not unsual to find beetroot borsch soup at the lunch cafeteria and Karelian pies are eaten by many on a weekly basis. Onion, garlic and cabbage are commonly used in soups, casseroles and sauces accompanied with potatoes or other starchy staples. As everywhere in the world, the emergence of the so-called westernized fast-food and diet culture, has changes the local food culture and preference a lot.

Many people eat porridge for breakfast, whereas bread is eaten throughout the day with meals and as a snack. In a national 24 hour dietary recall, 40 % of men and 45 % of women ate porridge on either one of the two study days (Valsta et al., 2018). Typically porridge is either made from oat or from a mixture of oat, rye, barley and wheat, and it is eaten with berries. Rye bread was voted as the national food of Finland in 2016, which shows how big a part it plays in the diet of many. According to the previously mentioned national 24 hour dietary recall, 80 % of Finnish men consumed rye bread during one of the two study days. This had a significant impact on fibre intake

as 30 % of their fibre intake was from rye bread (fresh and crisp bread) (Valsta et al., 2018). Women eat less, but even for them, fifth of fibre comes from rye bread produce. Potatoes are a common staple at meals, served typically boiled or as mashed potatoes. Different types of potatobased casseroles, mixed with ham or fish, are also common main courses.

A warm lunch is served through-out the school system, ranging from preschool to universities. From preschool to secondary school meals served are free of charge. Children who go to the day care, also get a meal provided by the municipality at the kindergarten. About a third of employees eat a warm lunch at a work canteen (Finnish institute of health and welfare, 2019), and often lunch is subsidised by the employer. Typically evening meals are consumed at home.

The free school meal system has taught Finns from early on that one of the main meals of the day is provided or at least made by someone else. This food system health benefits, as eating at school and work place canteen is associated with making healthier food choices (Raulio et al., 2010; Tilles-Tirkkonen et al., 2011). At the same time, this means that it is difficult to control the ingredients of one of the main meals of the day, making adhering to special diets more complicated.

2.8.2. FODMAP studies in Finland

A few studies done in Finland have utilised the low FODMAP diet or the knowledge of FODMAP content of specific foods. The main aims of these studies have been other than evaluating the the gut effects of the low FODMAP diet as such in people. These four studies are presented in Table 6.



Table 6. Studies performed in the Finnish population that have looked at the effect of LFD or individual FODMAPs on gut symptoms.

Publica tion	Research setting and the main aim of the study	Study participants (number)	Level of LFD or FODMAP content of food utilised and duration of the study	Amount of bread consumed	Amount of FODMAPs consumed/day	Main findings
Lappi et al., 2014	A randomized crossover study investigating the postprandial effects of wholegrain rye bread and a wheat bread enriched with bioprocessed rye bran.	Otherwise healthy people who reported having problems tolerating grains, especially rye bread. (n=21)	LFD used as a standardized diet during the 4-week run-in period prior to the study and during both 4-week study arm periods, but with the addition of different test breads. Use of LFD was 12 weeks in total.	Invervention bread intake was 6-10 slices (20-25 g each) depending on energy requirements.	Fructans intake ranged from 1,4 g/day (wheat bread containing bioprocessed rye bran) to 3,7 g/day (wholegrain rye bread).	The participants reported significantly (p < 0.01) better gastrointestinal quality of life during the 4-week run-in and during the test periods compared to their habitual diet during screening, even when consuming test breads that contained fructans.
Laatika inen et al., 2016	A randomised double-blind crossover study investigating the effect of low FODMAP ryebread vs. regular ryebread on gut symptoms.	IBS (n=87)	One week run-in period on usual diet + 4-week trial with either low- FODMAP rye bread or regular rye bread + 4-week trial with the other bread.	Rye bread intake was 7-8 slices per day depending on energy requirements.	Median fructan intake from low FODMAP rye bread 0.45 g/day (fructan + mannitol intake was 0,60 g/day) during weeks 2-4 (half a dose of bread was	There was no significant difference between the different groups with regards to IBS Symptom Severity Score (IBS-SSS) or quality of life. Individual symptoms, i.e.



Publica tion	Research setting and the main aim of the study	Study participants (number)	Level of LFD or FODMAP content of food utilised and duration of the study	Amount of bread consumed	Amount of FODMAPs consumed/day	Main findings
			Wash-out period ≥4 weeks between trials.		consumed during week 1). Median fructan intake from regular rye bread was 1,73 g/day (fructan + mannitol intake was 2,21 g/day).	flatulence (p = 0.04), abdominal pain (p = 0.049), cramps (p = 0.049) and rumbling (p = 0.001) were milder in subjects eating the low FODMAP bread than the regular one.
Laatika inen et al., 2017	A randomised, parallel, double- blind pilot study, looked at the effects of sourdough wheat bread to regular yeast-fermented wheat bread on gastrointestinal symptoms and analysed the effects of sourdough baking	IBS or subjective wheat-sensitivity (n=26). Sourdough group (n=13), yeast- fermented bread group (n=13).	One week run-in period, followed by a one week trial, in which the patients received either the sourdough wheat bread or yeast- fermented wheat bread. Gluten free diet was used as the standardised diet during the 2-week study duration.	Invervention bread intake was 6 slices per day.	Median fructan intake from sourdough bread 0,08 g/day. Median fructan intake from yeast- fermented bread 0,31 g/day.	There was no difference in gastrointestinal symptoms between the groups, nor was there a difference in low-grade inflammatory markers measured.



Publica tion	Research setting and the main aim of the study	Study participants (number)	Level of LFD or FODMAP content of food utilised and duration of	Amount of bread consumed	Amount of FODMAPs consumed/day	Main findings
Holmo	A maganastiva study	Colonatel concer	the study	_	The median	Detients who had
Holma et al., 2020	A prospective study looking at the associations of lactose and high FODMAP foods on gut symptoms after chemotherapy in colorectal cancer patients using food diaries.	Colorectal cancer patients (n=52)	FODMAP intake was measured by 4- day food diaries at baseline and during the third chemotherapy cycle. The FODMAP-rich food intake was categorised into three consumption groups (low, medium and high).	_	The median FODMAP-rich food intake was 5,5 portions/day at baseline and 5,4 portions/day during cancer treatments.	Patients who had high intake of lactose, especially together with high intake of other FODMAP foods were more likely to have diarrhea, the risk being over 4- fold compared with patients with low FODMAP intake. FODMAP content of the diet did not have a statistically significant association with other gastrointestinal symptoms.

The participants of Lappi et al. study used the LFD as a standardised diet and followed the diet total of 12 weeks, out of which 4 weeks were on the LFD only (Lappi et al., 2014). During the intervention arms, when they consumed either one of the test breads, the participants experienced slight to moderate flatulence, but this didn't decrease their quality of life. Over 90 % of participant listed none or slight gut symptoms during the test periods. In the discussion, the authors conclude that the improved gastrointestinal status seemed to be due to the low FODMAP diet utilised to standardise the diets of the participants, although the participants consumed fairly large amounts of bread, which was thought to be the culprit of their gut symptoms.

Both studies by Laatikainen et al. (2017, 2016) had a somewhat opposite study setting than Lappi et al., where the role of different types of breads on gut symptoms was investigated without changing the habitual diet of the participants. Neither one of these studies showed benefit of altering the FODMAP intake from bread only (Laatikainen et al., 2017, 2016). The sourdough fermentation did modify the FODMAP content, but not enough to alleviate IBS symptoms (Laatikainen et al., 2016). The second study looked at the effect of rye bread low in FODMAPs to gut symtoms and low-grade inflammatory markers, but no differences could be found between the low FODMAP rye bread and regular FODMAP rye bread arm (Laatikainen et al., 2017).

A recent study looked at the associations of lactose and high FODMAP foods on gut symptoms in patients with colorectal cancer (Holma et al., 2020). This study found that high intake of lactose increased the likelihood of diarrhea, especially if the intake of FODMAP-rich foods was high. As no data on FODMAP content of Finnish foods exist, the investigators evaluated FODMAP intake as portions from 4-day food diaries at baseline and during the third chemotherapy cycle. The authors concluded that there was no statistically significant difference in GI symptoms in patients who consumed FODMAP-rich foods above or below the median amount, even though FODMAP intake played a part in diarrhea aggrevation when in combination with lactose.

2.8.3. FODMAP intake in the Finnish diet

All described Finnish studies utilising the low FODMAP diet in some way, state that evaluation of FODMAPs from the typical Finnish diet is difficult, as there is no national database that would list detailed information on FODMAP content of produce. However, there is data from Sweden (Liljebo et al., 2020), where dietary habits are, to some extend, similar to Finland. Liljebo et al. (2020)

assessed in their study that in the Swedish population, the main sources of FODMAPs were rye and wheat products.

Australian FODMAP analysis can be used with regards to common grain, vegetables and fruit data (Biesiekierski et al., 2011; Muir et al., 2009; Varney et al., 2017), although, growing conditions, plant cultivar, climate, seasonal variation in growth temperature, ripeness and storage time and temperature are known to affect FODMAP content of produce (Huynh et al., 2008; Karppinen et al. 2003; Muir et al., 2009). In addition, cooking methods, such as pickling, activating seeds and nuts, sprouting, fermenting, and preparationg time alter the FODMAP content of food (Tuck et al., 2018). Some methods, such as pickling, reduced the FODMAP content greatly (87-97 %), where as other methods, such as sprouting reduced the FODMAP content, but not to the extend that the food could be classified as low FODMAP (Tuck et al., 2018). High, low and unknown FODMAP contents of food common to the Finnish cuisine are listed in Table 6.

Table 6. Estimated high, low and unknown sources of fermentable oligo-, di- and monosaccharides and polyols in the Finnish diet.

High FODMAP foods in the	Low FODMAP foods in the	Unknown FODMAP content
Finnish cuisine	Finnish cuisine	
Onion	Potato	Forest and garden berries
Garlic	Many root vegetables (carrot,	Fruit and berry juices
Beetroot	parsnip, celeriac, swede)	Gluten-free, wheat-starch
Apple	Common cabbage (when	products
Rye	consumed in moderation)	Spelt products
Barley	Oat	Forest mushrooms*
Wheat	Gluten-free products	
Xylitol-products	Low lactose and lactose-free	
* FODMAD	dairy products	

* FODMAP-content is assumed high based on data on cultivated mushrooms

Many gluten-free products are also low FODMAP, but not all (Whelan et al., 2011). One difference between Australian and European legistlation enables is the use of gluten-free wheat starch in the making of gluten-free bakery products. Australian baking industry is not using gluten-free wheat starch in their products, as they are more strict about the level of gluten traces in the food. No detectable gluten is allowed, neither is the use of oats or malted gluten-containing cereals or their products (https://www.coeliac.org.au/s/about-us). In the EU the threshold level for traces of gluten is 20 mg/kg (Regulation 828/2014). This also means that Australian gluten-free analysis data are mostly on products that differ from the ones used in the EU. As celiac disease is relatively common in in Finland, gluten-free wheat-starch products are widely available as breads, cakes and other bakery products. Little is known about the FODMAP content of these produce or their tolerability to people with gastrointestinal issues.

One study on the polyol content of Finnish berries exists from 1980, but due to the clear difference in order of magnitude and methodology, the data of this thesis and the 1980 study cannot be compared in a meaningful way (Mäkinen & Söderling, 1980). Based on the existing data, one cannot draw a comprehensive overview of the FODMAP content of berries. Only a few type of Australian berries have been analysed (Muir et al., 2009). Berries as a source of FODMAPs can

vary a lot, since over 65 year old Finns consume berries over 20 kg/person/year , whereas those under 25 years only consume 5 kg/person/year, average being 13 kg/person/year (Aalto, 2018).

Unique to Finland is the frequent consumption of xylitol products, most typically chewing gum or pastilles. Xylitol is also used in some cough and mouth-freshener drops and some vitamins. Xylitol products are known to be anticariogenic and are therefore recommended in Finland throughout life, starting from when children get their first teeth. The recommendated intake by the Finnish Dental Association of xylitol is five grams per day, which is equavalent to six xylitol chewing gum pieces (of which over 50 % of sweetener should be pure xylitol). These products are recommended to be eaten after a meal. Xylitol use is only an adjuvant dental care practise, as it does not replace teeth brushing of flossing. The laxative effects are also well-known, as this warning is written on packages. The laxatives effects are known to occur only after larger amounts, 20-30 g, are consumed (Oku & Nakamura, 2007). This is approximately the equivalent of half a box of xylitol pastilles. Xylitol is present is very small amounts in berries and vegetables (Oku & Nakamura, 2007), but most likely the main source in the Finnis diet are xylitol-sweetened products. It should be noted, that the FODMAP analyses have not taken into account the xylitol content of foods. The basic analysis measures sorbitol and mannitol only. Hence, foods that contain a lot of xylitol are not listed in the FODMAP content data.

2.8.4. IBS and FODMAPs in short

This literature review finds that IBS is a globally common condition, which causes a great economic burden on the health care system. Etiology of IBS is still unclear, but effective treatments have, nevertheless, been adopted ranging from dietary therapy to pharmacotherapy and psychotherapy. The low FODMAP diet has emerged as an efficient and evidence-based dietary therapy option. As it was developed in Australia, the question has been, whether it can be utilized in other cuisines. FODMAP content of Finnish foods has not been analysed systematically previously. The companies may have knowledge of the their products, but this information has not been used very much in marketing, excluding a few breads. Total intake of FODMAPs from the Finnish diet is not known and should be evaluated further to give a better understanding on the role of this specific features that may explain gut symptoms in the IBS population.

34



The overall aim of this research is to evaluate the FODMAP content of typical Finnish food products.

The specific aims of the study were :

To evaluate the FODMAP content of the products per 100 g.

To evaluate the FODMAP content of the products per typical portion size.

To assess, if the products pass the low FODMAP criteria.

4. MATERIALS AND METHODS

4.1. Sample collection

Typically the low FODMAP diet analysis starts from collecting products from the grocery shop systematically, after which products are pooled and mixed, and a sample for analysis is taken. In cases where the food needs to be prepared (e.g. soaking and cooking of legumes), this is done prior to taking the sample. This sample is then homogenized either by grinding by hand or using utensils suited for the purpose. Samples are freeze-dried, if they cannot be analysed straight away. There are some differences between how different food groups are sampled, which is shown in Figures 2 and 3 as flow charts.

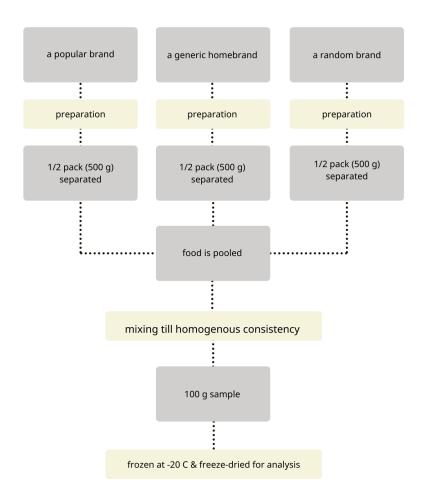


Figure 2. Grain and pulses product sampling procedure. Constructed on the basis of methods descriptions (Biesiekierski et al., 2011; Tuck et al., 2018; Varney et al. 2017).

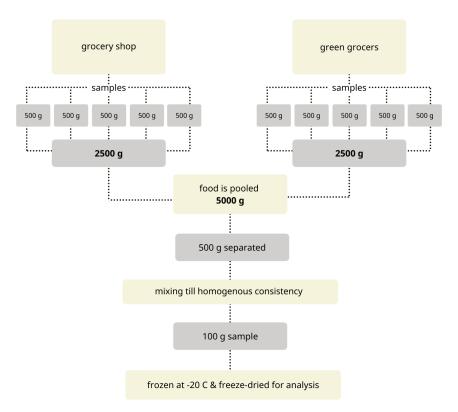


Figure 3. Vegetable, berry and fruit sampling procedure. Constructed on the basis of methods descriptions (Muir et al., 2009; Tuck et al., 2018; Varney et al. 2017).

