THE EFFECT OF LOW FODMAP DIET IN PATIENTS WITH RADIATION-INDUCED SMALL BOWEL DISEASE

Master's Thesis in Clinical Nutrition

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ABSTRACT/SUMMARY

Rationale: Patients suffering from chronic radiation-induced small bowel disease (RISBD) after cancer treatment have similar symptoms as patients with IBS (irritable bowel syndrome), despite dissimilar pathological origin. The low FODMAP (fermentable oligo-, di-, monosaccharides and polyols) diet (LFD) is a widespread management strategy for IBS. The aim of the conducted study was to investigate the effects of LFD on symptoms and health related quality of life (HRQOL) for patients with chronic RISBD.

Methods: In an open pilot study, 11 patients with RISBD related IBS symptoms were instructed to follow LFD throughout a 4-week intervention period. IBS Severity Scoring System (IBS-SSS) and IBS Symptom Questionnaire (IBS-SQ) were used to assess symptoms. An Ad hoc questionnaire measured grade of damage and typical RISBD complaints. Short Form Nepean Dyspepsia Index (SF-NDI) and 12-item Short Form Health Survey (SF-12) were used to evaluate HRQOL. A 3-day food record was used to estimate baseline intake of FODMAPs, to reveal dietary changes and to assess adherence to the diet. All schemes were completed at baseline and at 4 weeks.

Results: FODMAP intake was successfully reduced, and main additional changes in the diet were reduced intake of energy, carbohydrates and fiber. The adherence to the diet was high (mean 94.8%). IBS symptoms improved significantly based on mean total score of IBS-SSS and IBS-SQ, which changed from 310.2±60.7 to 171.4±107.2 ($p=0.001$) and 27.4±4.1 to 15.7±10.1 ($p=0.002$), respectively. The severity of abdominal pain, abdominal distension, belching/flatulence, constipation, diarrhea, early satiety, dissatisfaction with bowel habits and interference with life in general, improved significantly. Tendencies of improvement were also measured in comorbidity complaints and typical RISBD complaints. HRQOL improved based on SF-NDI total score, which changed from 30.5±9.4 to 18.3±8.2 ($p=0.001$) and based on mental ($p=0.047$) and physical ($p=0.134$) component summary score of SF-12.

Conclusions: The low FODMAP diet seems effective in alleviating IBS symptoms, and improving HRQOL in patients with RISBD. High compliance to LFD is possible with adequate diet counseling and continuous guidance. Further controlled studies with larger sample size should be conducted to verify our results and hopefully enable the implementation of LFD as a future management strategy for chronic RISBD.

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LIST OF ABBREVATIONS

BMI: Body mass index

CRP: C reactive protein

CTGF: Connective tissue growth factor

DNA: Deoxyribonucleic acid

FGID: Functional gastrointestinal disorders

FIGO: The International Federation of Gynecology and Obstetrics

FODMAP: Fermentable oligosaccharides, disaccharides, monosaccharides and polyols

FOS: Fructo-oligosaccharides

GI: Gastrointestinal

GIANT: GI and Nutrition team

GOS: Galacto-oligosaccharides

Gy: Gray

HBO: Hyperbaric oxygen

HMU: Hyperbaric Medical Unit

HRQOL: Health related quality of life

HUS: Haukeland University Hospital

IBD: Inflammatory bowel disease

IBS: Irritable bowel syndrome

IBS-C: Irritable bowel syndrome with constipation

IBS-D: Irritable bowel syndrome with diarrhea

IBS-M: Irritable bowel syndrome with a mixed bowel pattern

IBS-SQ: Irritable bowel syndrome symptom questionnaire

IBS-SSS: Irritable bowel syndrome severity scoring system

IL1: Interleukin 1

IL2: Interleukin 2

IMRT: Intensity-modulated radiotherapy

IQR: Interquartile range

Kcal: Kilocalorie

LENT/SOMA: Late Effect Normal Tissues/Subjective Objective Management Analysis

LFD: Low FODMAP diet

MCT: Medium-chain triglycerides

PAR-1: Protease-activated receptor-1

REC: The Regional ethics committee

RISBD: Radiation-induced small bowel disease

RT: Radiation treatment

RTOG: Radiation Therapy Oncology Group

SD: Standard deviation

SeHCAT: Selenium homocholic acid taurine scan

SF-12: 12-item Short Form Survey

SF-NDI: Short Form Nepean Dyspepsia Index

SIBO: Small intestine bacterial overgrowth

TGF-β1: Transforming growth factor β1

TNF-α: Tumor necrosis factor α

UiB: University of Bergen

UK: United Kingdom

VAS: Visual analogue scale

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1. INTRODUCTION

1.1 Radiation-induced Small Bowel Disease

1.1.1 Background

Radiation-induced small bowel disease (RISBD) is a common side effect following ionizing radiation treatment (RT) for cancer in the gastrointestinal (GI) tract, or in the surrounding organs (1). Because of localization close to specific organs, the cancer types related to this symptom disease are GI, gynecological and urological cancers. The terms used to describe this condition vary. Traditionally, the term "radiation enteritis/proctitis/colitis" has been used. However, inflammation may be misleading, as it is not a dominating feature. "Pelvic radiation disease" or "radiation-induced small bowel disease/damage" are probably more accurate. The designations "radiation enteropathy", "radiation proctopathy" and "radiation colopathy" may be useful to define the localization. Because of the proximity to the small bowel, symptoms arising from different parts of the intestines are often overlapping and the condition should perhaps not be named anatomically specified (1). Still, the focus in this paper is damage to the small bowel, because small bowel based symptoms are likely to be influenced by diet. RISBD is often subdivided in acute and chronic damage (2). The acute symptoms are self-limiting and only present during the treatment period, normally with an onset between the first three weeks of treatment and lasting for six weeks after treatment (3). In this study we will focus on patients who suffer from chronic radiation injury, developed (by definition) between 18 months and several years after completion of radiation therapy. Prolonged radiation injury can also occur as a chronic continuation of acute damage (2).

1.1.2 Pelvic radiation treatment

RT aims to damage tumor DNA (deoxyribonucleic acid) to prevent cell division, or promote apoptosis and cell death. High energy protons or neutrons evokes free radicals and DNA strain damage (4). The cells of normal tissue are less sensitive but are also affected in the process. To make it possible for normal tissue to regenerate, the radiation is given in fractions, *e.g*. one daily fraction five days a week for up to seven weeks. The dose, the radiation field and the fraction schedule are planned in advance. The administration of each fraction is painless and completed within a few minutes (5).

The dosage given is registered as total amount of Gray (Gy), which reflects how much energy the area receives. This normally varies from 50-70 Gy for pelvic tumors (6). RT can be given

as external radiation, internal radiation (brachytherapy) or as a combination. Brachytherapy, by insertion of radioactive needles, allows more localized treatment and hence less damage to normal tissue (5).

1.1.3 Epidemiology

The number of new-diagnosed cancer cases in Norway, was in 2015 about 32600 (7). The cancer types that poses a risk to develop RISBD are all among the 10 most frequent; prostate 29%, colon 18%, rectum 9% and gynecological 8%. This makes a total of about 11000 patients who hypothetically are at risk for RISBD if receiving RT (7). In the UK, 20% of pelvic cancer cases are treated with radiation (8). The trend since 1965 for all these cancer types is that mortality is decreasing while survival and prevalence are increasing. An exception is gynecological cancers, where a decreasing incidence has been observed. Diagnostic methods and routines have improved, and the simultaneous shift to an ageing/older population, can explain the increased prevalence (7). The number of cancer survivors is increasing as treatment has been steadily improved (2). In Norway, approximately two of three cancer patients live five years after diagnosis (all cancer types) (7). Consequently the number of patients suffering from RISBD may also increase. Some reports suggest that up to 90% of cancer patients receiving pelvic RT will, to some degree, perceive a permanent change of bowel habits (9). This may be an overestimation, but generally, the condition is underreported, although half of the patients report that the late effects reduce quality of life (2). Based on the number of people receiving pelvic RT globally, this is estimated to encompass half a million people (10). Fecal urgency is believed to affect quality of life to the largest extent, and is reported in 3-53% of the patients (11, 12). Only a minor part of the affected patients are referred to a gastroenterology specialist (2). Suggested reasons for underreporting of the condition, is first of all the current lack of a clear definition and a routine management (2). Secondly, the discharge from follow-up after five years combined with the slow progress of chronic symptoms play a major role. The Norwegian National guidance for Gynecological Cancers suggest controls to be carried out every 3rd-6th month the first two years after finishing treatment, and then every 6th month the next five years (13). The main aim of the controls is to detect late effects and recurrent cancer. The most common late effects after RT for this cancer type are fatigue, abdominal/pelvic pain, GI affliction, urinary incontinence and infertility (14). Third, the fact

that patients are relieved being cured for cancer gives them a high tolerance for GI symptoms and make them less likely to seek help (11).
Estimated proportions of patients affected by GI symptoms after RT are 66% for colorectal cancer, 40% for gynecological cancer and 30% for urological cancer (2). In the UK, this is equivalent to the number of patients diagnosed with inflammatory bowel disease (IBD) annually, but the medical attention and research funds are blatantly imbalanced (15).