In this case, it was impossible to collect samples according to this established and customary way. Firstly, the option of freeze-drying samples in Finland prior to taking them to Australia proved impossible, as facilities for this procedure were unable to assist in the endeavour. Secondly, due to student budget, taking in more food than was done, would have been too expensive. Most products were donated by the food companies and a few were purched from a regular grocery shop in Tampere, Finland. There was no support for the luggage cost.

At the time of preparation, in 2012, there were very little data on the FODMAP content of rye, gluten-free wheat-starch products and berries. Spelt was of interest as results from previous analysis (Biesiekierski et al., 2011) had shown that sourdought spelt bread is low in FODMAPs. There was, however, speculation on whether this is the case with spelt in other countries, as climate, soil and other factors are known to have an impact on the fructan content of grains (Huynh et al., 2008;

Karppinen et al. 2003; Muir et al., 2009). Oat was also of interest, as its nutrient and fibre content was known to be high, but FODMAP content was estimated to be low. Hundred percent oat bread had just made it's way to Finnish grocery shop shelves, so it was evident that it needed to be analysed for FODMAPs. Hence, samples from these categories were chosen to be analysed. The miscellaneous products came about mostly because of experience from clinical work. The patients with gut issues had trouble finding suitable snacks to carry easily with (müesli bars) and they too wanted to eat something sweet (sweets and biscuits).

Companies were approached by phone and email by the student. Samples that needed to be purchased were done so by the student. All packaging and labeling of products for customs was done by the the student. All preparations were done in collaboration with Monash University, and helpful negotions were held on which products to choose for analysis.

The products that were analysed are listed in table 7. The manufacturers (Vaasan, Fazer, Sunspelt, Birkkala, Biokia and Joswola) were asked to provide three packages preferably from different batches. They were able to do this in most parts.

Category	Туре	Product name	Package size	Number of packages
Berries	Lingonberry (Vaccinius vitis- idaea)	Biokia Lingonberry	100 g	1
		Joswolan Lingonberry	50 g	2
	Bilberry (Vaccinium myrtillus)	Biokia Bilberry	100 g	1
		Joswolan Bilberry	50 g	2
	Wild cranberry (<i>Vaccinium</i> oxycoccos)	Biokia Cranberry	100 g	1
		Joswolan Wild Cranberry	50 g	2
	Sea buckthorn (<i>Hippophae rhamnoides</i>)	Biokia Sea Buckthorn	100 g	1
	Blackcurrant (<i>Ribes nigrum</i>)	Joswolan Blackcurrant	50 g	2
Oat	Bread	Vaasan 100 % oat bread	400 g	3
Gluten- free,	Bread	Semper Trio three seed bread rolls	300 g	1
contains		Semper Minibaguetter	300 g	1

Table 7. Products selected for the FODMAP analysis.

Category	Туре	Product name	Package size	Number of packages
wheat starch				
Wheat	Bread	Vaasan Isopaahto, wheat toast	500 g	3
		Fazer Paahto Vehnä, white wheat toast	280 g	3
		Fazer Paahto Taysjyvä, wholemeal wheat toast	280 g	3
Spelt	Crisp bread	Sunspelt, organic, wholegrain crispbread	_*	3
		Birkkala, organic, wholegrain crackers	220 g	2
	Flour and flakes	Birkkala, organic, semi- course spelt flour	800 g	3
		Birkkala, organic, spelt flakes	600 g	3
	Pasta	Sunspelt wholegrain pasta	330 g	3
Rye	Crisp bread	Vaasan Koulunäkki crispbread	200 g	3
		Vaasan 100 % rye sourdough crackers	300 g	3
		Oululainen sourdough crackers	200 g	3
	Bread	Ruispalat, organic, 100 % rye	400 g	3
		Ruispala, original, contains wheat	330 g	3
		Oululainen Reissumies, fresh rye bread	235 g	3
		Oululainen Jälkiuunileipä, sourdough fresh bread	300 g	3
Snacks and sweets	Müesli bars	Jyväshyvä Paussi müesli 5 grains & chocolate	125 g	2
		Jyväshyvä Paussi müesli raspberry	108 g	2
	Biscuits	Jyväshyvä oat biscuits	175 g	2
	Sweets	Sunspelt organic spelt liquorice	80 g	_**

* Data missing. The product is no longer in production. ** Data missing. Written information could not be interpreted.

Australian border control is very particular about food stuff, so being able to bring in the food to the country was not certain at any point. All measures that could be done to ensure passing the border control were taken. Prior to entry to the country, thorough documentation of products was done and held at hand throughout the journey from Finland to Australia. The receiving institute, Monash University, prepared a reference letter stating that the purpose of bringing in the food was scientific,

which was also kept at hand. There were no issues at the customs bring the samples into the country.

No personal information was collected, hence there were no need to ethical approval for the data collection.

4.2. Sample preparation

Typically the procedure of acquiring a freeze-dried sample was explained in Sample collection section and shown as flow charts in figure 2 and 3. However, samples in pre-dried form, such as flour, or in a liquid form, such as dairy and plant-based milk products, are not freeze-dried (Tuck et al., 2018). Hence, there was no need to freeze-dry some of samples (e.g. flour, crispbread, berry powder. As mentioned previously, freeze-drying could not be done in Finland, hence, fresh products needed to be taken to Australia for the analysis.

Freeze-dried food stuff was prepared for HPLC and fructan assay analysis as described in Figure 4. The 100 g sample size is a normal size used by the Monash University for HPLC FODMAP analysis. Analysis was done in triple sets, ensuring accuracy. Double filtering is done to remove unwanted particles and noncarbohydrate substrates (Muir et al., 2009).

Pooling was done to the extend that was possible, i.e. there was several packages and bigger amounts available. For example, for the berry samples, only 100 g could be accuired and hence, this amount was used as the starting point.

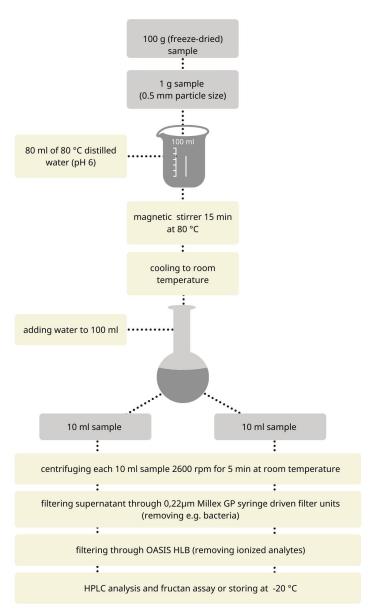


Figure 4. HPLC analysis methodology.

The actual analysis procedures were done by the qualified laboratory staff members. Here a detailed description of the methodology is presented.

4.2.1. Fructan assay

The analysis of sucrose, starch and fructans requires different methods (Muir et al., 2007). Total fructan is measured using an enzymatic hydrolysis method, namely Megazyme Fructan HK Assay kit (Megazyme International Ireland Ltd, Wicklow, Ireland; AOAC Method 999.03 and AACC

Method 32.32) (Varney et al., 2017). However, as this assay does not give the polymer lenght of fructans, but only the total fructan content, fructans are further enzymatically hydrolysed to release monosaccharides, glucose and fructose, that are then measured by HPLC (Muir et al., 2007).

4.2.2. <u>High-performance liquid chromatography (HPLC)</u>

HPLC technique is used to analyse different compounds in a mixture by separating and quantifying them. The FODMAP analysis utilises HPLC to measure fructose in excess of glucose, sorbitol, mannitol, lactose and raffinose and stachyose (two different type of galacto-oligosaccharides) (Varney et al., 2017). Also faster and less solvent-using ultra-high-performace liquid chromatography is used (Varney et al., 2017). HPLC is used in combination with evaporative light scattering detector (ELSD).

In HPLC a high-pressure pump is used to push the mobile phase (a solvent) together with the sample through the stationary phase (usually silica, alumina or cellulose), all of which are in a stainnless steel column (5-25 cm long, 4.5 mm in width) (Quick Biochemistry Basics, 2019). The stationary phase contains substrate that is small in particle size, giving therefore a larger surface area for the analysis. The column is attached to a detector, in this case the ELSD, which is connected to the computer. The different substrates, e.g. in this case, glucose, fructose, sorbitol, mannitol, lactose, raffinose and stachyose, are separated in the stationary phase, detected by the detector and drawn by the computer as peaks against retention time. Standard compounds, in this case, sugars, are used as they are needed to give meaning to the peaks on the graph. The concentration of a substrate is calculated by looking at the area under the curve.

4.2.3. Evaporative light scattering detector (ELSD)

The detector, ELSD, uses nebulasation, evaporation and scattering of light in substrate analysis (Agilent Techonologies, 2016). First the sample goes through nebulisation, which, with the help of an inert gas, forms fine and even droplet spray that is then heated in the evaporation chamber, so that volatile compounds are evaporated from the sample. The lowest possible temperature is used, in order to avoid sample degradation. A beam of light is then shone upon the non-volatile sample left after evaporation, and the light scattered is in proportion to the amount of sample that is present.

4.3. Sample analysis

The analysed FODMAP data are shown in mono- and disaccharides fructose, glucose (and calculated from this data, excess fructose) and lactose. Sugar polyols analysed are sorbitol and mannitol. The different galacto-oligosaccharides (GOS) are shown as raffinose and stachyose. Fructo-oligosaccharides (FOS) are shown as nystose and kestose, that according to email conversation with Dr. Jane Muir from Monash University, are of interest, as these FOS compouds are particularly readily fermentable, and hence, are likely to aggrevate symptoms. The amount of FOS is included in the fructan data, as fructo-oligosaccharides are types of fructans. FODMAP content data of the samples are reported as means (g per 100 g or per portion).

4.3.1. FODMAP content per portion of products

Portion sizes matter greatly in the low FODMAP diet contex. A given food may appeare as high FODMAP, if only the per 100 g data is evaluated. However, most foods are eaten in smaller amounts or on several sitting throughout the day, lessening the risk of typical gut symptoms related to IBS.

The weight of a given portion of food is taken from the manufacturer package information, but in the case of self-baked bread, cooked pasta and porridge flakes, Fineli composition database was used. Fineli is a national database maintained by the National Institute of Health and Welfare in Finland. Portion size was chosen as *medium* in all examples. In the case of flour and raw pasta, per portion data is not calculated, as these are not eaten as such. Raw and cooked pasta data are shown so that evaluations on the effect of cooking on FODMAP content can be discussed. All wheat bread samples were type toast bread, but were analysed as untoasted.

The manufacturer of berry powders name 12,5 grams as a portion and according to them this amount is equivalent to 1 deciliter of fresh berries. As it is not unlikely for Finns to consume more than this in a day, it was thought to be useful to also also calculate the FODMAP content of a 25 gram portion (equivalent to 2 deciliter of fresh berries).

Total FODMAP data are presented as graphs. The total FODMAP content is not shown in the results tables, as these calculations are more of relevance when looking at the FODMAP content per

portion and at one sitting. The total FODMAP figure is calculted by adding up excess fructose, lactose, sugar alcohols, GOS and fructans. As mentioned previously, FOS data is included in the fructan data, as fructo-oligosaccharides are types of fructans.

4.3.2. Analysing the data in relation to the FODMAP criteria

The analysed FODMAP data are also categorized as being below or above the cut-off values for low FODMAP criteria (Varney et al., 2017). These criteria are presented in detail in Table 4., but the relevant case-by-case criteria are also mentioned in the results table.

5. RESULTS

5.1. The FODMAP content of products per 100 grams

Different berries contained different FODMAP compounds. The results are presented in Table 8. Lingonberry and bilberry both contained only insignificant amounts of sorbitol per 100 grams, but no other FODMAP compounds. Cranberry (two brands) contained fructans (0.71-0.77 g/100 g) and insignificant amounts of polyols sorbitol and mannitol. Blackcurrant (one brand) contained plenty of sorbitol (3.49 g/100 g), whereas sea buckthorn (one brand) contained plenty of excess fructose (2.22 g/100 g). Sea buckthorn also contained insignificant amount of polyols sorbitol and mannitol.

The most common FODMAP compounds in grain products were fructans and some contain small amounts of excess fructose and GOS. Results are presented in Table 9 and the in results for rye products in Table 10. Oat bread (one brand) contained some excess fructose (0.14 g/100 g), an insignificant amount of mannitol, and some oligosaccharides (0.38 g/100 g). Fructan content was 0.19 g/100 g. Oligosaccharides are calculated combining the GOS and fructan values (see Table 9).

Gluten-free bread (two brands) contained some excess fructose (0.17-0.20 g/100 g) and oligosaccharides (0.32-0.41g/100 g). Fructan content was 0.28-0.34 g/100 g. Wheat bread (three brands) contained excess fructose (0.17-0.24 g/100 g), traces of sugar alcohols and oligosaccharides (0.84-1.37 g/100 g). Fructan content varied from 0.43 g/100 g to 1.13 g/100 g.

Spelt crispbread (two brands) contained insignificant amount of other FODMAPs, but fructan content was 1.03 g/100 g and 1.17 g/100 g. Spelt pasta (one brand), uncooked, contained mainly fructans (0.31 g/100 g). Cooking the pasta for 5 minutes lowered the fructan content slightly (0.28 g/100 g). Spelt flakes used for making spelt porridge contained very small amounts of other FODMAPs, except fructans (1.2 g/100 g). Sourdough spelt bread baked with only spelt flour contained some excess fructose (0.5 g/100 g) and fructans (1.51 g/100 g). It also contained insignificant amount of GOS. Sourdough spelt bread make with a combination of flour and flakes contained excess fructose (0.2 g/100 g) and fructans (0.19 g/100 g). It also contained traces of other polyols and GOS.

Rye crispbread (one brand) contained very little excess fructose and polyols. Oligosaccharide content was 3.22 g/100 g, of which fructans 2.99 g/100 g. Rye sourdough crackers (two brands) contained some excess fructose (0.12-0.27 g/100 g) and traces of polyols. Oligosaccharide content was 2.34-3.6, of which fructans 2.18-3.42 g/100 g. Rye fresh bread (four brands) contained excess fructose 0.16-0.38 g/100 g and some traces of mannitol. Total oligosaccharides content was 1.18-2.16 g/100 g. Fructan content varied from 1.04-1.93 g/100 g.

Snacks and sweets contained fructans and polyols. Some contained also small amounts of GOS. Data are presented in Table 11. Müesli bars (two brands) contained fructans (2.41-2.49 g/100 g. which was also the total oligosaccharide content. The raspberry müesli bar also contained polyols (1.63 g/100 g). Oat biscuits (one brand) contained 0.27 g/100 g fructans and little GOS, leading to total oligosaccharide content of 0.3 g/100 g. Spelt liquorice (one brand) contained plenty of sorbitol (2.71 g/100 g) and some mannitol (0.31 g/100 g). Oligosaccharide content was 0,25 g/100 g, of which fructans 0.14 g/100 g.

5.2. The FODMAP content of a typical portion

The detailed data for the FODMAP content of berries is shown in Table 8. Blackcurrants contained large amounts of sorbitol per 12.5 g and per 25 g portions (0.44 g/100 g and 0.88 g/100 g, respectively). A small portion (12,5 g) and a larger portion (25 g) of sea buckthorn contained excess fructose (0.28 g/100 g and 0.55 g/100 g, respectively), but only traces of other FODMAPs. Lingonberry and bilberry portions did not contain FODMAP compounds in significant amounts.

As with 100 grams of grain products, the grain portions contained fructans and some contained small amounts of excess fructose and GOS. Tables 9 and 10 show data for grain product portions, as does Figure 6. One slice of oat bread (one type) contained some excess fructose (0.04 g), and some oligosaccharides (0.12 g). Fructan content was 0.06 g. A piece or a roll of gluten-free bread (two types) contained some excess fructose (0.8-0.12 g) and oligosaccharides (0.16-0.24 g). Fructan content was 0.14-0.20 g. A slice of wheat bread (three types) contained excess fructose (0.04-0.05 g), traces of sugar alcohols and some oligosaccharides (0.21-0.32 g.). Fructan content varied from 0.11 g to 0.21 g.

One piece of spelt crispbread (2 types) contained 0.10-0.15 g of fructans, but no other FODMAPs. A medium portion (125 g) of cooked spelt pasta contained 0.49 g fructans, but no other FODMAPs. Typically 25 g of spelt flakes is used for a medium size portion of porridge. This amount contains 0.30 g of fructans, but no other FODMAPs. A 30 g slice of sourdough spelt bread baked with only spelt flour contained some excess fructose (0.2 g) and fructans (0.47 g). It also contained insignificant amount of GOS. A 30 g slice of sourdough spelt bread make with a combination of flour and flakes contained excess fructose (0.06 g) and fructans (0.10 g). It also contained traces of other polyols and GOS.

A slice of rye crispbread (one type) contained very little excess fructose and polyols. Oligosaccharide content was 0.52 g, of which fructans 0.48 g. Rye sourdough crackers are very thin. They weigh only 10 grams a piece. The two types analysed contained negligible amount of excess fructose (0.1-0.2 g). They contained 0.22-0.34 g of fructans a slice and 0.24-0.36 g of total oligosaccharides. A slice of rye fresh bread (four types) contained excess fructose 0.03-0.1 g. Total oligosaccharides content was 0.35-0.6 g. Fructan content varied from 0.31 g to 0.54 g.

Snacks and sweets contained fructans and polyols. Some contained also small amounts of GOS. Data are presented in Table 11. Müesli bars (two types) contained fructans 0.48-0.5 g. which was also the total oligosachharide content. The raspberry müesli bar also contained 0.32 g polyols. One oat biscuits (5 g) contained only traces of FODMAPs. A larger portion (3 biscuits) also contained very little FODMAPs, as the fructan content was only 0.4 g. A piece of spelt liquorice (4 g) contained 0.12 g polyols sorbitol and mannitol and traces of fructans. A whole bag (80 g) contained 2.42 g polyols sorbitol and mannitol and 0.11 g fructans.



5.3. Products meeting the low FODMAP criteria

Berries that fulfil the low FODMAP criteria are lingonberry, bilberry in all portions, and cranberry in both 12.5 g and 25 g portions. This is shown in Table 8 and in Figure 5. Content for wild cranberries is high only in large amounts, as shown in per 100 g data. The smallest portion (12.5 g) of sea buckthorns was low FODMAP according to the criteria. The berry is typically eaten in small amounts, as the it is very sour.

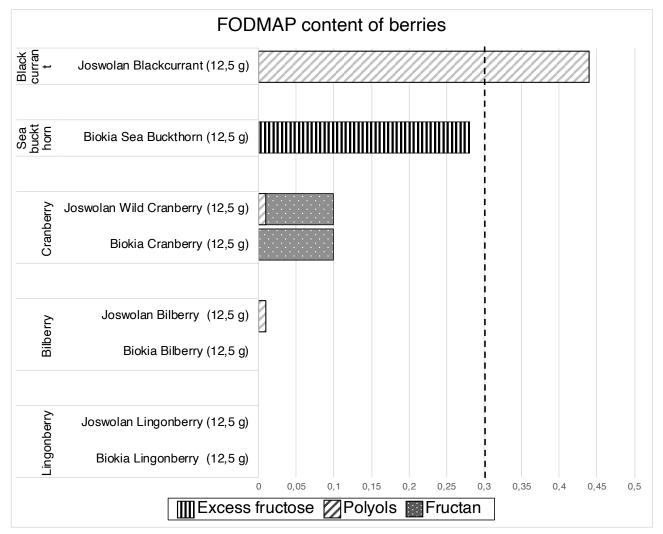


Figure 5. The FODMAP content of different Nordic berries calculated for a small portion of berries (12,5 g dry, 1 dl fresh). The cut-off value is set at 0,3 g per portion, as this is commonly used as a rough figure for the FODMAP threshold. Different patterns show different FODMAPs present.

Oat bread fullfilled the low FODMAP criteria best (Figure 6). One wheat toast (Vaasan Isopaahto vehnä) could be considered low FODMAP, when only one slice is eaten. The spelt crispbreads and one rye crispbread (Oululainen) were below the criteria threshold.

Spelt pasta was below the FODMAp criteria, but since a medium portion of spelt pasta is larger than 100 grams, the portion was well above the cut-off value. A portion of spelt porridge is typically made with 25 grams of flakes, which would make spelt porridge suitable for the low FODMAP diet, as it is just at the cut-off value of 0.3 g/portion (see Figure 6).

One of the self-baked spelt breads was below the low FODMAP criteria (flour + flakes), the other one was not (flour only). One of the gluten-free, wheat starch based products was below the cut-off value (Semper Minibaguetter) and the other one was above the cut-off value (Trio three seed bread rolls). All fresh rye breads were well above the criteria threshold, as were most rye crispbreads.



Figure 6. The FODMAP content of grain products. The cut-off value is set at 0,3 g per portion, as this is commonly used as a rough figure for the FODMAP threshold. Different patterns show different FODMAPs present. GOS = Galacto-oligosaccharides.

The cut-off value (0.5 g) was chosen as a snack is considered a small meal on its own. Below the FODMAP cut-off value were oat biscuits, which contained very little FODMAPs. Also a piece of

spelt liquorice was well below the cut-off value, but a small bag of liquorice contained plenty of FODMAPs, especially the polyol sorbitol (data not shown in Figure 7, but presented in Table 11).

The 5 grain & chocolate müesli bar was just below the cut-off value, where as the raspberry müesli bar contained much more FODMAPs, especially polyols sorbitol and mannitol (data not shown in Figure 7, but presented in Table 11).

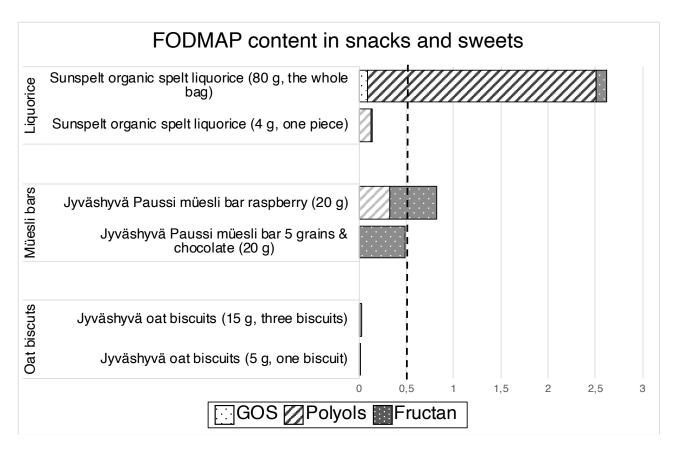


Figure 7. The FODMAP content of snacks and sweets. The cut-off value is set at 0.5 g, as this is commonly used as a rough figure for the FODMAP threshold for a meal at one sitting. Different patterns show different FODMAPs present. GOS = Galacto-oligosaccharides.



Table 8. Different FODMAP compounds measured by HPLC and enzymatic assay in different Nordic berries per 100 g and per two typical portions that berries are eaten in. Abbreviations: GOS = Galacto-oligosaccharides. FOS= fructo-oligosaccharides.

	Mono- and disaccharides		Sugar polyols GOS				FOS					
Food	Fructos e	Glucose	Excess fructose	Lactose	Sorbitol	Mannito l	Raffinos e	Stachyose	Nystose	Kestose	Total fructan	FODMAP rating*
Lingonberry (Vaccinius vitis-idaea)												
Biokia Lingonberry												
g per 100 g as eaten weight	7.18	9.11	0	0	.01	0	0	0	0	0	0	Low. Sorbitol < 0.2 g.
g per 12,5 g (1 dl fresh)	.9	1.14	0	0	0	0	0	0	0	0	0	Low.
g per 25 g (2 dl fresh)	1.8	2.28	0	0	0	0	0	0	0	0	0	Low.
Joswolan Lingonberry												
g per 100 g as eaten weight	7.15	10.76	0	0	.01	0	0	0	0	0	0	Low. Sorbitol < 0.2 g.
g per 12,5 g (1 dl fresh)	.89	1.35	0	0	0	0	0	0	0	0	0	Low.
g per 25 g (2 dl fresh)	1.79	2.69	0	0	0	0	0	0	0	0	0	Low.
Bilberry (<i>Vaccinium myrtillus</i>) Biokia Bilberry												
g per 100 g as eaten weight	4.81	8.62	0	0	0	.02	0	0	.03	.17	0	Low. Mannitol < 0.2 g. Oligosaccharides 0.2 g.
g per 12,5 g (1 dl fresh)	.6	1.08	0	0	0	0	0	0	0	.02	0	Low. **
g per 25 g (2 dl fresh)	1.2	2.16	0	0	0	0	0	0	.01	.04	0	Low. **
Joswolan Bilberry												
g per 100 g as eaten weight	4.46	8.49	0	0	.04	.01	0	0	0	0	0	Low. Total polyols < 0.4 g.
g per 12,5 g (1 dl fresh)	.56	1.06	0	0	.01	0	0	0	0	0	0	Low. Sorbitol < 0.2 g.
g per 25 g (2 dl fresh)	1.12	2.12	0	0	.01	0	0	0	0	0	0	Low. Sorbitol < 0.2 g.
Cranberry (Vaccinium oxycoccos)												



	Mono- and disaccharides			Sugar	polyols	G	OS	FO	8			
Food	Fructos e	Glucose	Excess fructose	Lactose	Sorbitol	Mannito l	Raffinos e	Stachyose	Nystose	Kestose	- Total fructan	FODMAP rating*
Biokia Cranberry												
g per 100 g as eaten weight	14.88	21.02	0	0	.04	.02	0	0	0	0	.77	High. Total polyols > 0.4 , oligosaccharides > 0.2 g.
g per 12,5 g (1 dl fresh)	1.86	2.63	0	0	0	0	0	0	0	0	.10	Low. Oligosaccharides < 0.2 g.
g per 25 g (2 dl fresh)	3.72	5.26	0	0	.01	.01	0	0	0	0	.19	Low. Oligosaccharides < 0.2 g. ***
Joswolan Wild Cranberry												
g per 100 g as eaten weight	13.48	19.72	0	0	.04	.03	0	0	0	0	.71	High. Total polyols > 0.4 g, oligosaccharides > 0.2 g.
g per 12,5 g (1 dl fresh)	1.69	2.47	0	0	.01	0	0	0	0	0	.09	Low. Sorbitol < 0.2 g, oligosaccharides < 0.2 g
g per 25 g (2 dl fresh)	3.37	4.93	0	0	.01	.01	0	0	0	0	.18	Low. Total polyols < 0.4 g, oligosaccharides < 0.2 g.
Blackcurrant (<i>Ribes nigrum</i>)												
Joswolan Blackcurrant												
g per 100 g as eaten weight	1.35	2.76	0	0	3.49	0	0	0	0	.01	0	High. Sorbitol > 0.2 g. **
g per 12,5 g (1 dl fresh)	.17	.35	0	0	.44	0	0	0	0	0	0	High. Sorbitol > 0.2 g.
g per 25 g (2 dl fresh)	.34	.69	0	0	.87	0	0	0	0	0	0	High. Sorbitol > 0.2 g.
Sea buckthorh (<i>Hippophae rhamnoides</i>) Biokia Sea buckthorn												
g per 100 g as eaten weight	3.13	.91	2.22	0	.01	.02	0	0	0	.03	0	High. Total polyols < 0.4 g, but excess fructose > 0.15 g.
g per 12,5 g (1 dl fresh)	.39	.11	.28	0	0	0	0	0	0	0	0	Low. Excess fructose < 0.4 g.
g per 25 g (2 dl fresh)	.78	.23	.55	0	0	.01	0	0	0	0	0	High. Mannitol < 0.2 g, but excess fructose > 0.15 g.

* FODMAP criteria presented in Varney et al. (2017) publication.** Insignificant amount of FOS.*** Insignificant amount of polyols. Abbreviations: GOS = Galacto-oligosaccharides. FOS= fructo-oligosaccharides.



Table 9. Different FODMAP compounds measured by HPLC and enzymatic assay in a selection of oat, gluten-free, wheat and spelt products a per 100 g and per portion.

	Mono- and disaccharides			Sugar	Sugar polyols GOS		SOS	FOS				
Food	Fructo se	Glucos e	Excess fructos e	Lactos e	Sorbito 1	Mannit ol	Raffin ose	Stachy ose	Nystos e	Kestos e	Total fruct an	FODMAP rating*
Oat bread												
Vaasan 100 % oat bread												
g per 100 g as eaten weight	.17	.03	.14	0	0	.01	.19	0	0	0	.19	High. Excess fructose < 0.15 g, mannitol < 0.2 g, but oligosaccharides > 0.3 g.
g per 30 g (one slice)	.05	.01	.04	0	0	0	.06	0	0	0	.06	Low. Excess fructose < 0.15 g. Oligosaccharides < 0.3 g.
Gluten-free, wheat starch bread												
Semper Trio three seed bread rolls												
g per 100 g as eaten weight	.67	.47	.20	0	0	0	.07	0	0	0	.34	High. Excess fructose > 0.15 g. Oligosaccharides > 0.3 g.
g per 60 g (one roll)	.40	.28	.12	0	0	0	.04	0	0	0	.20	Low. Excess fructose < 0.15 g. Oligosaccharides < 0.3 g.
Semper Minibaguetter												U
g per 100 g as eaten weight	.44	.27	.17	0	0	0	.04	0	0	0	.28	High. Excess fructose > 0.15 g. Oligosaccharides > 0.3 g.
g per 50 g(one piece)	.22	.14	.08	0	0	0	.02	0	0	0	.14	Low. Excess fructose < 0.15 g. Oligosaccharides < 0.3 g.
Wheat bread												

54



	Mono- and disaccharides		ides	Sugar	polyols	G	OS	FOS				
Food	Fructo se	Glucos e	Excess fructos e	Lactos e	Sorbito 1	Mannit ol	Raffin ose	Stachy ose	Nystos e	Kestos e	- Total fruct an	FODMAP rating*
Vaasan Isopaahto Vehnä, wheat toast												
g per 100 g as eaten weight	.48	.31	.17	0	.01	.01	.27	0	.13	0	.57	High. Excess fructose > 0.15 g. Total polyls 0.2 g. Oligosaccharides > 0.3 g.
g per 25 g (one slice)	.12	.08	.04	0	0	0	.07	0	.03	0	.14	Low. Excess fructose < 0.15 g. Oligosaccharides < 0.3 g.
Fazer Paahto Vehnä, white wheat toast												
g per 100 g as eaten weight	.48	.24	.24	0	0	0	.24	0	.06	0	1.13	High. Excess fructose > 0.15 g. Oligosaccharides > 0.3 g.
g per 19 g (one slice)	.09	.05	.04	0	0	0	.05	0	.01	0	.21	Low. Excess fructose < 0.15 g. Oligosaccharides < 0.3 g.
Fazer Paahto Täysjyvä, wholemeal wheat toast												c .
g per 100 g as eaten weight	.34	.14	.20	0	0	.01	.26	.33	.11	0	.43	High. Excess fructose > 0.15 g. Oligosaccharides > 0.3 g. **
g per 25 g (one slice)	.09	.04	.05	0	0	0	.07	.08	.03	0	.11	Low. Excess fructose < 0.15 g. Oligosaccharides < 0.3 g.
Spelt												
Sunspelt, organic, wholegrain crispbread												
g per 100 g as eaten weight	.09	.08	.01	0	0	0	0	0	0	0	1.03	High. Excess fructose < 0.15 g, but oligosaccharides > 0.3 g.