1.1.4 Pathophysiology

The GI symptoms following pelvic radiation injury vary individually but include post-prandial pain, abdominal discomfort/pain, diarrhea, constipation, obstruction, nausea, anorexia (reduced appetite), weight loss, bloating, steatorrhea, rectal bleeding, fecal urgency/incontinence and malabsorption of specific or multiple nutrients (4).

The causes of symptoms are complex and multifactorial (Figure 1). It is important to remember, that not all symptoms seen after radiation are caused solely by the treatment, but could be due to *e.g.* already existing vulnerability for irritable bowel syndrome (IBS), celiac disease, small intestine bacterial overgrowth (SIBO), thyroid dysfunction, pancreatic insufficiency, drug side effects or change in dietary habits, indirectly connected to the cancer disease (2, 16). Also psychological stress, which cancer patients often suffer from, can promote GI symptoms. Despite of that, data suggesting organic causes for the symptoms do exist (2).

The acute phase of radiation injury is histologically dominated by inflammation (6), and presents with clinical symptoms like loose stools, abdominal cramps, nausea and bleeding, normally managed by symptomatic and dietary treatment (11). Repetitive injury from radiation and free radicals provoke cell death, cytokine activation, abscess formation and arteriole swelling in intestinal cell layers. The cells of the small intestinal mucosa are rapidly dividing, and are therefor especially vulnerable (4). Lacking or abnormal neovascularization promotes ischemia and telangiectasia formation (17). The latter, can lead to rectal bleeding which occurs frequently in this patient group (2). The acute reaction is self-limiting and usually subsides soon after cessation of RT (11).
In contrast, delayed/chronic radiation injury is dominated by progressive vascular changes, resulting in the hall-mark of the condition; fibrosis, which leads to both structural and

functional deteriorations, and also metabolic derangements (11). Inflammatory changes are less prominent. Clinical GI features are mainly dysmotility and malabsorption, but also fecal incontinence and bleeding. Severe situations can occur due to intestinal obstructions, fistulas or bowel perforation, but the main problem is often compromised quality of life due to diarrhea, fecal urgency, abdominal pain, bloating and flatulence (11).

The underlying pathophysiology is not fully understood, but endothelial dysfunction is central in causing and perpetuating the delayed effect of radiation injury (17, 18). Prolonged thrombotic obstruction of small vessels releases multiple pro-inflammatory cytokines (IL1, IL2, TNF-α) and growth factors (TGF-β1, CTGF) (17, 19). A dose-dependent down-regulation of thrombomodulin results in a consistent shift in the coagulation equilibrium towards reduced anticoagulation (20). The persisting pro-thrombotic state promotes low-grade inflammation and visa versa, resulting in a chronic vicious circle. A simultaneous up-regulation of protease-activated receptor-1 (PAR-1) in intestinal muscle cells may represent a link between endothelial dysfunction and radiation-induced fibrosis (21). In addition, RT-provoked increased Rho Kinase signaling induces intestinal barrier dysfunction, leading to exposed mucosa and compromised secretory and absorptive functions (22). Some of the common symptoms can be explained directly by these mechanisms, but there are also secondary phenomena that contribute to GI symptoms. Examples are SIBO due to motility changes, bile salt malabsorption due to damage in terminal ileus and malabsorption of specific nutrients such as vitamin B_{12}, lactose or other carbohydrates (4).

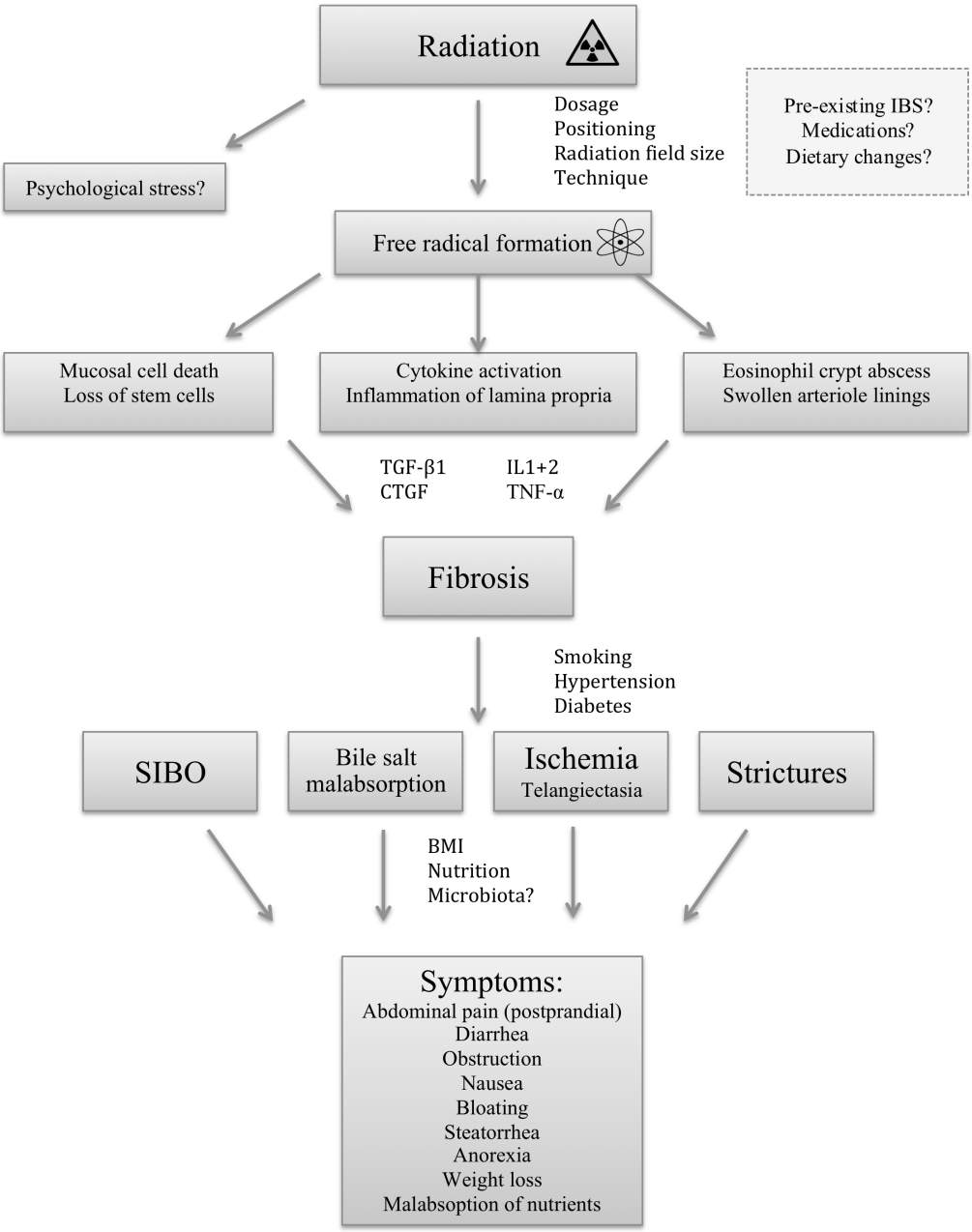

Figure 1: Overview over RISBD pathophysiology
Radiation treatment induces the formation of free radicals, which promote changes in the cells of the bowel wall. Cell death, vascular changes, inflammation and swelling lead to fibrotic tissue with malfunctions that express as clinical symptoms (17-22). IBS; Irritabel bowel syndrome, TGF-β1; Transforming growth factor β1, CTGF; Connective tissue growth factor, IL; Interleukin, TNF-α; Tumor necrosis factor α, SIBO; Small intestine bacterial overgrowth.