	Ν	Iono- and	disacchari	ides	Sugar	polyols	G	OS	F	OS		
Food	Fructo se	Glucos e	Excess fructos e	Lactos e	Sorbito 1	Mannit ol	Raffin ose	Stachy ose	Nystos e	Kestos e	Total fruct an	FODMAP rating*
g per 10 g (one piece)	.01	.01	0	0	0	0	0	0	0	0	.10	Low. Oligosaccharides < 0.3 g.
Birkkala, organic, wholegrain crackers												
g per 100 g as eaten weight	.09	.07	.02	0	0	0	0	.03	0	Data missing	1.17	High. Exess fructose < 0.15 g, but oligosaccharides > 0.3 g. Missing data does not alter outcome.
g per 12,5 g (one piece)	.01	.01	0	0	0	0	0	0	0	Data missing	.15	Low. Oligosaccharides < 0.3 g. Missing data does not alter outcome.
Sunspelt wholegrain												
pasta, cooked 5 min												
g per 100 g as eaten weight	.05	.08	0	0	0	0	0	0	0	0	.28	Low. Oligosaccharides < 0.3 g.
g per 125 g (one medium portion)	.09	.14	0	0	0	0	0	0	0	0	.49	High. Oligosaccharides > 0.3 g.
Sunspelt wholegrain pasta, raw												
g per 100 g	.06	.08	0	0	0	0	0	.02	0	0	.31	High. Oligosaccharides > 0.3 g. ***
Birkkala, organic, spelt flakes												c .
g per 100 g as eaten weight	.03	.02	.01	0	0	0	.01	0	0	.14	1.2	High. Excess fructose < 0.15 g, but oligosaccharides > 0.3 g.
g per 25 g used for a medium porridge portion Birkkala, organic, semi-	.01	.01	0	0	0	0	0	0	0	.04	.30	Low. Oligosaccharides 0.3 g.
course spelt flour												



	Ν	Iono- and	disacchari	ides	Sugar	polyols	G	OS	F	OS		
Food	Fructo se	Glucos e	Excess fructos e	Lactos e	Sorbito l	Mannit ol	Raffin ose	Stachy ose	Nystos e	Kestos e	Total fruct an	FODMAP rating*
g per 100 g	.12	.05	.07	0	0	0	.11	0	0	.27	1.51	High. Excess fructose < 0.15 g, but oligosaccharides > 0.3 g.
Sourdough spelt bread baked with Birkkala semi-course flour												
g per 100 g as eaten weight	.09	.04	.05	0	0	0	.05	0	0	.26	1.51	High. Excess fructose < 0.15 g, but oligosaccharides > 0.3 g.
g per 30 g (one medium slice)	.03	.01	.02	0	0	0	.02	0	0	.08	.45	High. Excess fructose > 0.15 g, oligosaccharides > 0.3 g.
Sourdough spelt bread baked with Birkkala semi-course flour + flakes												
g per 100 g as eaten weight	.25	.05	.20	0	0	.01	.14	0	0	0	.19	High. Mannitol < 0.2 g, but excess fructose > 0.15 g and oligosaccharides > 0.3 g.
g per 30 g (one medium slice)	.08	.02	.06	0	0	0	.04	0	0	0	.06	Low. Excess fructose < 0.15 g, oligosaccharides < 0.3 g.

* FODMAP criteria presented in Varney et al. (2017) publication. .** Insignificant amount of polyols. *** Insignificant amount of GOS. Abbreviations: GOS = Galacto-oligosaccharides. FOS= fructo-oligosaccharides.



Mono- and disaccharides FOS GOS **Sugar polyols** Food Glucos Excess Lactos Sorbit Manni Raffin Stachy Nystos Kestos Total FODMAP rating* Fructo e fructos e ol tol e fructa se ose ose e e n Vaasan Koulunäkki crispbread .07 .23 .28 High. Excess fructose < g per 100 g as eaten weight .31 .24 0 .02 0 0 0 2.99 0.15 g, sorbitol < 0.2 g, but oligosaccharides > 0.3 g. .01 .04 High. Excess fructose < .04 0 0 0 .04 0 0 g per 16 g (one slice) .05 .48 0.15 g, but oligosaccharides > 0.3 g. Vaasan 100 % rye sourdough crackers .01 .71 .64 g per 100 g as eaten weight .43 .16 .27 0 0 .18 0 3.42 High. Mannitol < 0.2 g, but excess fructose > 0.15 g and oligosaccharides > 0.3g High. Excess fructose < 0.2g per 10 g (one slice) .04 .02 .02 0 0 0 .02 0 .07 .06 .34 g, but oligosaccharides > 0.3 g **Oululainen sourdough** crackers .12 .71 g per 100 g as eaten weight .23 High. Excess fructose < .11 0 0 .02 .16 0 .18 2.18 0.15 g and mannitol < 0.2g, but oligosaccharides > 0.3 g. g per 10 g (one slice) .02 .01 .01 0 0 0 .02 0 .07 .02 .22 Low. Excess fructose < 0.15 g, mannitol < 0.2 and oligosaccharides < 0.3 g. Ruispalat, organic, 100 % rve g per 100 g as eaten weight .29 0 .01 0 0 .43 .14 0 .24 0 1.55 High. Mannitol < 0.2 g, but excess fructose > 0.15 g

Table 10. Different FODMAP compounds measured by HPLC and enzymatic assay in rye bread and crispbread a per 100 g and per portion.



	Mono- and disaccharides			Sugar polyols GOS		F	OS					
Food	Fructo se	Glucos e	Excess fructos e	Lactos e	Sorbit ol	Manni tol	Raffin ose	Stachy ose	Nystos e	Kestos e	Total fructa n	FODMAP rating*
												and oligosaccharides > 0.3 g
g per 28 g (one slice)	.12	.04	.08	0	0	0	.07	0	0	0	.43	High. Excess fructose < 0.15, but oligosaccharides > 0.3 g.
Ruispala, original, contains wheat												0
g per 100 g as eaten weight	.55	.17	.38	0	0	.01	.18	.05	.71	.24	1.93	High. Mannitol < 0.2 g, but excess fructose > 0.15 g and oligosaccharides > 0.3 g.
g per 28 g (one slice)	.15	.05	.10	0	0	0	.05	.01	.20	.07	.54	High. Excess fructose < 0.15 g, but oligosaccharides > 0.3 g.
Oululainen Reissumies, fresh rye bread												
g per 100 g as eaten weight	.24	.12	.16	0	0	0	.14	0	0	0	1.11	High. Excess fructose > 0.15 g and oligosaccharides > 0.3 g.
g per 30 g (one slice)	.07	.04	.03	0	0	0	.04	0	0	0	.33	High. Excess fructose < 0.15 g, but oligosaccharides > 0.3 g.
Oululainen Jälkiuunileipä, sourdough fresh bread												
g per 100 g as eaten weight	.31	.09	.22	0	0	0	.14	0	0	0	1.04	High. Excess fructose > 0.15 g and oligosaccharides > 0.3 g.
g per 30 g (one slice)	.09	.03	.06	0	0	0	.04	0	0	0	.31	High. Excess fructose < 0.15 g and oligosaccharides > 0.3 g.

* FODMAP criteria presented in Varney et al. (2017) publication. Abbreviations: GOS = Galacto-oligosaccharides. FOS= fructo-oligosaccharides.



Table 11. Different FODMAP compounds measured by HPLC and enzymatic assay in a selection of snacks and sweets per 100 g and per portion.

Fructo se	Glucos e	Excess fructos e	Lactos e	Sorbit ol	Manni tol	Raffin ose	Stachy ose	Nystos e	Kestos e	Total fructa n	6
5.26	7.03	0	0	0	0	0	0	0	0	2.41	High. Oligosaccharides > 0.3 g.
1.05	1.41	0	0	0	0	0	0	0	0	0.48	High. Oligosaccharides > 0.3 g.
5.21	7.39	0	0	.91	.72	0	0	.19	0	2.49	High. Total polyols > 0.4 g and oligosaccharides > 0.3 g.
1.04	1.48	0	0	.18	.14	0	0	.04	0	.50	High FODMAP. Total polyols < 0.4 g, but oligosaccharides > 0.3 g.
											0 0
1.07	1.35	0	0	0	0	.03	0	0	0	.27	Low. Oligosaccharides 0.3 g.
.05	.07	0	0	0	0	0	0	0	0	.01	Low. Oligosaccharides < 0.3 g.
.16	.20	0	0	0	0	0	0	0	0	.04	Low. Oligosaccharides < 0.3 g.
	se 5.26 1.05 5.21 1.04 1.07 .05	se e 5.26 7.03 1.05 1.41 5.21 7.39 1.04 1.48 1.07 1.35 .05 .07	se e fructos e 5.26 7.03 0 5.26 7.03 0 1.05 1.41 0 5.21 7.39 0 1.04 1.48 0 1.07 1.35 0 .05 .07 0	se e fructos e 5.26 7.03 0 0 1.05 1.41 0 0 5.21 7.39 0 0 1.04 1.48 0 0 1.07 1.35 0 0 .05 .07 0 0	seefructoseol e e e ol 5.26 7.03 0 0 0 1.05 1.41 0 0 0 5.21 7.39 0 0 $.91$ 1.04 1.48 0 0 $.18$ 1.07 1.35 0 0 0 05 $.07$ 0 0 0	seefructos e eoltol5.267.030001.051.410005.217.3900.911.041.4800.181.071.35000.05.07000	se e fructos e ol tol ose 5.26 7.03 0 0 0 0 0 1.05 1.41 0 0 0 0 0 5.21 7.39 0 0 .91 .72 0 1.04 1.48 0 0 .18 .14 0 1.07 1.35 0 0 0 0 .03 .05 .07 0 0 0 0 0 .03	seefructoseoltoloseoseeeoltoloseoseose5.267.03000001.051.41000005.217.3900.91.7201.041.4800.18.14001.071.350000.030.05.070000000	seefructoseoltoloseose $osee^{-1}5.267.0300000001.051.410000005.217.3900.91.7200.191.041.4800.18.1400.041.071.350000000.05.070000000$	seefructos e eoltoloseose e^{-1} <th< td=""><td>se e fructos e ol tol ose ose e fructa n 5.26 7.03 0 0 0 0 0 0 0 2.41 1.05 1.41 0 0 0 0 0 0 0 0.48 5.21 7.39 0 0 .91 .72 0 0 .19 0 2.49 1.04 1.48 0 0 .18 .14 0 0 .50 .50 1.07 1.35 0 0 0 .03 0 0 .27 .05 .07 0 0 0 .03 0 0 .27</td></th<>	se e fructos e ol tol ose ose e fructa n 5.26 7.03 0 0 0 0 0 0 0 2.41 1.05 1.41 0 0 0 0 0 0 0 0.48 5.21 7.39 0 0 .91 .72 0 0 .19 0 2.49 1.04 1.48 0 0 .18 .14 0 0 .50 .50 1.07 1.35 0 0 0 .03 0 0 .27 .05 .07 0 0 0 .03 0 0 .27

liquorice



	Mono- and disaccharides			des	Sugar	polyols	s GOS FOS					
Food	Fructo se	Glucos e	Excess fructos e	Lactos e	Sorbit ol	Manni tol	Raffin ose	Stachy ose	Nystos e	Kestos e	Total fructa n	FODMAP rating*
g per 100 g as eaten weight	.17	.37	0	0	2.71	.31	0	.11	0	0	.14	High. Oligosaccharides < 0.3 g, but total polyols > 0.4 g.
g per 4 g (one liquorice)	.01	.01	0	0	.11	.01	0	0	0	0	0,01	Low. Total polyols < 0.4 g and oligosaccharides < 0.2 g.
g per 80 g (the whole bag)	.14	.30	0	0	2.17	.25	0	.09	0	0	.11	High. Oligosaccharides < 0.2 g, but total polyols > 0.4 g.

* FODMAP criteria presented in Varney et al. (2017) publication. Abbreviations: GOS = Galacto-oligosaccharides. FOS= fructo-oligosaccharides.



6. **DISCUSSION**

6.1. Main findings

The FODMAP analysis of typical Finnish products provided information on the content of FODMAPs per 100 grams. This data were used to further calculate the FODMAP content of products per typical portion size. It was then evaluated whether the products passed the low FODMAP criteria for both foods per 100 g and in the case of a typical portion size of a given food.

Products such as lingonberry, bilberry and oat bread and biscuits proved out to contain very little FODMAP compounds, especially per portion, and hence, these could be safely included in the low FODMAP diet. On the other hand, some products, especially rye bread and crispbreads all contained plenty of FODMAPs, especially fructans.

6.2. Specific finding by category

6.2.1. Berries

Lingonberry (*Vaccinium vitis-idaea*) and bilberry (*Vaccinium myrtillus*) were both low FODMAP is all portions (per 100 g, per 12,5 g portion, and per 25 g portion). According to the producers package information, 12,5 g portion is equivalent to 1 dl of fresh berries and 25 g then being equivalent to 2 dl of fresh berries. The Finnish national database Fineli estimates that 1 dl of fresh berries is 60 g. This is an interesting finding as previously analysed cultivated blueberries (*Vaccinium corymbosum*), are high in FODMAPs according to the Monash University low FODMAP diet smartphone application. Only a small portion of 40 grams is listed as low FODMAP. There were no previous FODMAP data on lingonberries.

Blackcurrant (*Ribes nigrum*) is a typical garden berry in the Nordic countries, but also a popular berry all around the world, especially as a juice or jam ingredient. Hence, this unpublished preliminary data should be of interest to many. Blackcurrant was high in sorbitol in all portions, but there was either none or just traces of other FODMAPs. Therefore, only people who are sensitive to sorbitol need to avoid blackcurrant, if they wish to avoid GI symptoms. There are other popularly

grown *Ribes* family garden berries, namely redcurrant and white currants, that should also be investigated in the future.

Sea buckthorn (*Hippophae rhamnoides*) was analysed to contain plenty of excess fructose, whereas none of the other berries contained excess fructose. There were either none or only trace amounts of other FODMAPs in sea buckthorn. This means that only people whose small intestine does not absorb fructose efficiently, may be intolerant to sea buckthorns. However, it should also be noted that normally only large amounts of fructose are able to trigger GI symptoms (Barrett et al., 2010).

The berry data from this study are unique and interesting for people involved in counselling IBS patients, but also to the food industry. This study acts as an incentive to study berries further and according to the systematic sampling protocol.

6.2.2. Grains

Grain FODMAP content, mainly fructans, has been previously published (Biesiekierski et al., 2011; Karppinen et al., 2003; Whelan et al., 2011), making it possible to compare data from this work to previous findings. However, FODMAP content of oat bread has previously been unpublished. Oat bread proved out to pass the low FODMAP criteria (see Figure 6). As the sampling was not done in the hoped manner, comparing these findings to previous data can provide an estimation of data reliability.