There are many factors that determine the degree of damage to the bowel tissue, and how prominent the symptoms become (23). First of all, clinical/technical factors play a major role, like radiation technology, dosage, regimen, size and site of radiation field and concurrent chemotherapy (1). It is estimated that a total dosage of 50 Gy will result in 50% of the patients developing RISBD within five years (24). The fact that concurrent use of

chemotherapy deteriorates the acute side effects of radiation, does not necessarily lead to worsen chronic late effects (4). In addition, there are patient-related factors involved in the risk of developing RISBD. Examples are cancer type and localization, comorbidities, previous abdominal surgery, genetic disposition and concurrent medications (1, 11). As endothelial vascularization is a central aspect of RISBD, conditions that reduce blood flow in general, like hypertension, diabetes, smoking and poor nutrition, can predispose to more severe late effects (23). Reduced body mass index (BMI) also contributes to a higher risk of developing chronic symptoms (4). Lately, it has been suggested that the composition and functionality of microbiota could play a role in the pathophysiological picture of RISBD (25). Andreyev et al. emphasize the importance of aiming to detect and understand the changes in GI physiology rather than focusing on the underlying pathology of the symptoms (10). They address 22 symptoms of pelvic radiation injury, and point out that by systematic investigation and treatment of the discovered abnormalities; improvement is possible (10, 26).

1.1.5 Diagnosis

RISBD patients are under-diagnosed and few are referred to further management. However, there are tools available to detect and assess the degree of tissue damage and symptom severity (11). Examples are the Royal Marsden Algorithm, the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) tissue damage grading system and the Late Effect Normal Tissues/Subjective Objective Management Analysis (LENT/SOMA) table (11, 27, 28). These tools investigate the presence of damage based on symptoms, not by endoscopic or histologic examination. Therefore no distinction is made between different possible pathologies (4). This can be a major limitation when it comes to the choice of treatment, as for example diarrhea can have many possible causes. For initial diagnosis it is recommended to perform Selenium Homocholic acid taurine scan (SeHCAT)(bile acid malabsorption), glucose hydrogen/methane breath test, upper GI endoscopy with duodenal biopsies and flexible sigmoidoscopy (2). In addition, evaluation of biological markers such as C reactive protein (CRP), calprotectin and lactoferrin has been suggested, but they provide limited information (4). Possible differential diagnoses are recurrent neoplasia, colorectal cancer, celiac disease, IBD or thyrotoxicosis, and these should be eliminated before concluding with a diagnose (4).

1.1.6 Management

The diverse and complex symptomatology of RISBD demands a comprehensive history taking and systematic investigation (2). This calls for a multidisciplinary cooperation and a holistic view on diagnosis, treatment and care. Practice guidance and an algorithm-based follow-up approach have been designed at the Royal Marsden Hospital (2, 29). This underlines the importance of collaboration between gastroenterologist, oncologist, surgeons, radiologist, laboratory service, dietitians, nurses, psychologist etc.

The management of acute and chronic radiation injury can be subdivided into prophylactic approaches and treatment approaches. Radiation technology/methodology, and use of various medications can have a preventive effect on the development of RISBD (acute and delayed). Conformal radiotherapy techniques and intensity-modulated radiotherapy (IMRT) reduce the extent of radiation damage to normal surrounding tissue. Multiple beam intensity in a three-dimensional manner narrows the radiation region and consequently allows higher doses to the tumor (30). The use of IMRT has expanded in Norway since the 1980's (31). Other influencing factors are patient positioning, use of belly board, use of absorbable mesh slings, timing of treatment (circadian rhythm) and patients bladder content during RT (1, 32). Pharmacological agents can be used as protectors, mitigators or therapeutics and include antioxidants (like vitamin E gamma-tocotrienol), statins, somatostatin analoges (like pasireotide), sucralfate, teduglutide, balsalazide and nutritional supplements like glutamine and arginine (1, 4, 33, 34). They act by decreasing inflammation, improving the vascular function, or protecting the intestinal wall through various mechanisms. Some of these are already used in the clinic (*e.g*. statins), but others are hypothetically prophylactic and still under the scope of animal and human studies (*e.g.* pasireotide).

Suggested treatment approaches are usually focused either on the symptoms or on complications. Some common symptoms can be alleviated by medications like anti-motility agents (Loperamide) or bile salt sequestering agents (cholestyramine) for diarrhea, analgesics for abdominal pain, and anti-emetics for nausea (1, 35). Loperamid is used regularly in this patient group. The effect is not well documented, and it only attenuates the symptoms without resolving the underlying problem (4). Anti-inflammatory agents like corticosteroids and sulphasalazine have shown to be effective in acute RISBD, but a recommendation for use in the chronic situation is not established (4).

Probiotics and antibiotics can be used both to prevent and treat the commonly occurring SIBO. The effect is best documented for acute radiation injury and the optimal regimen,

dosage and duration is not clear (4, 36). If antibiotics are used to treat SIBO-induced diarrhea, this is normally only a temporary solution, as the cause of SIBO (motility change) is still present. It has been suggested that probiotics, prebiotics and dietary changes which reduce the thriving potential for the bacteria, can be a useful alternative approach (16). Other suggested dietary approaches include supplements of micronutrients, use of medium chained triglycerides (MCT), exclusion diets, supportive enteral diets and parenteral nutrition (1, 4, 37-41). Surgery and endoscopic therapies should be avoided because of the vulnerability of the abnormal fibrotic and hypoxic tissue, but is necessary in some cases. This includes situations of sever strictures, fistulas, perforation, recurrent cancer or extensive and persisting symptoms that favor the establishment of short bowel syndrome (2, 4).

The ischemic environment in fibrotic and/or necrotic tissue in the small bowel wall of RISBD patients is characterized by cell hypoxia, hypocellularity and hypovascularity, which can explain many of the known findings and symptoms. Hyperbaric oxygen (HBO) treatment has shown to promote angiogenesis, fibroplasia and tissue restructuring, resulting in an increased number of small blood vessels and better function of the ischemic tissue (16, 42, 43). The core-mechanism is a massive increase in tissue oxygen pressure, which stimulates neoangiogenesis in ischemic tissues due to a steep fall of the pO_2. Patients are placed in a hyperbaric chamber, usually pressurized to 2.4 atmospheres (ATA), breathing 100% oxygen for 90 minutes daily until a total of 30-40 treatments (43). A review from 2002 found that 67 of 74 studies have published positive results of HBO for chronic radiation damage (44). This is compatible with the results of a Norwegian study looking at health related quality of life (HRQOL) after HBO (43). Results from blinded, randomized, placebo-controlled trials are lacking on the field. Therefore, the Hyperbaric Oxygen Therapy II (HOT-II) study was conducted and published by Glover et al. in 2016 (45). This phase III study on 84 participants, found no significant difference in change of symptom or HRQOL in the intervention group vs. the sham-group. This result is contradictory to the result of the first study of this type, the HORTIS study from 2008 (46), and Glover et al. stress the need for more level 1 evidence of this treatment type (45). The availability of hyperbaric oxygen treatment is generally limited to specialized centers (4). In Norway, treatment for not-acute indications is localized to the Center for hyperbaric medicine in Bergen, implying a long travel and an extensive treatment stay for many patients.

1.1.7 Role of diet in RISBD

It is well known that a diet providing good nutritional status has impact the tolerance, completion and late effect development during and after pelvic RT. The relationship is also visa versa, as acute and chronic GI symptoms can lead to insufficient diet and reduced nutritional status (47). It is reported that 11-33% of patients receiving pelvic radiation are undernourished before starting treatment, and that 83% loose weight during the radiation period (39). At the Royal Marsden NHS Foundation, a specialist center for cancer treatment in London, the focus on RISBD has been emphasized for a long time (48). They started in 2000 the GI and Nutrition Team (GIANT). From a one-year study from this clinic, it was reported that 36% (n=326) of the patients referred had a need for dietetic interventions (48). A review from UK found dietary advises to be the second most used treatment for late GI symptoms after the use of anti-diarrhea agents (49). Many factors in the clinical picture of RISBD, imply a risk for malnutrition and weight loss, like diarrhea, steatorrhea and vomiting, but also decreased intake, digestion or absorption (50).

In Norway, brochures are available and handed out to patients after completing RT, where RISBD is noted as a possible late effect. These brochures include counseling information about food groups that could be excluded to reduce GI symptoms. The patients are encouraged to eat a diet low in lactose and fat, and to avoid spicy foods, foods with hard baking crust and foods that induce bowel gas. It also recommend to eat small and frequent meals, and to distribute the daily fat intake over several meals (51). To what extent this approach is presented and followed, or to what degree it has an effect, is not known. A study from UK used a questionnaire to evaluate how women at risk of RISBD where coping with GI symptoms (52). About half of the 95 women included, had changed their diet, but at the same time only half of them had received dietary advises. There seemed to be no correlation in who received counseling, and who changed diet. The most prominent diet changes were eating less fruit, fiber and vegetables. When avoiding these foods without sufficient supervision, the diet can be unbalanced, low in important micronutrients, and not in line with a healthy diet that reduces risk of lifestyle diseases (52).

In clinical practice, a diet low in fermentable oligosaccharides, disaccharides, monosaccarides and polyols (FODMAP), has been tested for this group of patients. The experienced results seem promising in form of improvements of GI symptoms, but clinical trials have not yet been published (1). Many RISBD patients report postprandial discomfort,

and relate the severity and onset of symptoms to dietary intake. In a study, RISBD patients reported exacerbated GI symptoms after intake of bran muffin, berries, cabbage, brussels sprouts, broccoli, mixed salad, Ceaser salad, baked beans, lentils and nuts (53). Fifty percent of women with RISBD reported increased symptoms after consumption of these foods, compared to 21% of controls. Many of these foods contain FODMAPs. In addition, only 20% of the RISBD-group felt symptoms after eating food with high fat intake, despite the fact that many of them were trying to avoid high-fat foods (53).

The rationale behind the idea that a low FODMAP diet (LFD) could have an effect on RISBD patients includes the fact that their symptoms are similar to what is seen in IBS, a condition successfully treated with LFD. In addition, the physiological damage to the small bowel can reduce the function of brush-border enzymes and luminal transport proteins, resulting in decreased carbohydrate breakdown and uptake (16). IBS patients often experience visceral hypersensitivity. This causes pain-related neural stimulation after normal postprandial distention of the gut lumen, followed by an abnormal motility response of distention. This again can explain symptoms like diarrhea and/or constipation often seen in RISBD patients (16). Many patients report their symptoms to be postprandial and related to intake of specific foods. Consequently, a large proportion of them have excluded different foodstuffs from their diet, either by own initiative, or after advise from health professionals (53). Based on this, studies investigating dietary interventions to limit the symptom-burden have been, and should be conducted.

1.1.8 Associated conditions

Urological problems, fertility- and sexual problems, lymphedema, neuropathy, fatigue, emotional and psychological problems are all conditions that are associated with pelvic radiation, and should be taken into account in a holistic management for these patients (2, 14).

1.2 The low FODMAP diet

1.2.1 Rationale for the low FODMAP diet

The low FODMAP diet was primarily introduced mainly for functional gastrointestinal disorders (FGID) like IBS and functional bloating (54). The acronym FODMAP is short for fermentable oligosaccharides, disaccharides, monosaccharides and polyols. This includes oligosaccharides known as fructans (fructo-oligosaccharides, FOS) and galactans (galacto-oligosaccharides, GOS), the disaccharide lactose, the monosaccharide fructose in excess over glucose and polyols (sugar alcohols) (55). The rationale why these carbohydrates can promote symptoms in vulnerable guts is that they through different mechanisms give distension in the wall of the small and large bowel (Figure 2). The five different nutrients have different chemical characteristic and sources, but they all have in common that they are small (<10 sugar units) and therefore osmotic active, and that they are not fully absorbed in the small intestine and hence rapidly fermented by GI bacteria. Ingestion of FODMAP will therefore increase the volume in the intestines in form of gases (hydrogen, methane and carbon dioxide), liquid (osmotic activity draws water into the gut lumen) and also solids (FODMAP containing grains, fruits and vegetable are fiber sources *i.e.* bulking). In addition, the bacterial fermentation will result in production of short chain fatty acid (acetic, propionic and butyric acids), which can affect the motility of the intestinal wall. The distention of the bowel wall promotes pain and alters colonic motility and transit time (56). As in IBS, RISBD patients may have a dysbiosis in microbiota, which means an abnormal location or composition of bacteria (57). The increased luminal volume itself, together with motility changes, can explain the known symptoms of both IBS and RISBD (pain, discomfort, diarrhea, constipation, bloating, flatulence and fecal incontinence) (55).

Poor uptake of most FODMAPs is common, but this physiological malabsorption is usually well tolerated in healthy people. Although everyone will experience some abnormal symptoms when consuming large enough quantities of FODMAPs, the threshold and the severity of symptoms vary individually. FODMAP intake is more problematic when having a vulnerable or damaged intestine by any cause (57). LFD has been studied extentively and the evidence for its effect for IBS is well documented (56, 58, 59). Because of this, and because of similar symptoms and disease characteristics, the diet has also been tried for other conditions like inflammatory bowel disease (IBD), diverticulitis, ileal pouch, celiac disease and also exercise-induced GI symptoms (57, 60-63).

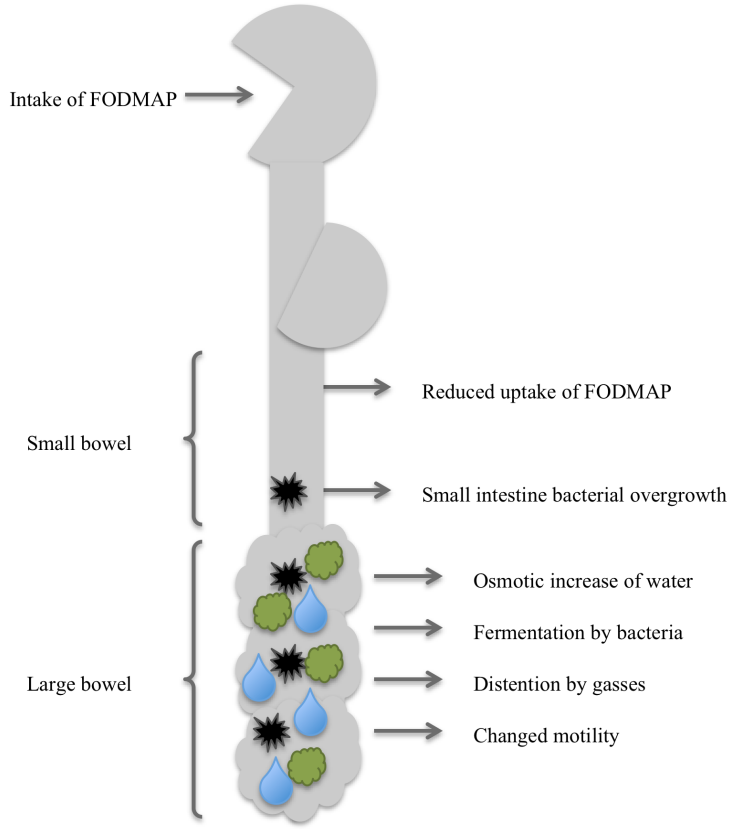

Figure 2: The progress from FODMAP intake to IBS symptoms
FODMAPs are poorly absorbed in the small intestine and can cause bowel distention by gas, water and solids, which promote GI symptoms. FODMAP; Fermentable oligosaccharides, disaccharides, monosaccharides and polyols, IBS; Irritable bowel syndrome

1.2.2 Different FODMAP groups

The tolerance for the different FODMAP groups and the quantities vary between individuals (63). Distinctive subgroups of these carbohydrates will consequently be of individual importance when restricting FODMAPs from diet. Therefore, the rationale for the problematic digestion for each subgroup should be explained briefly for patients converting to the diet. This can improve the compliance (55).