As in all previous analysis, the highest fructan content was found in rye products (Biesiekierski et al., 2011; Karppinen et al., 2003; Whelan et al., 2011). The fructan content of fresh rye bread in this study varied between 1.04-1.93 g/100 g. This is similar to the Australian findings, 1.05-1.42 g/100 g (Biesiekierski et al., 2011), and the UK findings, 1.94 g/100 g (Whelan et al., 2011). The previous data from Finland by Karppinen et al. provided higher content that of 2.1-2.8 g/100 g (Karppinen et al., 2003).

Variation in fructan content of grains can be due to climate and seasonal variation (Huynh et al., 2008), or due to baking methods, which can influence the FODMAP content too, as yeast and sourdough leavened bread may have different FODMAP content (Loponen et al., 2018). Even

toasting of bread can alter the fructan content of a slice slightly (Whelan et al., 2011). This is though to be due to thermal degradation (Whelan et al., 2011).

It is not unsuprising that drying bread increases its fructan content per 100 grams. This was verified in this study, as the rye crispbread and crackers, both of which are very commonly consumed in Finland, were both high in fructans (2.18-3.42 g/100 g). These findings are consistent with previous Finnish data (2.2-2.6 g/100 g; Karppinen et al., 2003), but being less than Australian data (4.6 g/100 g; Biesiekierski et al., 2011). The difference could possible be explained by baking methods, as Finnish crispbread and rye crackers are typically baked using the sourdough method, which can break down some of the FODMAP compouds during leavening (Loponen et al., 2018). The companies, whose products were analysed for the Biesiekierski et al. (2011) study (Ryvita, Arnott's), confirmend through email communication that neither one of the rye crispbreads use the sourdough method.

The Finnish spelt FODMAP content was at the time of sample collection of interest, as previous measurements had shown that sourdough spelt bread could pass the low FODMAP criteria. In fact, that is what also happened in this study, although the findings were not consistent. The sourdough spelt bread that was baked with spelt flour and flakes contained dramatically less fructans (0.19 g/100 g) than the sourdough flour-only spelt bread (1.51 g/100 g), although same flour and baking methods were used. This finding remains a mystery, although Biesiekierski et al. have found similar findings in Australia from regular non-sourdough spelt bread (0.20 g/100 g). Perhaps, more interest should be directed in understanding the differences of dough composition (flour, flakes, or a combination) and also the effect size baking methods can have. The composition and type of bacteria in sourdough culture should be studied in depth as has been done in the case of rye in an effort to find ways to lower the FODMAP content of bread (Loponen et al., 2018).

In addition to the berry data, spelt pasta data were, at the time of analysis, unique. There was little difference between the fructan content of the raw pasta (0.31 g/100 g) and the cooked pasta (0.28 g/100 g). Fructans are water-soluble, but since the cooking time for spelt pasta is only 5 minutes, cooking process was irrelevant to the fructan content. A small portion of spelt pasta would pass for the low FODMAP criteria, but a medium size portion was above the cutoff value (0,3 g/portion), being 0.49 g/100 g. However, if spelt pasta is the only major FODMAP source of a meal, this portion could pass the cutoff value of a whole meal (0.5 g/100 g; Varney et al., 2017).

Wheat bread fructan content varied from 0.43 to 1.13 g/100 g. In the Australia data fructan content were 0.68-0.69 g/100 g (Biesiekierski et al., 2011). Whelan et al. analysed several different white breads, many of which contained soy flour (Whelan et al., 2011), which is an untypical ingredient in Finnish breads and could, in theory, influence the FODMAP content of bread, as soy products is known to be high in FODMAPs (Tuck et al., 2018). The fructan content of white baker's toast, which did not contain soy flour, was 1.02 g/100 g, being similar to the highest fructan content of this study.

If only one slice of bread is eaten, all study wheat breads were below the low FODMAP cutoff value, emphasising yet again that portion sizes matter in the context of the low FODMAP diet.

Of the two gluten-free, wheat starch products analysed, one product was below the FODMAP cutoff value and the other just above it (0.28 and 0.34 g/100 g, respectively). In the study by Whelan et al. two gluten-free wheat starch products were analysed, with varying results (Whelan et al., 2011). One sample contained 0.36 g/100 g and the other 1.15 g/100 g, which could be explained by other ingredients and the baking method.

6.2.3. Snacks and sweets

Some data exists also on snacks, such as müesli bars and biscuits (Biesiekierski et al., 2011), making it possible to see, whether these findings are similar. In the Australian FODMAP analysis, müesli bars with fruit contained 2.53 g/100 g fructans, which is similar to the data in this study, were one contained 2.41 and the other 2.49 g/100 g fructans. The raspberry müesli bar contained also polyols. Both were considered above the 0.3 g/portion cut-off value for grains, but as these products are normally consumed as a snack on their own, the cut-off value was during data presentation was set to 0.5 g/portion. If eaten alone, both bars are below or exactly at the cut-off point.

Oat biscuits are typical biscuits served with coffee, tea or with juice for children. The tested oat biscuits were below the low FODMAP criteria cut-off value even at 100 grams, equivalent to 20 biscuits, as these biscuits tend to be small. In the light of these preliminary results, these biscuits are therefore, a gut-friendly option for people sensitive to FODMAP compounds.

Spelt liquirice was a curiosity product provided by the company SunSpelt that also donated some of the spelt products. Liquirice as such is indeed a popular sweet in Finland, but normally wheat is used in its making. Spelt liquirice proved out to contain plenty of sorbitol. The origin of it is a bit of a mystery as neither one of the sweetening ingredients, the coconut palm sugar nor the sugarbeet syrup, should contain sorbitol according to Monash University low FODMAP diet smartphone application. Neither is sorbitol present in spelt flour nor flakes, as shown in this study at by Australian group (Biesiekierski et al., 2011). There is also the possibility that an error has occurred in the analysis process.

6.3. Weaknesses of the study

As mentioned earlier, due to the lack of adequate sampling process, these presented findings represent only the preliminary FODMAP data of given products, which can be regarded as a weakness of the study. Generalisations on the FODMAP content of given type of foods should be done with caution.

Sample information could have been handled better, as there was some confusion on the package amounts and certain products. At one point, the files for these notes were missing. Data was recovered, but in the future data should be handled with more care.

Results were interpretated and presented several years after the analysis, which is certainly another weakness, although, several products analysed are still in production. Had the results been interpreted earlier, it could have been used as an incentive to investigate these products special to the Nordic countries earlier on.

6.4. Strengths of the study

The study provided data that verifies earlier FODMAP content analysis and it also provided information that is completely new, and hence, of interest to the field of GI and food development research. This study also further elucidates regional specialities that need to be taken into consideration when using the LFD approach. Having had the analysis done at the institute that is specialised in FODMAP analysis could also be considered a strength.



6.5. What can be learned

This study taught about the methodology of FODMAP analysis in depth. It also emphasises the need to evaluate cultural and regional varieties of produce in order for the low FODMAP diet to be utilized more effective in the management of gastrointestinal symptoms of patients such as people with IBS. The results also show that portion sizes matter. There is no need to strictly exclude, for example rye crisps or sea buckthorn, as these foods can be enjoyed in small amounts per sitting.

It should also be noted that the FODMAP cut-off values are highly arbitrary and based on clinical experience (Varney et al., 2017). As the individual threshold for FODMAP tolerance varies, the somewhat strict cut-off values raise the question whether they in fact lead patients to exclude foods too easily.

On a personal level, the work taught especially scientific writing. The delay in sample processing can be regarded as a weakness, but it does have some benefits. Many more publications have been published since sample collection year of 2012, having made it possible to discuss both IBS research and FODMAP research in a more comprehensive way.

6.6. Future perspective

In the future, it would be interesting to systematically sample commonly used rye, spelt, wheat, gluten-free and berry products, but also some old (xylitol) and some new (vegan protein alternatives) food innovations and wild produce that are commonly consumed.

The Finnish market has seen a rise in vegan and vegetarian protein products that are an alternative to traditional meat-based products. Typically, protein-rich foods are not on top of the high FODMAP list, but as these novel products contain both grains and pulses (e.g., fava beans), the FODMAP content may be of concern for people with gut issues. Had these products existed in year 2012, they would have been most certainly been included in the analysis. There is no official information open to the general public on the possible FODMAP content of these products.

It should be noted that xylitol chewing gum was taken to Australia with the purpose of conducting a small-scale comparative study looking at whether sorbitol-sweetened and xylitol-sweetened chewing gum cause gut symptoms and to what extend. The anticariogenic xylitol products have been little researched or even used and marketed, outside Finland and Japan. Indeed, several clarifications were requested by the Monash University ethics committee, possibly because they were unfamiliar with xylitol as a sweetener. Unfortunately, the ethics approval for this study came already after the student had returned to Finland.

Xylitol is known to have prebiotic properties in vitro and in animal models (Salli et al., 2019) unlike artificial sweeteners that are known to be harmful to gut microbiota (Rinninella et al., 2019), xylitol could be investigated further as a tooth- and gut-friendly sweetener. As a polyol it could have negative effects too (Oku & Nakamura, 2007), but the threshold and likelihood of symptom aggravation should be investigated further.

Wild produce, berries, mushrooms, and herbs may contribute to some individuals' FODMAP intake greatly, but this is only speculation, as actual data was missing. For clinical patient consultations, evaluating the FODMAP content of these foods would be useful. Berries and mushrooms are known to contain prebiotic compounds, as they are high in different types of fibre and polyfenols, and could therefore, contribute to a a gut-friendly Nordic diet, even with less FODMAPs as in the case of oat, lingonberry and bilberry.

Celiac disease is common in Finland, as the estimated prevalence is 2 %, which is why the food industry is well-accustomed in producing gluten-free foods for this consumer group. Excluding gluten-containing rye, wheat and barley from the diet, is thought to lead to a reduction in FODMAP intake, but this cannot be said of all gluten-free products (Whelan et al., 2011). A systematic analysis of key gluten-free products from various grain product groups, i.e. sweet and savoury bakery goods, porridges, pastas and breakfast cereals, would be beneficial, as it is possible for a patient to have celiac disease (in remission) and functional gut symptoms concomitantly.

6.7. Future of FODMAPs

The low FODMAP diet has been shown to be effective in treating the IBS population in many countries. The most restrictive phase only lasts for some weeks and it has been shown that most

patients can reintroduce foods back into their diet (Harvie et al., 2017; Maagard et al. 2016; O'Keeffe et al, 2018).

The diet may seem laboursome for an outsider, but it should be noted that the diet is accepted by the patients and they feel it increases their quality of life, in addition to also treating the physical gut symptoms (Harvie et al., 2017; O'Keeffe et al., 2018). The fact that dietary counselling is not always given by qualified dietitians, may lead to misuse of the diet and poor patient satisfaction sometimes experiences in the clinical setting (Trott et al., 2019). The recommended three-phase procedure of elimination, reintroduction and personalisation (Whelan et al., 2018) eventually leads to and individualised "adapted FODMAP diet" (O'Keeffe et al., 2018). It should be also emphasised that the LFD is a voluntary diet. No patient should ever be forced to follow the diet, and they should be informed on its pros and cons.

The low FODMAP diet is not a treatment to IBS, as it is merely a way to manage symptoms. Twothirds who try it, benefit, the rest need other treatments to manage their IBS symtoms. Possible confounders that influence the diet efficacy could be e.g. impaired gut-brain axis, or other malabsorption conditons, such as sucrase-isomaltase deficiency or intolerances, like wheat sensitivity. Efforts to identify diet responders are being made. One promising testing with strong accuracy is measuring of volative organic compouds from feaces (Rossi et al., 2018). Aggressively marketed gut microbiota profiling has been suggested as means to individualize diets further, but according to a recent review, the inconsistent evidence from studies, do not support their use in IBS (Biesiekierski et al., 2019).

One answer to dealing with gut symptoms inducing FODMAPs may be bioprocessing of food. At the moment it is possible to alleviate the negative effects of GOS by taking an enzymatic supplement (Tuck et al., 2018a) or using a lactase enzyme when eating lactose containing foods. This strategy relies on the purchase of enzymes and carrying them with oneself, if eating out. These enzymes can be costly. Nyyssölä et al. (2020) suggests that the enzymatic process could take place already at the manufacturing stage (Nyyssölä et al., 2020). This could be also more effective, as reaction conditions (pH, incubation time) can be more altered in at a manufacturing site. Bioprocessing is certainly an option for the food industry, but as people are encouraged to consume a highly plant-based and unprocessed diet, this enzymatic application is only helpful for some foods.

The major question regarding the LFD has been its long-term effects especially with regards to the gut microbiota. More information should be gathered on the reintroduction phase of the diet. It should be investigated whether there are ways to inhibit the negative effects on gut microbiota with for example diet, probiotics or prebiotics. Nutrients other than fibre, such as antioxidants, are known to stimulate the growth of micro-organisms in the gut. There is already evidence that taking a probiotic is beneficial in curbing the decline of bifidobacterial during the LFD elimination phase (Staudacher et al., 2017).

7. CONCLUSIONS

FODMAP analysis has been done on a vast array of products from several countries and continents. These preliminary finding from Finnish products show that there are still food groups, such as berries, that require further analysis. More accurate data would make it easier to apply the LFD in perhaps new regions, and with better efficacy.

Based on the results of this study, people on the low FODMAP diet can add lingonberry, bilberry and some slices of oat bread, spelt porridge and biscuits to their diet. Some foods, like sea buckthorn and wild cranberries, can also be included in the diet in small amounts. There are not many spelt products or producers on the market in Finland, but spelt bread baked with the sourdough method could be a nice addition to the selection of cereal products suitable for people with a sensitive gut, as these products could be lower in FODMAP compounds.

The iconic Finnish rye bread is popular, but due to its fructan content, can cause gut symptoms to many. It is a typical complaint in Finland that rye bread upsets one's stomach, especially if eaten in large amounts. This is where the trick often lies: in the portion sizes. These preliminary finding show that even a rye crispbread could pass the low FODMAP criteria, if eaten in small amounts. People on the LFD can savour the taste of rye, when they just limit the amounts.

Motivated by these results, the student plans to analyse at least the berry data futher, as there is no comprehensive literature on the topic, as was discussed earlier in this publication. Adequately collected samples could be analysed in the same manner as was done in the previous FODMAP content studies, and indeed, in this study. In the dietetic practise, the suitability of wild mushrooms is a annual topic brought about by the autumn mushroom season. Hence, collecting and analysing wild mushroom data would be helpful for the purpose of dietary counselling and more comprehensive FODMAP databases.

8. ACKNOWLEDGEMENTS

I would sincerely like to thank the Monash University staff and especially associate professor Dr. Jane Muir at the Department of Gastroenterology with all the analysis work and guidance with the data. My visit to Monash University enriched my life both professional and personally, as I made many close friends and colleagues in that time.

A very special thanks to my Master's thesis supervisor, Tarja Kinnunen, for her patience and excellent instructions that helped me turn an Excel document into a comprehensive Master's thesis. I've learned a lot from you.

Thank you for the companies for your sample donations.



9. REFERENCES

Aalto, U. K. (2018). Elintarvikkeiden kulutus kotitalouksissa vuonna 2016 ja muutokset vuosista 2012, 2006 ja 1998. (Faculty of Social Sciences - Publications; No. 2018:80). Helsinki: Helsingin yliopisto, Kuluttajatutkimuskeskus. (In Finnish.)

Agilent Technologies. (2016, February 19). *True Universal Detection* [Video]. YouTube. <u>https://www.youtube.com/watch?v=bLgl_TiPv0A</u>

Alfaro-Cruz, L., Kaul, I., Zhang, Y., Shulman, R. J., & Chumpitazi, B.P. (2019). Assessment of Quality and Readability of Internet Dietary Information on Irritable Bowel Syndrome. *Clinical Gastroenterology and Hepatology*, 17(3):566-567. <u>http://doi.org/10.1016/j.cgh.2018.05.018</u>

Arkkila, P. (2015). Protonipumpun estäjien pitkäaikaisen käytön haitat. *Suomen Lääkärilehti*, 70(18):1235-1240 (In Finnish.)

Balemans, D., Aguilera-Lizarraga, J., Florens, M. V., Jain, P., Denadai-Souza, A., Viola, M. F., Alpizar, Y. A., Van Der Merwe, S., Vanden Berghe, P., Talavera, K., Vanner, S., Wouters, M. M., & Boeckxstaens, G.E. (2019). Histamine-mediated potentiation of transient receptor potential (TRP) ankyrin 1 and TRP vanilloid 4 signaling in submucosal neurons in patients with irritable bowel syndrome. *The American Journal of Physiology: Gastrointestinal and Liver Physiology*, 316(3):G338-G349. http://doi.org/10.1152/ajpgi.00116.2018

Ballou, S., & Keefer, L. (2017). Psychological Interventions for Irritable Bowel Syndrome and Inflammatory Bowel Diseases. *Clinical and Translational Gastroenterology*, 8(1): e214. http://doi.org/10.1038/ctg.2016.69

Barbara, G., Cremon, C., De Giorgio, R., Dothel, G., Zecchi, L., Bellacosa, L., Carini, G., Stanghellini, V., & Corinaldesi, R. (2011). Mechanisms underlying visceral hypersensitivity in irritable bowel syndrome. *Current Gastroenterology Reports*, 13(4):308-15. <u>http://doi.org/10.1007/s11894-011-0195-7</u>

Barrett, J. S., Gearry, R. B., Muir, J. G., Irving, P. M., Rose, R., Rosella, O., Haines, M. L., Shepherd, S. J., & Gibson, P. R. (2010). Dietary poorly absorbed, short-chain carbohydrates increase delivery of water and fermentable substrates to the proximal colon. *Alimentary Pharmacology & Therapeutics*, 31(8):874-82. <u>http://doi.org/10.1111/j.1365-2036.2010.04237.x</u>

Bennet, S. M. P., Böhn, L., Störsrud, S., Liljebo, T., Collin, L., Lindfors, P., Törnblom, H., Öhman, L., & Simrén, M. (2018). Multivariate modelling of faecal bacterial profiles of patients with IBS predicts responsiveness to a diet low in FODMAPs. *Gut*, 67(5):872-881. http://doi.org/10.1136/gutjnl-2016-313128

Bernard, Kristine. (2018, January 5). The Top Coffee Consuming Countries. Retrieved from https://www.worldatlas.com/articles/top-10-coffee-consuming-nations.html

Beyder, A., Mazzone, A., Strege, P. R., Tester, D. J., Saito, Y. A., Bernard, C. E., Enders, F. T., Ek, W. E., Schmidt, P. T., Dlugosz, A., Lindberg, G., Karling, P., Ohlsson, B., Gazouli, M., Nardone, G., Cuomo, R., Usai-Satta, P., Galeazzi, F., Neri, M., Portincasa, P., ... Farrugia, G. (2014). Loss-

of-function of the voltage-gated sodium channel NaV1.5 (channelopathies) in patients with irritable bowel syndrome. *Gastroenterology*. 146(7):1659-1668. <u>http://doi.org/10.1053/j.gastro.2014.02.054</u>

Biesiekierski, J. R., Jalanka, J., & Staudacher, H. M. (2019). Can Gut Microbiota Composition Predict Response to Dietary Treatments?. Nutrients, 11(5), 1134. https://doi.org/10.3390/nu11051134

Biesiekierski, J. R., Rosella, O., Rose, R., Liels, K, Barrett, J. S., Shepherd, S. J., Gibson, P. R., & Muir, J. G. (2011). Quantification of fructans, galacto-oligosacharides and other short-chain carbohydrates in processed grains and cereals. *Journal of Human Nutrition and Dietetics*, 24(2):154-76. <u>http://doi.org/10.1111/j.1365-277X.2010.01139.x</u>

Boekema, P. J., Samsom, M., van Berge Henegouwen, G. P., & Smout, A. J. (1999). Coffee and gastrointestinal function: facts and fiction. A review. Scandinavian journal of gastroenterology. Supplement, 230, 35–39. <u>https://doi.org/10.1080/003655299750025525</u>

Bradford, K., Shih, W., Videlock, E., Presson, A. P., Naliboff, B. D., Mayer, E. A., & Lin Chang, L. (2012). Association between Early Adverse Life Events and Irritable Bowel Syndrome. *Clinical Gastroenteroly and Hepatology*, 10(4): 385–390.e3. <u>http://doi.org/10.1016/j.cgh.2011.12.018</u>

Buchanan, D. T., Cain, K., Heitkemper, M., Burr, R., Vitiello, M. V., Zia, J., & Jarrett, M. (2014). Sleep Measures Predict Next-Day Symptoms in Women with Irritable Bowel Syndrome. The Journal of Clinical Sleep Medicine, 10(9): 1003–1009. <u>http://doi.org/10.5664/jcsm.4038</u>

Böhn, L., Störsrud, S., Liljebo, T., Collin, L., Lindfors, P., Törnblom, H., & Simrén, M. (2015). Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: a randomized controlled trial. *Gastroenterology*, 149(6):1399-1407.e2. http://doi.org/10.1053/j.gastro.2015.07.054

Böhn, L., Störsrud, S., Törnblom, H., Bengtsson, U., & Simrén, M. (2013). Self-reported foodrelated gastrointestinal symptoms in IBS are common and associated with more severe symptoms and reduced quality of life. *The American Journal of Gastroenterology*, 108(5):634-41. <u>http://doi.org/10.1038/ajg.2013.105</u>

Canavan, C., West, J., & Card, T. (2014a). The epidemiology of irritable bowel syndrome. *Clinical Epidemiology*, 6: 71–80. <u>http://doi.org/10.2147/CLEP.S40245</u>

Canavan C., West J., & Card T. (2014b). Review article: the economic impact of the irritable bowel syndrome. *Alimentary Pharmacology & Therapeutics*, 40(9):1023-34. http://doi.org/10.1111/apt.12938

Chumpitazi, B. P., Cope, J. L., Hollister, E. B., Tsai, C. M., McMeans, A. R., Luna, R. A., Versalovic, J., & Shulman, R. J. (2015). Randomised Clinical Trial: Gut Microbiome Biomarkers are Associated with Clinical Response to a Low FODMAP Diet in Children with Irritable Bowel Syndrome. *Alimentary Pharmacology & Therapeutics*, 42(4): 418–427. http://doi.org/10.1111/apt.13286



Cole, J. A., Rothman, K. J., Cabral, H. J., Zhang, Y., & Farraye, F. A. (2006). Migraine, fibromyalgia, and depression among people with IBS: a prevalence study. *BMC Gastroenterology*, 6:26. <u>http://doi.org/10.1186/1471-230X-6-26</u>

Cox, S. R., Lindsay, J. O., Fromentin, S., Stagg, A. J., McCarthy, N. E., Galleron, N., Ibraim, S. B., Roume, H., Levenez, F., Pons, N., Maziers, N., Lomer, M. C., Ehrlich, S. D., Irving, P. M., & Whelan, K. (2020). Effects of Low FODMAP Diet on Symptoms, Fecal Microbiome, and Markers of Inflammation in Patients With Quiescent Inflammatory Bowel Disease in a Randomized Trial. *Gastroenterology*, 158(1):176-188.e7. <u>http://doi.org/10.1053/j.gastro.2019.09.024</u>

Cummings, J. H., & Macfarlane, G. T. (1997). The role of intestinal bacteria in nutrient metabolism. *Clinical Nutrition*, *16*, 3–11.

Daileda, T., Baek, P., Sutter, M. E., & Thakkar, K. (2016). Disaccharidase activity in children undergoing esophagogastroduodenoscopy: A systematic review. *World Journal of Gastrointestinal Pharmacology and Therapeutics*, 7(2):283-93. <u>http://doi.org/10.4292/wjgpt.v7.i2.283</u>

Dinan, T. G., Cryan, J., Shanahan, F., Keeling, P. W., & Quigley, E. M. (2010). IBS: An epigenetic perspective. *Nature Clinical Practice Gastroenterology and Hepatology*, 7(8):465-71. <u>http://doi.org/10.1038/nrgastro.2010.99</u>

Dior, M., Delagrèverie, H., Duboc, H., Jouet, P., Coffin, B., Brot, L., Humbert, L., Trugnan, G., Seksik, P., Sokol, H., Rainteau, D., & Sabate, J.M. (2016). Interplay between bile acid metabolism and microbiota in irritable bowel syndrome. *Neurogastroenterology and Motility*, 28(9):1330-40. http://doi.org/10.1111/nmo.12829

Drossman, D. A., Morris, C. B., Schneck, S., Hu, Y. J., Norton, N. J., Norton, W. F., Weinland, S. R., Dalton, C., Leserman, J., & Bangdiwala, S.I. (2009). International survey of patients with IBS: symptom features and their severity, health status, treatments, and risk taking to achieve clinical benefit. *Journal of Clinical Gastroenterology*, 43(6):541-50. http://doi.org/10.1097/MCG.0b013e318189a7f9

Drossman, D. A. (1995). Sexual and Physical Abuse and Gastrointestinal Illness. *Scandinavian Journal of Gastroenterology*, 30:sup208, 90-96. <u>http://doi.org/10.3109/00365529509107768</u>

El-Salhy, M., Gilja, O. H., Gundersen, D., Hatlebakk, J. G., & Hausken, T. (2014a). Endocrine cells in the ileum of patients with irritable bowel syndrome. *World Journal of Gastroenterology*, 20(9): 2383-2391. <u>http://doi.org/10.3748/wjg.v20.i9.2383</u>

El-Salhy, M., Gilja, O. H., Gundersen, D., Hatlebakk, J. G., & Hausken, T. (2014b). Interaction between ingested nutrients and gut endocrine cells in patients with irritable bowel syndrome (review). *International Journal of Molecular Medicine*, 34(2):363-71. http://doi.org/10.3892/ijmm.2014.1811

El-Salhy, M., Hatlebakk, J. G., Gilja, O. H., & Hausken, T. (2015). Densities of rectal peptide YY and somatostatin cells as biomarkers for the diagnosis of irritable bowel syndrome. *Peptides*, 67:12-9. <u>http://doi.org/10.1016/j.peptides.2015.02.008</u>



Elsenbruch, S., Schmid, J., Bäsler, M., Cesko, E., Schedlowski, M., & Benson, S. (2012). How positive and negative expectations shape the experience of visceral pain: an experimental pilot study in healthy women. *Neurogastroenterology and Motility*, 24(10):914-e460. http://doi.org/10.1111/j.1365-2982.2012.01950.x

Enck, P., Aziz, Q., Barbara, G., Farmer, A. D., Shin Fukudo, S., Mayer, E. A. 5, Niesler, B., Quigley, E. M. M., Rajilic -Stojanovic, M., Schemann, M., Schwille-Kiuntke, J., Simren, M., Zipfel, S, & Spiller, R.C. (2016). Irritable bowel syndrome. Nature Reviews Disease Primer, 2:16014. <u>http://doi.org/10.1038/nrdp.2016.14</u>

Eswaran, S. L., Chey, W. D., Han-Markey, T., Ball, S., & Jackson K1. (2016). A Randomized Controlled Trial Comparing the Low FODMAP Diet vs. Modified NICE Guidelines in US Adults with IBS-D. *The American Journal of Gastroenterology*, 111(12):1824-1832. http://doi.org/10.1038/ajg.2016.434

Fabisiak, A., Włodarczyk, J., Fabisiak, N., Storr, M., & Fichna, J. (2017). Targeting Histamine Receptors in Irritable Bowel Syndrome: A Critical Appraisal. *Journal of Neurogastroenterology and Motility*, 23(3):341-348. <u>http://doi.org/10.5056/jnm16203</u>

Finnish institute of health and welfare. (2019, May 23). Työpaikkaruokailu. (Eating at the work place.) <u>https://thl.fi/fi/web/elintavat-ja-ravitsemus/ravitsemus/ruokapalvelut/tyopaikkaruokailu (</u>In Finnish)

Ford, A. C., & Moayyedi, P. (2010). Meta-analysis: factors affecting placebo response rate in the irritable bowel syndrome. *Alimentary Pharmacology & Therapeutics*, 32(2):144-58. http://doi.org/10.1111/j.1365-2036.2010.04328.x

Gatta, L., & Scarpignato, C. (2017). Systematic review with meta-analysis: rifaximin is effective and safe for the treatment of small intestine bacterial overgrowth. *Alimentary Pharmacology & Therapeutics*, 45(5):604-616. <u>http://doi.org/10.1111/apt.13928</u>

Garcia-Etxebarria, K., Zheng, T., Bonfiglio, F., Bujanda, L., Dlugosz, A., Lindberg, G., Schmidt, P. T., Karling, P., Ohlsson, B., Simren, M., Walter, S., Nardone, G., Cuomo, R., Usai-Satta, P., Galeazzi, F., Neri, M., Portincasa, P., Bellini, M., Barbara, G., ... D'Amato, M. (2018). Increased Prevalence of Rare Sucrase-isomaltase Pathogenic Variants in Irritable Bowel Syndrome Patients. *Clinical Gastroenterology and Hepatology*, 16(10):1673-1676. http://doi.org/10.1016/j.cgh.2018.01.047

Gearry, R. B., Irving, P. M., Barrett, J. S., Nathan, D. M., Shepherd, S. J., & Gibson, P. R. (2009). Reduction of dietary poorly absorbed short-chain carbohydrates (FODMAPs) improves abdominal symptoms in patients with inflammatory bowel disease-a pilot study. *Journal of Crohn's and Colitis*, 3(1):8-14. <u>http://doi.org/10.1016/j.crohns.2008.09.004</u>

Ghoshal, U. C., Shukla, R., & Ghoshal, U. (2017). Small Intestinal Bacterial Overgrowth and Irritable Bowel Syndrome: A Bridge between Functional Organic Dichotomy. *Gut Liver*, 11(2):196-208. <u>http://doi.org/10.5009/gnl16126</u>

Gonsalkorale, W. M., Perrey, C., Pravica, V., Whorwell, P. J., & Hutchinson, V. (2003). Interleukin 10 genotypes in irritable bowel syndrome: evidence for an inflammatory component? *Gut*, 52(1): 91–93. <u>http://doi.org/10.1136/gut.52.1.91</u>

Halmos, E. P., & Gibson, P. G. (2019). Controversies and reality of the FODMAP diet for patients with irritable bowel syndrome. Journal of Gastroenterology and Hepatology, 34 (7), 1134-1142. http://doi.org/10.1111/jgh.14650

Halmos, E. P., Christophersen, C. T., Bird, A. R., Shepherd, S. J., Gibson, P. R., & Muir, J. G. (2015). Diets that differ in their FODMAP content alter the colonic luminal microenvironment. *Gut*, 64(1):93-100. <u>http://doi.org/10.1136/gutjnl-2014-307264</u>

Halmos, E. P., Power, V. A., Shepherd, S. J., Gibson, P. R., & Muir, J. G. (2014). A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology*, *146*(1), 67–75.e5. https://doi.org/10.1053/j.gastro.2013.09.046