Fructose has a transport mechanism with low capacity when the monosaccharide is in excess over glucose. This is the case in some fruits, sweeteners like honey and in concentrated fruit (juice, dried fruit and large serves). The reason for this is that the fructose transporter with highest capacity, GLUT-2, demands coexistence of glucose for absorption. The individual capacity for free fructose can be measured by a hydrogen breath test. Low activity/lack of the lactose cleaving hydrolase, lactase, at the brush border is the reason why lactose is scarcely absorbed. This can be permanent or temporary, and can also be measured by a breath test.

Low amounts/activity of hydrolases also explains the reduced absorption of fructans and galactans. Fructans are chains of fructose and appear as storage of carbohydrates in cereals, fruits and vegetables. Sources of galactans are beans, lentils and peas. They are thought to be non-absorbable, and are either excreted or fermented by microbiota. Polyols can be problematic due to the lack of an active absorption mechanism, and therefore the uptake depends only on passive diffusion through pores. The amount absorbed consequently depends on molecule size, transit time and pore size (which vary throughout the small intestine and is affected by epithelial damage). Polyols are present in some fruits, mushrooms and as sweeteners (55).

1.2.3 Application/implementation of the diet

As the tolerance for FODMAPs will be exceeded if the total amount consumed is large enough, FODMAPs need to be restricted completely, not only certain subgroups individually (55). To see the effects on symptoms, the diet need to be withheld for 2-6 weeks (56). The approach will not cure the cause of the symptoms, but can potentially be symptom relieving. The diet has until now mostly been studied counseled by a dietitian in a one-to-one approach. This permits the counseling to be focused on food alternatives relevant for the individual patient, based on their regular eating habits (56). If symptom relief is achieved after some weeks on strict diet, the next step is to reintroduce FODMAP groups one by one, to find out which one, and in which amount the subgroups are tolerated. This second phase is called the reintroduction phase, and aims to customize a diet with minimal restrictions and at the same time minimal symptoms. The procedure is to systematically introduce specific amounts of foodstuff that are high in one FODMAP group but low in the others when being symptom free. If it's tolerated, larger amounts are consumed over three days, and thereafter a new subgroup can be tried. If symptoms reoccur, the subgroup is not tolerated and a strict diet should be restarted until symptom control is re-achieved, before testing the next group.

1.2.4 Limitations of the diet

LFD has some disadvantages and is not the right solution for all individuals. For instance, prolonged adherence to the diet possibly reduces fructose absorption capacity. This, together with a restricted food variety, can imply a risk for inadequate intake of specific nutrients and prebiotics. Furthermore, some recent studies report that it can alter the composition of gut microbiota in an unfavorable way (55, 56). A study comparing LFD and a traditional

Australian diet, found that after 6-8 weeks on LFD, the abundance of health benefitting bacterial groups was reduced (61, 64). These groups of gut bacteria are the butyrate-producing ones (Faecalibacterium Prausnitzii), which seem to be generally reduced also in patients with IBD. This underlines the uncertainty for safety of long-term restriction of FODMAPs. Not all IBS patients seem to be responders to the diet, reflecting the unclear mechanisms behind the symptoms, but also individual compositions of the intestinal microbiota (59, 65).

Risks for inadequate intake of specific essential nutrients on a strict LFD is especially important for the intake of fiber and calcium. Close continuous counseling from a dietitian seems necessary both for adherence and safety, and this limits its accessibility (64). Combined with the lack of information about FODMAP content on food packages, the diet is resource-demanding in many ways (59).

1.3 Study rationale

The main reason to introduce the LFD for patients with RISBD is the similarity in symptoms between this condition and IBS. Symptoms like abdominal pain/discomfort, abnormal bowel habits, bloating and flatulence are seen in both illnesses, even though RISBD has an organic cause unlike IBS. In addition, the LFD shares some of the principles seen in the traditionally dietary advises given to patients after pelvic radiation. This is why clinical dietitians in Norway have tried the LFD approach for this patient group. The effect on symptoms seems promising, but there is lack of clinical trials to confirm (or disprove) this. The aim of our study was to investigate the effect of LFD on symptoms and quality of life in patients with RISBD.

2. SUBJECTS AND METHODS

2.1 The study

The study was conducted as a master thesis in clinical nutrition at the Faculty of Medicine and Dentistry at the University of Bergen (UiB), in collaboration with the Section of Gastroenterology, Medical Department at Haukeland University Hospital (HUS). The study coordinator was master student Trine Larsen. The study protocol was approved by the Regional committee for medical and health research ethics (REC) for western Norway, May 2016 (2016/567)(Appendix 1).

2.2 Patient recruitment

The period of recruitment was from late August 2016 to January 2017. Patient recruitment was conducted using multiple approaches to reach patients who fulfilled the inclusion criteria. This was necessary since this patient group is relatively under-diagnosed, and defined as outpatients who no longer suffer from cancer. Patients were recruited by advertisement through the Association of Gynecological Cancer in Norway; a patient association affiliated with the Norwegian Cancer Society. Advertisement was published on the webpage and on the Facebook page of both the national and the regional association in Bergen. In addition, the regional association sent information about the study to all their members as private e-mails. A call for participants was also made through the web page for Prostate Cancer, the National Association against Digestive Disorders and through lecturers at the National Healthcare Institution for Cancer; Montebello center, in Mesnali. Recruitment was also attempted through the list of patients referred to The Hyperbaric Medical Unit (HMU) at the Department of occupational medicine, the outpatient service at the Department of Gynecology and the Department of Medicine, all at HUS.

The patients who filled the inclusion criteria were contacted by phone, and some contacted the master student unprompted by phone or email. The participants considered eligible for the study received a detailed, oral and written presentation of the study, and a written informed consent was signed (Appendix 2). As patients from many parts of Norway were included, the consent was handed in by e-mail, mail or during personal meeting. All participants were informed about the right to self-determination and that withdrawal from the study at any time would not affect further treatment.

2.2.1 Inclusion criteria

- Subjects between 18-70 years of age
- Signed informed written consent
- Patients who suffer from radiation-induced small bowel disease
- Patients with radiation-induced IBS symptoms referred to and/or accepted for HBO treatment
- IBS symptoms confirmed by the Rome III-criteria
- IBS symptoms with/without rectal bleeding

2.2.2 Exclusion criteria

- Patients already eating a diet low in FODMAPs (if so they have to stop the diet at least 3 weeks before entering the study)
- Patients already receiving HBO treatment

2.3 Study design

This pilot study used a quantitative open, prospective, intervention design with an intervention group consisting of 11 subjects. After signing written consent, a start date for the 4-week diet period was settled. The participants started the diet period consecutive according to recruitment and what was suitable for the individual participant. Figure 3 illustrates the chronological progress of the clinical study. Prior to the diet period, all subjects received counseling in how to follow the LFD. Written diet information, and lists of foodstuffs to exclude and alternatives to eat were handed out. The participants made a 3-day food record (Appendix 3), and questionnaires regarding IBS criteria, RISBD grading, GI symptoms and quality of life were completed. There were also made a short interview to collect baseline characteristics and information about the details of the cancer treatment. This was done in a one-to-one meeting at HUS. For participants who lived elsewhere in Norway than in the Bergen-area, the questionnaires were filled out at home and sent by e-mail or mail. These participants were given diet counseling by phone. The written information about the diet was developed by the master student in clinical nutrition (*i.e.* study coordinator), and was based on a booklet from the dietitians at HUS, supplemented by details from materials published by writer and blogger Julianne Lyngstad and the low FODMAP Diet Application from the Monash University, Australia. (Appendix 4 and 5)

During the diet period, the participants were encouraged to contact the master student by phone or email at any time in case of questions or ambiguities of any kind regarding the diet.

During the last days of the diet period the subjects again made a 3-day food diary, and filled out new questionnaires. At this point they also filled a compliance scheme to register to what degree the diet had been followed, and how demanding the diet felt for them (Appendix 6). A similar scheme was completed also 4-6 weeks after the diet period (Appendix 7).

After completing the study, the participants who achieved a decrease in IBS symptoms and/or an increased quality of life, were offered counseling in the second phase of the LFD. This phase is the reintroducing phase that aims to uncover the type and amount of the FODMAP subgroups that cause the individual subject symptoms, and which groups can be reintroduced to the diet (Appendix 8).

2.3.1 Study timeline

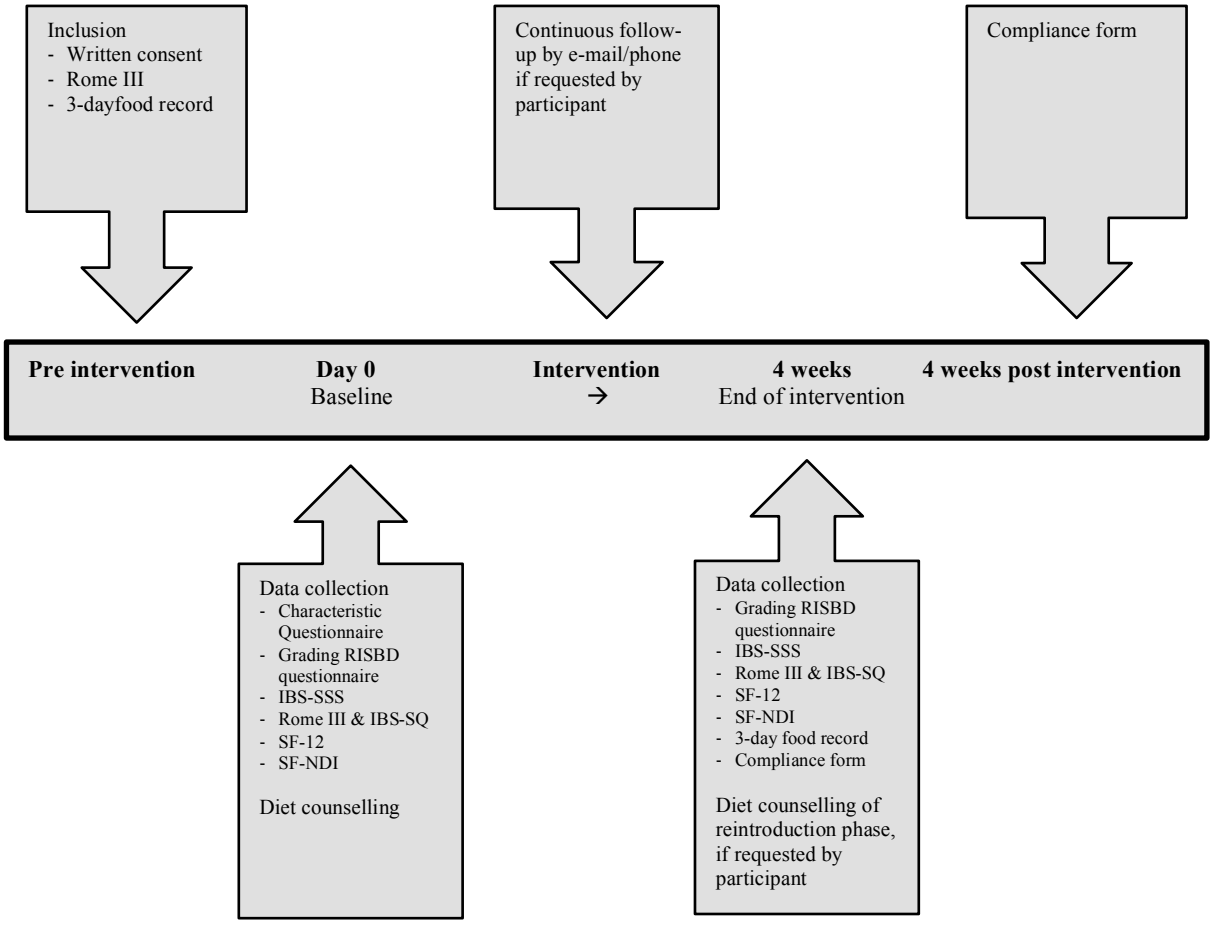

Figure 3: Study timeline
RISBD; Radiation-induced small bowel disease, IBS-SSS; Irritable Bowel Syndrome Severity Scoring System, IBS-SQ; Irritable Bowel Syndrome Symptom Questionnaire, SF-12; 12-item Short Form Survey, SF-NDI; Short Form Nepean Dyspepsia Index

2.4 Hypothesis

The aim of this pilot study was to answer the following questions:

1. Are GI symptoms alleviated in patients suffering from RISBD when adapting to a low FODMAP diet? If so, which symptoms are alleviated and to what degree?
2. Will a low FODMAP diet have any influence on health related quality of life in subjects with RISBD?

Null hypothesis: There will be no differences in symptoms or health related quality of life before and after an intervention with the low FODMAP diet.

Alternative hypothesis: The study participants will experience a relief in symptoms and an increased health related quality of life after an intervention with the low FODMAP diet.

2.5 Data collection methods

2.5.1 Food record

The participants were asked twice during the study period to do a prospective food record for three coherent days, including two weekdays and one weekend day. This method implies a self-reported registration off all foods and beverages consumed. In addition to the type, brand, ingredients and preparation method, the amount of food should be registered as accurate as possible. This can be done by either weighing all foods in advance or by estimating amounts by household utensils (66). The food record was a standardized scheme developed at the Department for Clinical Nutrition at HUS (Appendix 3). The method of using a 3-day prospective food record is the most validated one for measuring dietary intake (67). The first record was used to estimate the participants' intake of FODMAP at baseline, and the second was used to evaluate adherence to LFD. Information about intake of energy, macronutrients, dietary fiber and calcium was also registered from the records, to evaluate possible changes from baseline to end of intervention. These data were obtained by plotting the food records into the Norwegian online diet tool *Kostholdsplanleggeren* (68).

The baseline intake of FODMAP was calculated from the baseline food record, using the Swedish nutritional calculation program, *Dietist Net Free.* The program contains a recently added database developed by three former master students at UiB. They plotted FODMAP values from Australia, Denmark and Norway (63, 69-72). Norwegian values were only available for the content of lactose in dairy products. For mixed products the database values

of FODMAPs were estimated from Norwegian recipes at *matprat.no*, and the recalculation of household utilities to grams found in the Norwegian diet tool *Kostholdsplanleggeren.* Still the database in *Dietist Net* has limitations for mixed foods. For example was the FODMAP content of instant tomato soup and chocolate chip cookie registered as 0 g in the database. To estimate the content of such foods, we used traditional recipes and the ingredient list for the products together with values from Australian and Norwegian analysis. This was done for all the FODMAP containing foods and ingredients and thereafter the sum of FODMAPs in the respective meal was calculated. In addition to the sum of overall FODMAP intake, the contribution from different FODMAP-groups was registered to state the main source of FODMAPs for each participant. The FODMAP groups in the database are fructose, lactose, fructans, galactans, free fructose, polyols, GOS and FOS. The FODMAP intake was estimated only at baseline, not at 4 weeks. The FODMAP intake was assumed to be so negligible if the diet was followed properly, that the calculation would have been inaccurate. Instead, the compliance form filled at the same time point, was used to evaluate if the FODMAP intake was sufficiently low.

2.5.2 Baseline characteristics questionnaire

An Ad hoc questionnaire was used to register baseline characteristic of the participants and information about their former cancer treatment (Appendix 9). This questionnaire was, in contrast to the others, not handed out to the subjects to fill on their own. In stead, the study coordinator asked the questions verbally. This made it possible to ask follow-up questions if needed. The information collected by this form included details about the RT received; like number of fractions, dosage size, other concurrent treatment forms, medications, and also GI symptoms. In addition, factors that affect blood circulation like smoking, diabetes, blood pressure and earlier pelvic surgery, were noted.

2.5.3 Ad hoc questionnaire for grading of radiation injury based on RTOG

In order to register to what extent the participants suffered from RISBD, we used the Radiation Therapy Oncology Group and European Organization for Research and Treatment of Cancer (RTOG/EORTC) late radiation morbidity scoring scheme (27). It includes characteristics that classify five different grades of radiation damage to specific organs and tissue types. Grade 0 means absence of damage, and 5 means the damage led to death. Based on the characteristics for small and large intestine a questionnaire was compiled and handed

out to the patients (Appendix 10). This form was initially supposed to be completed only before the diet period, with intention to include the resulting grade as a baseline characteristic. However, the scheme was also completed after the diet period, as it in retrospect seemed suitable also to measure change in symptom severity.