Han, C. J., & Yang, G. S. (2016). Fatigue in Irritable Bowel Syndrome: A Systematic Review and Meta-analysis of Pooled Frequency and Severity of Fatigue. *Asian Nursing Research (Korean Society of Nursing Science)*, 10(1):1-10. <u>http://doi.org/10.1016/j.anr.2016.01.003</u>

Hajizadeh Maleki, B., Tartibian, B., Mooren, F. C., Fitzgerald, L. Z., Krüger, K., Chehrazi, M., & Malandish, A. (2018). Low-to-moderate intensity aerobic exercise training modulates irritable bowel syndrome through antioxidative and inflammatory mechanisms in women: Results of a randomized controlled trial. *Cytokine*, 102:18-25. <u>http://doi.org/10.1016/j.cyto.2017.12.016</u>

Harvie, R. M., Chisholm, A. W., Bisanz, J. E., Burton, J. P., Herbison, P., Schultz, K., & Schultz, M. (2017). Long-term irritable bowel syndrome symptom control with reintroduction of selected FODMAPs. *World journal of gastroenterology*, *23*(25), 4632–4643. https://doi.org/10.3748/wjg.v23.i25.4632

Heitkemper, M., Jarrett, M., Bond, E. F., & Chang, L. (2003). Impact of Sex and Gender on Irritable Bowel Syndrome. *Biological Research For Nursing*, 5(1), 56-65. <u>https://doi-org.libproxy.tuni.fi/10.1177/1099800403005001006</u>

Henström, M., & D'Amato, M. (2016). Genetics of irritable bowel syndrome. *Molecular and Cellular Pediatrics*, 3: 7. <u>http://doi.org/10.1186/s40348-016-0038-6</u>

Hewawasam, S. P., Iacovou, M., Muir, J. G., & Gibson, P. R. (2018). Dietary practices and FODMAPs in South Asia: Applicability of the low FODMAP diet to patients with irritable bowel syndrome. J *Journal of Gastroenterology and Hepatology*, 33(2):365-374. http://doi.org/10.1111/jgh.13885

Hillilä, M. T., Färkkilä, N. J., & Färkkilä, M. A. (2010a). Societal costs for irritable bowel syndrome – a population based study, Scandinavian Journal of Gastroenterology, 45:5, 582-591, <u>http://doi.org/10.3109/00365521003637211</u>

Hillilä, M. (2010b). Irritable bowel syndrome in the general population: epidemiology, comorbidity, and societal costs. [Doctoral dissertation, University of Helsinki] <u>https://helda.helsinki.fi/bitstream/handle/10138/22826/irritabl.pdf?sequence=1</u>



Holma, R., Laatikainen, R., Orell, H., Joensuu, H., Peuhkuri, K., Poussa, T., Korpela, R., & Österlund P. (2020). Consumption of Lactose, Other FODMAPs and Diarrhoea during Adjuvant 5-Fluorouracil Chemotherapy for Colorectal Cancer. *Nutrients*, 12(2). pii: E407. <u>http://doi.org/10.3390/nu12020407</u>

Hod, K., Dickman, R., Sperber, A., Melamed, S., Dekel, R., Ron, Y., Halpern, Z., Berliner, S., & Maharshak, N. (2011). Assessment of high-sensitivity CRP as a marker of micro-inflammation in irritable bowel syndrome. *Neurogastroenterology and Motility*, 23(12):1105-10. <u>http://doi.org/10.1111/j.1365-2982.2011.01788.x</u>

Hustoft, T. N., Hausken, T., Ystad, S. O., Valeur, J., Brokstad, K., Hatlebakk, J. G., & Lied, G. A. (2017). Effects of varying dietary content of fermentable short-chain carbohydrates on symptoms, fecal microenvironment, and cytokine profiles in patients with irritable bowel syndrome. *Neurogastroenterology & Motilility*, 29(4). <u>http://doi.org/10.1111/nmo.12969</u>

Huynh, B. L., Palmer, L., Mather, D., Wallwork, H., Graham, R., Welch, R., & Stangoulis, J. (2008). Genotypic variation in wheat grain fructan content revealed by a simplified HPLC method. *Journal of Cereal Science*, 48. 369-378. <u>http://doi.org/10.1016/j.jcs.2007.10.004</u>

Iacovou, M., Craig, S. S., Yelland, G. W., Barrett, J. S., Gibson, P. R., & Muir, J. G. (2018). Randomised clinical trial: reducing the intake of dietary FODMAPs of breastfeeding mothers is associated with a greater improvement of the symptoms of infantile colic than for a typical diet. *Alimentary Pharmacology & Therapeutics*, 48(10):1061-1073. <u>http://doi.org/10.1111/apt.15007</u>

IrritableBowelSyndrome.net. (2016, December 13). *New Rome IV Diagnostic Criteria for IBS*. <u>https://irritablebowelsyndrome.net/clinical/new-rome-iv-diagnostic-criteria/</u>

Janakiram, C., Deepan Kumar, C. V., & Joseph, J. (2017). Xylitol in preventing dental caries: A systematic review and meta-analyses. *Journal of natural science, biology, and medicine*, 8(1), 16–21. <u>https://doi.org/10.4103/0976-9668.198344</u>

Johannesson, E., Ringström, G., Abrahamsson, H., & Sadik, R. (2015). Intervention to increase physical activity in irritable bowel syndrome shows long-term positive effects. *World Journal of Gastroenterology*, 21(2):600-8. <u>http://doi.org/10.3748/wjg.v21.i2.600</u>

Karppinen, S., Myllymäki, O., Forssell, P., & Poutanen, K. (2003). Fructan Content of Rye and Rye Products. *Cereal Chemistry*, 80(2):168–171.

Khanna, R., MacDonald, J. K., & Levesque, B. G. (2014). Peppermint oil for the treatment of irritable bowel syndrome: a systematic review and meta-analysis. *Journal of clinical gastroenterology*, *48*(6), 505–512. <u>https://doi.org/10.1097/MCG.0b013e3182a88357</u>

Kolehmainen, M., Ulven, S. M., Paananen, J., de Mello, V., Schwab, U., Carlberg, C., Myhrstad, M., Pihlajamäki, J., Dungner, E., Sjölin, E., Gunnarsdottir, I., Cloetens, L., Landin-Olsson, M., Akesson, B., Rosqvist, F., Hukkanen, J., Herzig, K. H., Dragsted, L. O., Savolainen, M. J., ... Dahlman, I. (2015). Healthy Nordic diet downregulates the expression of genes involved in inflammation in subcutaneous adipose tissue in individuals with features of the metabolic

syndrome. *The American Journal of Clinical Nutrition*, 101(1):228-39. http://doi.org/10.3945/ajcn.114.092783

Konturek, P. C., Brzozowski, T., & Konturek, S. J. (2011). Stress and the gut: pathophysiology, clinical consequences, diagnostic approach and treatment options. *Journal of Physiology and Pharmacology*, 62(6):591-9

Lacy, B. E., & Patel, N. K. (2017). Rome Criteria and a Diagnostic Approach to Irritable Bowel Syndrome. *Journal of Clinical Medicine*, 6(11): 99. <u>http://doi.org/10.3390/jcm6110099</u>

Laatikainen, R., Koskenpato, J., Hongisto, S. M., Loponen, J., Poussa, T., Huang, X., Sontag-Strohm, T., Salmenkari, H., & Korpela R. (2017). Pilot Study: Comparison of Sourdough Wheat Bread and Yeast-Fermented Wheat Bread in Individuals with Wheat Sensitivity and Irritable Bowel Syndrome. *Nutrients*, 9(11). pii: E1215. <u>http://doi.org/10.3390/nu9111215</u>

Laatikainen, R., Koskenpato, J., Hongisto, S. M., Loponen, J., Poussa, T., Hillilä, M., & Korpela, R. (2016). Randomised clinical trial: low-FODMAP rye bread vs. regular rye bread to relieve the symptoms of irritable bowel syndrome. Aliment Pharmacol Ther. 2016 Sep;44(5):460-70. http://doi.org/10.1111/apt.13726

Lahtinen, P., Jalanka, J., Hartikainen, A., Mattila, E., Hillilä, M., Punkkinen, J., Koskenpato, J., Anttila, V.J., Tillonen, J., Satokari, R., & Arkkila, P. (2020). Randomised clinical trial: faecal microbiota transplantation versus autologous placebo administered via colonoscopy in irritable bowel syndrome. Alimentary Pharmacology & Therapeutics, <u>http://doi.org/10.1111/apt.15740</u>

Lappi, J., Mykkänen, H., Bach Knudsen, K. E., Kirjavainen, P., Katina, K., Pihlajamäki, J., Poutanen, K., & Kolehmainen, M. (2014). Postprandial glucose metabolism and SCFA after consuming wholegrain rye bread and wheat bread enriched with bioprocessed rye bran in individuals with mild gastrointestinal symptoms. *Nutrition Journal*, 13:104. http://doi.org/10.1186/1475-2891-13-104

Lau, C. I., Lin, C. C., Chen, W. H., Wang, H. C., & Kao, C. H. Association between migraine and irritable bowel syndrome: a population-based retrospective cohort study. *European Journal of Neurology*, 21: 1198–1204. <u>http://doi.org/10.1111/ene.12468</u>

Levy, R. L., Jones, K. R., Whitehead, W. E., Feld, S. I., Talley, N. J., & Corey, L. A. (2001). Irritable bowel syndrome in twins: heredity and social learning both contribute to etiology. *Gastroenterology*, 121(4):799-804

Lewis, S. J., & Heaton, K. W. (1997). Stool form scale as a useful guide to intestinal transit time. *Scandinavian journal of gastroenterology*, *32*(9), 920–924. <u>https://doi.org/10.3109/00365529709011203</u>

Liebregts, T., Adam, B., Bredack, C., Röth, A., Heinzel, S., Lester, S., Downie-Doyle, S., Smith, E., Drew, P., Talley, N. J., & Holtmann, G. (2007). Immune activation in patients with irritable bowel syndrome. *Gastroenterology*, 132(3):913-20

Liljebo, T., Störsrud, S., & Andreasson, A. (2020). Presence of Fermentable Oligo-, Di-, Monosaccharides, and Polyols (FODMAPs) in commonly eaten foods: extension of a database to

indicate dietary FODMAP content and calculation of intake in the general population from food diary data. *BMC nutrition*, *6*, 47. <u>https://doi.org/10.1186/s40795-020-00374-3</u>

Lis, D. M., Stellingwerff, T., Kitic, C. M., Fell, J. W., & Ahuja, K. D. K. (2018). Low FODMAP: A Preliminary Strategy to Reduce Gastrointestinal Distress in Athletes. *Medicine and Science in Sports and Exercise*, 50(1):116-123. <u>http://doi.org/10.1249/MSS.000000000001419</u>

Lovell, R. M., & Ford., A. C. (2012). Global Prevalence of and Risk Factors for Irritable Bowel Syndrome: A Meta-analysis. *Clinical Gastroenterology and Hepatology*, 10:712–721

Maagaard, L., Ankersen, D. V., Végh, Z., Burisch, J., Jensen, L., Pedersen, N., & Munkholm, P. (2016). Follow-up of patients with functional bowel symptoms treated with a low FODMAP diet. *World journal of gastroenterology*, *22*(15), 4009–4019. https://doi.org/10.3748/wjg.v22.i15.4009

Masuy, I., Van Oudenhove, L., Tack, J., & Biesiekierski, J. R. (2018). Effect of intragastric FODMAP infusion on upper gastrointestinal motility, gastrointestinal, and psychological symptoms in irritable bowel syndrome vs healthy controls. *Neurogastroenterology & Motilility*, 30(1). <u>http://doi.org/10.1111/nmo.13167</u>

Marum, A. P., Moreira, C., Tomas-Carus, P., Saraiva, F., & Guerreiro, C. S. (2017). A low fermentable oligo-di-mono saccharides and polyols (FODMAP) diet is a balanced therapy for fibromyalgia with nutritional and symptomatic benefits. *Nutrición Hospitalaria*, 34:667-674. http://doi.org/10.20960/nh.703

Marynowski, M., Likońska, A., Zatorski, H., & Fichna, J. (2015). Role of environmental pollution in irritable bowel syndrome. *World Journal of Gastroenterology*, 21(40): 11371-11378. http://doi.org/<u>10.3748/wjg.v21.i40.11371</u>

Maxion-Bergemann, S., Thielecke, F., Abel, F., & Bergemann, R. (2006). Costs of Irritable Bowel Syndrome in the UK and US. *Pharmacoeconomics*, 24 (1): 21-37.

McIntosh, K., Reed, D. E., Schneider, T., Dang, F., Keshteli, A. H., De Palma, G., Madsen, K., Bercik, P., & Vanner, S. (2017). FODMAPs alter symptoms and the metabolome of patients with IBS: a randomised controlled trial. Gut, 66(7):1241-1251. <u>http://doi.org/10.1136/gutjnl-2015-311339</u>

Mearin, F. (2012). Editorial: From the acute infection to the chronic disorder "Don't worry it's just a viral gastroenteritis". *The American Journal of Gastroenterology*, 107(6):900-1. http://doi.org/10.1038/ajg.2012.105

Mearin, F., Caballero, A. M., Serra, J., Brotons, C., Tantiñà, A., Fort, E., Martínez-Cerezo, F. J., Perelló, A., Sánchez-Antolín, G., Rey, E., Angós Musgo, R., Berdier, R., Gómez-Rodríguez, B., Clavé, P., García-Alonso, M., Torán-Monserrat, P., & Tack, J. (2019). A retrospective and prospective 12-month observational study of the socioeconomic burden of moderate to severe irritable bowel syndrome with constipation in Spain. *Gastroenterologia y hepatologia*, *42*(3), 141–149. <u>https://doi.org/10.1016/j.gastrohep.2018.10.008</u>

Merskey H. (1994). Logic, truth and language in concepts of pain. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation, 3 Suppl 1*, S69–S76. <u>https://doi.org/10.1007/BF00433379</u>

Mudyanadzo, T. A., Hauzaree, C., Yerokhina, O., Architha, N. N., & Ashqar, H. M. (2018). Irritable Bowel Syndrome and Depression: A Shared Pathogenesis. Cureus, 10(8):e3178. http://doi.org/10.7759/cureus.3178

Muir, J. G., Rose, R., Rosella, O., Liels, K., Barrett, J. S., Shepherd, S. J., & Gibson, P. R. (2009). Measurement of short-chain carbohydrates in common Australian vegetables and fruits by high-performance liquid chromatography (HPLC). *Journal of Agricultural and Food Chemistry*, 57(2):554-65. <u>http://doi.org/10.1021/jf802700e</u>

Munukka, E., Ahtiainen, J. P., Puigbó, P., Jalkanen, S., Pahkala, K., Keskitalo, A., Kujala, U. M., Pietilä, S., Hollmén, M., Elo, L. Huovinen, P., D'Auria ,G., & Pekkala, S. (2018). Six-Week Endurance Exercise Alters Gut Metagenome That Is not Reflected in Systemic Metabolism in Overweight Women. *Frontiers in Microbiology*, 9:2323. <u>http://doi.org/10.3389/fmicb.2018.02323</u>

Myers, B., & Greenwood-Van Meerveld, B. (2009). Role of anxiety in the pathophysiology of irritable bowel syndrome: importance of the amygdala. Frontiers in Neuroscience, 3:47. http://doi.org/10.3389/neuro.21.002.2009

Myneedu, K., Deoker, A., Schmulson, M. J., & Bashashati, M. (2019). Fecal microbiota transplantation in irritable bowel syndrome: A systematic review and meta-analysis. *United European Gastroenterology Journal*, 7(8): 1033–104. <u>http://doi.org/10.1177/2050640619866990</u>

National Institute for Health and Care Excellence (NICE). (2015, February). *Irritable bowel syndrome in adults: diagnosis and management*. https://www.nice.org.uk/guidance/cg61/chapter/1-Recommendations#dietary-and-lifestyle-advice

Neal, K. R., Barker, L.,& Spiller, R.C. (2002). Prognosis in post-infective irritable bowel syndrome: a six year follow up study. *Gut*, 51(3):410-3

Nee, J., Zakari, M., & Lembo, A. J. (2015). Current and emerging drug options in the treatment of diarrhea predominant irritable bowel syndrome. *Expert Opinion on Pharmacotherapy*, 16(18):2781-92. <u>http://doi.org/10.1517/14656566.2015.1101449</u>

Nordic Nutrition Recommendations 2012(2014),5(11):1. http://dx.doi.org/10.6027/Nord2014-002

Nyyssölä, A., Ellilä, S., Nordlund, E., Poutanen, K. (2020). Reduction of FODMAP content by bioprocessing. *Trends in Food Science & Technology*, 99: 257-72. <u>https://doi.org/10.1016/j.tifs.2020.03.004</u>

O'Keeffe, M., Jansen, C., Martin, L., Williams, M., Seamark, L., Staudacher, H. M., Irving, P. M., Whelan, K., & Lomer, M. C. (2018). Long-term impact of the low-FODMAP diet on gastrointestinal symptoms, dietary intake, patient acceptability, and healthcare utilization in irritable bowel syndrome. *Neurogastroenterology and Motility*, 30(1). http://doi.org/10.1111/nmo.13154



O'Keeffe, M., & Lomer, M. C. (2017). Who should deliver the low FODMAP diet and what educational methods are optimal: a review. *Journal of Gastroenterology and Hepatology*, 32 Suppl 1:23-26. <u>http://doi.org/10.1111/jgh.13690</u>

Ong, D. K., Mitchell, S. B., Barrett, J. S., Shepherd, S. J., Irving, P. M., Biesiekierski, J. R., Smith, S., Gibson, P. R., & Muir, J. G. (2010). 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*, 25(8):1366-73. <u>http://doi.org/10.1111/j.1440-1746.2010.06370.x</u>

Oku, T., & Nakamura, S. (2007). Threshold for transitory diarrhea induced by ingestion of xylitol and lactitol in young male and female adults. *Journal of Nutritional Science and Vitaminology*, 53(1):13-20

Peters, S. L., Yao, C. K., Philpott, H., Yelland, G. W., Muir, J. G., & Gibson, P. R. (2016). 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*, 44(5):447-59. <u>http://doi.org/10.1111/apt.13706</u>

Pérez y López, N., Torres-López, E., & Zamarripa-Dorsey, F. (2015). Clinical response in Mexican patients with irritable bowel syndrome treated with a low diet low in fermentable carbohydrates (FODMAP). *Revista de Gastroenterología de México*, 80(3):180-5. http://doi.org/10.1016/j.rgmx.2015.06.008

Piche, T., Saint-Paul, M.C., Dainese, R., Marine-Barjoan, E., Iannelli, A., Montoya, M. L., Peyron, J. F., Czerucka, D., Cherikh, F., Filippi, J., Tran, A., & Hébuterne, X. (2008). Mast cells and cellularity of the colonic mucosa correlated with fatigue and depression in irritable bowel syndrome. *Gut*, 57(4):468-73. <u>http://doi.org/10.1136/gut.2007.127068</u>

Porter, C. K., Gormley, R., Tribble, D. R., Cash, B. D., & Riddle, M. S. (2011). The Incidence and gastrointestinal infectious risk of functional gastrointestinal disorders in a healthy US adult population. *The American Journal of Gastroenterology*, 106(1):130-8. <u>http://doi.org/10.1038/ajg.2010.371</u>

Quick Biochemistry Basics. (2019, July 17). HPLC | High performance liquid chromatography.

[Video]. YouTube. <u>https://www.youtube.com/watch?v=ZN7euA1fS4Y</u>

Raulio, S., Roos, E., & Prättälä, R. (2010). School and workplace meals promote healthy food habits. *Public Health Nutrition*, 13(6A):987-92. <u>http://doi.org/10.1017/S1368980010001199</u>

Regulation 828/2014. On the requirements for the provision of information to consumers on the absence or reduced presence of gluten in food. European Parliament, Council of the European Union. <u>http://data.europa.eu/eli/reg_impl/2014/828/oj</u>

de Roest, R. H., Dobbs, B. R., Chapman, B. A., Batman, B., O'Brien, L. A., Leeper, J. A., Hebblethwaite, C. R., & Gearry, R. B. (2013). The low FODMAP diet improves gastrointestinal symptoms in patients with irritable bowel syndrome: a prospective study. *International Journal of Clinical Practice*, 67(9):895-903. <u>http://doi.org/10.1111/ijcp.12128</u>



Rinninella, E., Cintoni, M., Raoul, P., Lopetuso, L. R., Scaldaferri, F., Pulcini, G., Miggiano, G., Gasbarrini, A., & Mele, M. C. (2019). Food Components and Dietary Habits: Keys for a Healthy Gut Microbiota Composition. *Nutrients*, 11(10), 2393. <u>https://doi.org/10.3390/nu11102393</u>

Rossi, M., Aggio, R., Staudacher, H. M., Lomer, M. C., Lindsay, J. O., Irving, P., Probert, C., & Whelan, K. (2018). Volatile Organic Compounds in Feces Associate With Response to Dietary Intervention in Patients With Irritable Bowel Syndrome. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*, *16*(3), 385–391.e1. <u>https://doi.org/10.1016/j.cgh.2017.09.055</u>

Salli, K., Lehtinen, M. J., Tiihonen, K., & Ouwehand, A. C. (2019). Xylitol's Health Benefits beyond Dental Health: A Comprehensive Review. *Nutrients*, *11*(8), 1813. <u>https://doi.org/10.3390/nu11081813</u>

Sanders, M. E., Merenstein, D. J., Reid, G., Gibson, G. R., & Rastall, R. A. (2019). Probiotics and prebiotics in intestinal health and disease: from biology to the clinic. *Nature Clinical Practice Gastroenterology and Hepatology*, 16(10):605-616. <u>http://doi.org/10.1038/s41575-019-0173-3</u>

Simrén, M., Svedlund, J., Posserud, I., Bjornsson, E. S., & Abrahamsson, H. (2008). Predictors of subjective fatigue in chronic gastrointestinal disease. *Alimentary Pharmacology & Therapeutics*, 28(5):638-47. <u>http://doi.org/10.1111/j.1365-2036.2008.03770.x</u>

Sebastián Sánchez, B., Gil Roales-Nieto, J., Ferreira, N. B., Gil Luciano, B., & Sebastián Domingo, J. J. (2017). New psychological therapies for irritable bowel syndrome: mindfulness, acceptance and commitment therapy (ACT). *Revista española de enfermedades digestivas : organo oficial de la Sociedad Española de Patología Digestiva*, 109(9):648-657. http://doi.org/10.17235/reed.2017.4660/2016

Serra, J., Azpiroz, F., & Malagelada, J. R. (2001). Impaired transit and tolerance of intestinal gas in the irritable bowel syndrome. *Gut*, 48(1):14-9

Sniffen, J. C., McFarland, L. V., Evans, C. T., & Goldstein, E. J. C. Choosing an appropriate probiotic product for your patient: An evidence-based practical guide. *PLoS One*, 13(12):e0209205. http://doi.org/10.1371/journal.pone.0209205

Staudacher, H. M., Lomer, M. C. E., Farquharson, F. M., Louis, P., Fava, F., Franciosi, E., Scholz, M., Tuohy, K. M., Lindsay, J. O., Irving, P. M., & Whelan, K. (2017). A Diet Low in FODMAPs Reduces Symptoms in Patients With Irritable Bowel Syndrome and A Probiotic Restores Bifidobacterium Species: A Randomized Controlled Trial. *Gastroenterology*,153(4):936-947. http://doi.org/10.1053/j.gastro.2017.06.010

Staudacher, H. M., Irving, P. M., Lomer, M. C., & Whelan, K. (2014). Mechanisms and efficacy of dietary FODMAP restriction in IBS. *Nature Reviews Gastroenterology & Hepatology*, 11(4):256-66. <u>http://doi.org/10.1038/nrgastro.2013.259</u>

Staudacher, H. M., Lomer, M. C., Anderson, J. L., Barrett, J. S., Muir, J. G., Irving, P. M., & Whelan, K. (2012). Fermentable carbohydrate restriction reduces luminal bifidobacteria and

gastrointestinal symptoms in patients with irritable bowel syndrome. *Journal of Nutrition*, 142(8):1510-8. <u>http://doi.org/10.3945/jn.112.159285</u>

Stermer, E., Bar, H., & Levy, N. (1991). Chronic functional gastrointestinal symptoms in Holocaust survivors. *The American Journal of Gastroenterology*, 86(4):417-22. [Abstract].

Tana, C., Umesaki, Y., Imaoka, A., Handa, T., Kanazawa, M., & Fukudo, S. (2010). Altered profiles of intestinal microbiota and organic acids may be the origin of symptoms in irritable bowel syndrome. *Neurogastroenterology and Motility*, 22(5):512-9, e114-5. <u>http://doi.org/10.1111/j.1365-2982.2009.01427.x</u>

Tilles-Tirkkonen, T., Pentikäinen, S., Lappi, J., Karhunen, L., Poutanen, K., & Mykkänen, H. (2011). The quality of school lunch consumed reflects overall eating patterns in 11-16-year-old schoolchildren in Finland. *Public Health Nutrition*, 14(12):2092-8. http://doi.org/10.1017/S1368980011001388

Tillisch, K., Mayer, E. A., & Labus, J. S. (2011). Quantitative meta-analysis identifies brain regions activated during rectal distension in irritable bowel syndrome. *Gastroenterology*, 140(1):91-100. http://doi.org/10.1053/j.gastro.2010.07.053

The Rome Foundation. (2020). <u>https://theromefoundation.org/</u>

Trott, N., Aziz, I., Rej, A., & Surendran Sanders, D. (2019). How Patients with IBS Use Low FODMAP Dietary Information Provided by General Practitioners and Gastroenterologists: A Qualitative Study. *Nutrients*, 11(6). pii: E1313. <u>http://doi.org/10.3390/nu11061313</u>

Tuck, C. J., Taylor, K. M., Gibson, P. R., Barrett, J. S., & Muir, J. G. (2018a). Increasing Symptoms in Irritable Bowel Symptoms With Ingestion of Galacto-Oligosaccharides Are Mitigated by α-Galactosidase Treatment. *The American journal of gastroenterology*, *113*(1), 124–134. https://doi.org/10.1038/ajg.2017.245

Tuck, C., Ly, E., Bogatyrev, A., Costetsou, I., Gibson, P., Barrett, J., & Muir, J. (2018b). Fermentable short chain carbohydrate (FODMAP) content of common plant-based foods and processed foods suitable for vegetarian- and vegan-based eating patterns. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association*, *31*(3), 422–435. https://doi.org/10.1111/jhn.12546

Yoon, S. L., Grundmann, O., Koepp, L., & Farrell, L. (2011). Management of irritable bowel syndrome (IBS) in adults: conventional and complementary/alternative approaches. *Alternative Medicine Review*, 16(2):134-51.

Youn, Y. H., Kim, H. C., Lim, H. C., Park, J. J., Kim, J-H., & Park, H. (2016) Long-term Clinical Course of Post-infectious Irritable Bowel Syndrome After Shigellosis: A 10-year Follow-up Study Journal of Neurogastroenterology and Motility. 22(3): 490–496. <u>http://doi.org/10.5056/jnm15157</u>

Valsta, L., Kaartinen, N., Tapanainen, H., Männistö, S., Sääksjärvi, K. (2018). Ravitsemus Suomessa - Nutrition in Finland — FinRavinto 2017 -tutkimus - The National FinDiet 2017 Survey. Finnish Institute for health and welfare. Report 12/2018. https://www.julkari.fi/handle/10024/137433



Varney, J., Barrett, J., Scarlata, K., Catsos, P., Gibson, P. R., & Jane G Muir, J. G. (2017). FODMAPs: food composition, defining cutoff values and international application. *Journal of Gastroenterology and Hepatology*, 32 (Suppl. 1): 53–61. <u>http://doi.org/10.1111/jgh.13698</u>

Waehrens, R., Ohlsson, H., Sundquist, J., Sundquist, K., & Zöller, B. (2013). Risk of irritable bowel syndrome in first-degree, second-degree and third-degree relatives of affected individuals: a nationwide family study in Sweden. *Gut*, 64(2):215-21. <u>http://doi.org/10.1136/gutjnl-2013-305705</u>

Whelan, K., Martin, L. D., Staudacher, H. M., & Lomer, M. C. E. (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. *Journal of Human Nutrition and Dietetics*, 239-255. <u>http://doi.org/10.1111/jhn.12530</u>

Wilder-Smith, C. H., Olesen, S. S., Materna, A., & Drewes, A. M. (2017). Predictors of response to a low-FODMAP diet in patients with functional gastrointestinal disorders and lactose or fructose intolerance. *Alimentary Pharmacology & Therapeutics*, 45(8):1094-1106. http://doi.org/10.1111/apt.13978

Wiffin, M., Smith, L., Antonio, J., Johnstone, J., Beasley, L., & Roberts, J. (2019). Effect of a short-term low fermentable oligiosaccharide, disaccharide, monosaccharide and polyol (FODMAP) diet on exercise-related gastrointestinal symptoms. *Journal of the International Society of Sports Nutrition*, 16(1):1. <u>http://doi.org/10.1186/s12970-019-0268-9</u>

Williams, R. E., Black, C. L., Kim, H. Y., Andrews, E. B., Mangel, A. W., Buda, J. J., & Cook, S. F. (2006). Determinants of healthcare-seeking behaviour among subjects with irritable bowel syndrome. *Alimentary Pharmacology & Therapeutics*, 23(11):1667-75.

Wouters, M. M., Van Wanrooy, S., Nguyen, A., Dooley, J., Aguilera-Lizarraga, J., Van Brabant, W., Garcia-Perez, J. E., Van Oudenhove, L., Van Ranst, M., Verhaegen, J., Liston, A., & Boeckxstaens, G. (2016). Psychological comorbidity increases the risk for postinfectious IBS partly by enhanced susceptibility to develop infectious gastroenteritis. *Gut*, 65(8):1279-88. http://doi.org/10.1136/gutjnl-2015-309460

Zhou, S. Y., Gillilland, M., Wu ,X., Leelasinjaroen, P., Zhang G, Zhou, H., Ye, B., Lu, Y., & Owyang, C. (2018). FODMAP diet modulates visceral nociception by lipopolysaccharide-mediated intestinal inflammation and barrier dysfunction. *Journal of Clinical Investigation*, 128(1):267-280. http://doi.org/10.1172/JCI92390

Zhou, Q., Fillingim, R. B., Riley, J. L., Malarkey, W. B., & Verne, G. N. (2010). Central and peripheral hypersensitivity in the irritable bowel syndrome. *Pain*, 148(3):454-61. <u>http://doi.org/10.1016/j.pain.2009.12.005</u>

Zomorodi, S., Abdi, S., & Tabatabaee, S. K. (2014). Comparison of long-term effects of cognitivebehavioral therapy versus mindfulness-based therapy on reduction of symptoms among patients suffering from irritable bowel syndrome. *Gastroenterology and hepatology from bed to bench*, 7(2), 118–124.