2.5.4 Rome III Diagnostic criteria for functional gastrointestinal disorders

The Rome III Diagnostic criteria for IBS were used to assure that the subjects fulfilled the inclusion criteria for the study (73). The criteria are as follows:
"Recurrent abdominal pain or discomfort at least 3 days/month in the last 3 months, associated with two or more of the following:

- Improvement with defecation
- Onset associated with a change in stool frequency
- Onset associated with a change in form (appearance) of stool

Symptom onset at least 6 months prior to the diagnosis, with the above criteria fulfilled for the last 3 months" (73)

A Norwegian translation of the Rome III Diagnostic Questionnaire for Adult Functional GI Disorders was used to evaluate if the criteria were met (Appendix 11)(74). In addition, the participants were asked the criteria directly through questions in the Rome III and Kane et al. IBS-symptom questionnaire (described later).

2.5.5 Assessment of symptoms

To measure the intervention's effect on symptoms, we used two different questionnaires. Despite the fact that the forms have some overlapping items, we wanted to assess the change in symptoms as accurate as possible, and therefor asked the participants to complete both.

2.5.5.1 IBS-SSS: IBS-Severity Scoring System

To measure subjective alteration of symptoms, the standardized and validated questionnaire Irritable Bowel Syndrome Severity Scoring System (IBS-SSS), was filled before and after the diet period (75). The scoring system contains five items rated with a 0-100 point visual analog scale (VAS). The items include severity and frequency of abdominal pain, severity of abdominal bloating, dissatisfaction with bowel habits and interference with life in general. Frequency of pain is rated as 1-10 days, and the answer is thereafter multiplied by 10 to

enable incorporation with the other items. The maximum total score of 500 indicates the worst degree of symptoms and the score can be used to classify IBS as in remission (<75), mild (75-175), moderate (175-300) or severe (>300). A reduction in the total score of ≥50 points is considered a significant improvement. The scoring system fits the purpose of measuring improvement since it is known to be sensitive to change in a relative short period of time (75). In this study an extended version of IBS-SSS was used. In addition to the above-mentioned five items, 10 questions regarding GI complaints and comorbidity symptom severity was asked (Appendix 12). The supplied questions are also rated as 0-100 point VAS scores and cover nausea, vomiting, early satiety, headache, backache, tiredness, belching and/or gas passing, heartburn, sudden urge to urinate, thigh-pain and pain in muscles and/or joints. The additional questions were compiled in Sweden but translated to Norwegian by master students at UiB in 2014.

2.5.5.2 IBS-SQ: Rome III and IBS symptom questionnaire

A combined questionnaire including the Rome III criteria for IBS, characterization of IBS subtype, and grading of symptoms was completed by participants before and after the diet period (Appendix 13). The first two parts are based on the IBS criteria from Rome III, and formulated by a Norwegian researcher group (76). The first part contains questions answered yes/no to judge if Rome III criteria are met. The second part asks about stool consistency and problems regarding defecation to characterize which subtype of IBS the subject suffers from; IBS-diarrhea (IBS-D), IBS-constipation (IBS-C) or IBS-mixed (IBS-M).

The last part of this scheme is called IBS symptom questionnaire (IBS-SQ) and was created by Kane et al. and Mathias et al. (77, 78). It contains six items were the subjects grade their symptom severity from 0-10 for nausea, bloating, abdominal pain, constipation, diarrhea and anorexia (loss of appetite). The IBS-SQ defines participants to have active IBS symptoms if the total score (max 60) of all six items is ≥15.

2.5.6 Assessment of quality of life

To measure the intervention's effect on health related quality of life we used two different questionnaires. Despite the fact that the forms have some overlapping items, we wanted to assess the change in quality of life as accurate as possible, and therefor asked the patients to complete both.

2.5.6.1 SF-NDI

Health related quality of life was measured by Short Form Nepean Dyspepsia Index (SF-NDI) (79). This questionnaire consists of 10 questions that can be divided in five sub-scales; tension, interference with daily activity, eating/drinking, knowledge/control and work/studies. The original version of NDI was developed in Australia, and consisted of 42 items. This has later been shortened to 25 items, and thereafter 10 items, but still holds a high responsiveness (ability to measure change). The questions are asked by selecting alternatives from 1 (not at all/never) to 5 (extremely/all the time). This gives a total score of 10-50 points, with the higher score indicating worse functioning/ quality of life. An individual score for all five of the sub-scales was also calculated. A Norwegian translation of the SF-NDI has been validated for patients with subjective food hypersensitivity, including IBS, and this version was used in the current study (Appendix 14) (80).

2.5.6.2 SF-12

The generic Medical Outcome 12 item Short Form Health Survey (SF-12) was also used to measure HRQOL (Appendix 15). This questionnaire is a shortened version of the 36 item Short Form Health Survey (SF-36) that was developed for the Medical Outcomes Study (MOS) by RAND Health (81). This was translated to Norwegian in 1998 (82). Like in the original form the results of SF-12 are also obtained by eight domain scores, a physical composite summary score (PCS) and the mental composite summary score (MCS)(83). The PCS are derived from the domain scores for general health, vitality, physical functioning, role-physical and bodily pain, while the MCS derives from the domains for general health, vitality, social functioning, role-emotional and mental health. As the scheme is generic, it can be used to measure HRQOL in different diseases (83).
The total score for PCS, MCS and the domain scores of SF-12 ranges from 0 to 100, with higher scores indicating better quality of life.

2.5.7 Dietary compliance during 4-week diet period

To measure adherence to LFD during the intervention period, a questionnaire developed in 2014 by four former nutritional students at UiB was applied (Appendix 6). The questions ask about satisfaction with the diet, to what extent the diet was followed, details about possible deviations from the diet, how straining the diet was perceived and satisfaction with diet counseling. The form includes a combination of VAS-scales and multiple-choice questions.

2.5.8 Dietary compliance 4-6 weeks after diet period

About one month after completing the study, the participants were asked to fill another compliance form. The aim was to assess the likelihood of adapting to the LFD as their regular diet, and to assess the progress of the reintroduction phase. This form was developed by the same group of students mentioned before, and includes both VAS-scale and multiple-choice questions (Appendix 7).

2.6 Ethical considerations

The study protocol (Appendix 16) was approved by REC west (Regional committee for medical and health research ethics, western Norway), May 2016 (protocol number: 2016/567)(Appendix 1).

Before inclusion all participants gave signed written informed consent. All personal data were kept anonymous and handled in a confidential manner. Participation in the study was voluntary and withdrawal was possible at any point without providing any justification.

2.7 Data analysis

All data from questionnaires and food records were plotted consecutively into a Microsoft Excel® data file. Statistical analyses were performed in GraphPad Prism version 7.0 for Macintosh (GraphPad Software Inc., San Diego, California, USA). Data were transferred to Prism after all data from 11 subjects had been collected.

To test data normality D'Agustino & Pearson omnibus test was used. Data following a normal distribution were presented as mean ± SD (standard deviation), otherwise as median with IQR (interquartile range). Paired t-test was used to compare the two sets of data from baseline and after 4 weeks with LFD. To quantify associations between FODMAP intake, symptoms and quality of life, Pearson correlation analyses were performed. A P-value of 0.05 or less was considered significant (*: $p \leq 0.05$, **: $p \leq 0.01$, ***: $p \leq 0.001$).

2.7.1 SF-12 scoring

To be able to calculate the PCS and MCS scores for SF-12 a free student licensure and an activation key for the use of scoring credits in the QualityMetric Health Outcomes™ Scoring Software 5.0, were requested and provided from *Optum QualityMetric Incorporated*. In prior to set PCS and MCS, four of the items in the questionnaire needed to be recoded. This was

necessary to achieve that higher values count for better quality of life for all items to enable comparison. The recoding was performed automatically when plotting the respondent's results into the software, so that 1=5, 2=4, 3=3, 4=2 and 5=1. Scoring algorithms converted all eight dimension scaled from 0-100 were 100 is the highest possible HRQOL state. The PCS and the MCS are known to change with age and also depend on sex. SF-12 scores presented are not adjusted for age and sex, and hence the results of this study can only be used for individually comparison from baseline to end of intervention, not to compare HRQOL from other studies using SF-12.

3. RESULTS

3.1 Recruitment

Recruitment was done continuously from late August 2016 until January 2017. The study coordinator/master student contacted 11 potential participants, and 12 made contact after seeing advertisements. Nine patients did not fulfill the inclusion criteria, leaving 14 participants for study inclusion (Figure 4). Of these 14 participants the majority (n=10) was recruited directly or indirectly through the National or Regional Association for Gynecological Cancer in Norway and Bergen. Five subjects contacted the study coordinator by own initiative through information from the advertisement. The remaining five of these participants were called via contact information given by already included participants. One patient showed interest after receiving information during a course at the Montebello center, and one saw the advertisement on the web page of the National Association against Digestive Disorders. An attempt to recruit patients through the Hyperbaric Medical Unit at HUS was made by calling patients on the referral and waiting list. This resulted in one included participant. The last patient was included after being referred to the study coordinator by a gastroenterologist from the Department of Medicine at HUS (Figure 5). Announcements through the Association for Prostate Cancer and the Department of Gynecology at HUS lead some patients to enquire more information about the study, but did for various reasons not contribute any extra participants to the study.

Three patients dropped out of the study after being included. Two of these dropped out during the first week of intervention and reasons for withdrawal were that the diet seemed too demanding and not suitable with own experience of tolerable and problematic foodstuff, or that the timing was poor regarding the family life situation. A third participant dropped out during the last days of the LFD period. The reason was acute sickness in the close family preventing her to complete the last food record and questionnaires. Eleven participants completed the study.

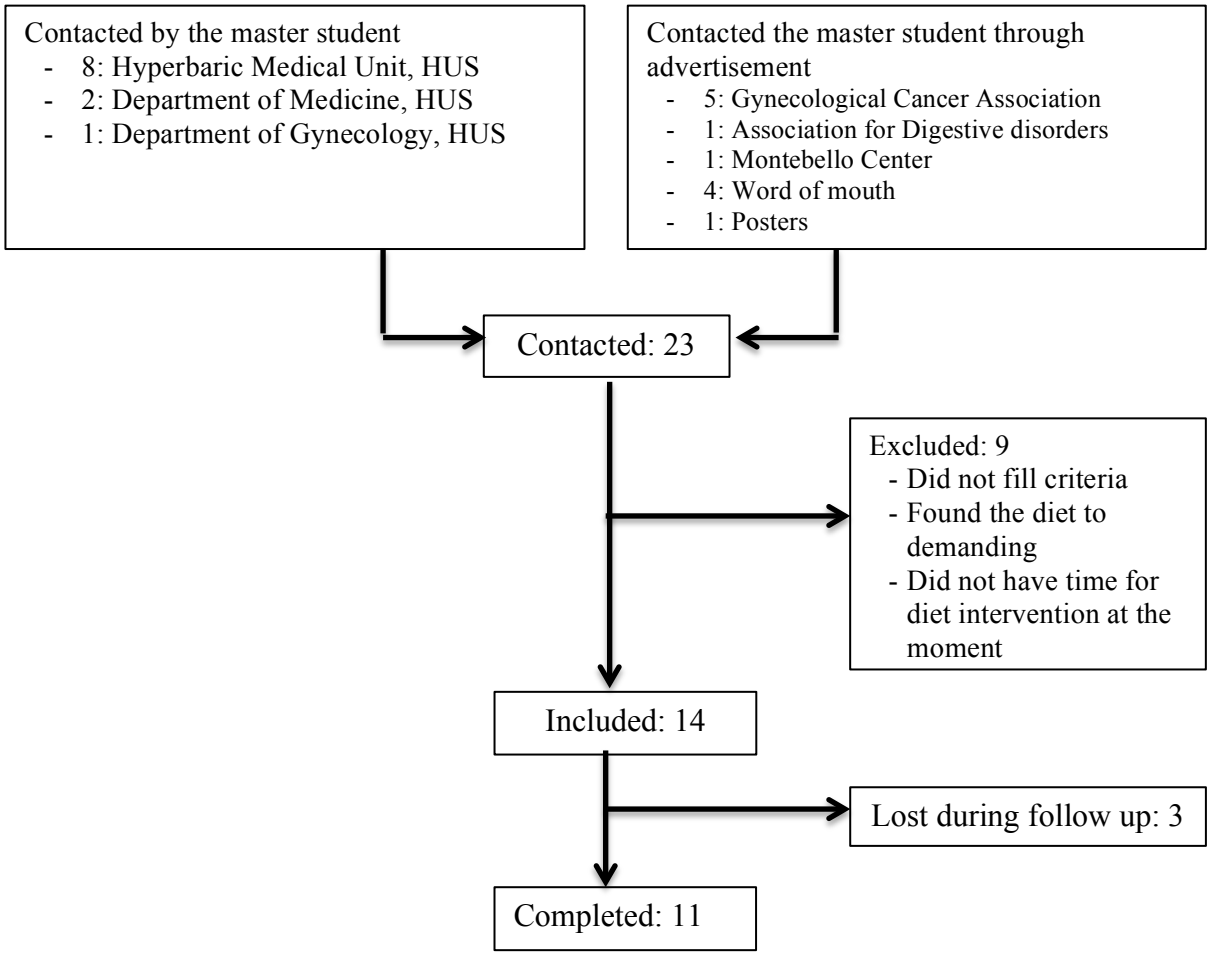

Figure 4: Flow chart of the recruitment process
HUS; Haukeland university hospital

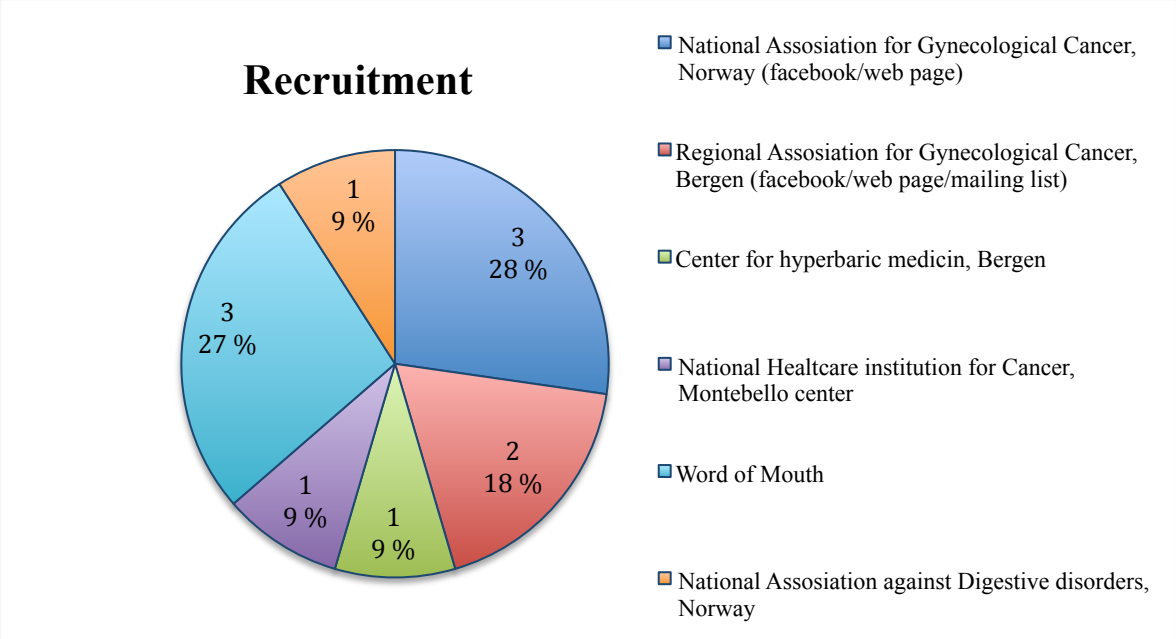

Figure 5: Pie chart of how patients were recruited to the study

3.2 Demographics

Baseline characteristics of the study population show a mean age of 46.6 years, mean BMI of 27.7 kg/m^2 and inclusion of exclusively female participants. Three male patients made contact/were contacted but they all found the diet to demanding, and therefor none were included. The complete baseline demographics are presented in Table 1.

Table 1: Baseline demographics for the study population (n=11) at baseline

Participants, n	**11**
Male/Female, n	0/11
Age, years, mean ± SD	46.6 ± 4.5
BMI, kg/m^2, mean ± SD	27.7 ± 6.9
Cancer type, n	
Cervix cancer	9
Ovarian cancer	1
Vulva cancer	1
Total radiation dosage, Gy, mean± SD	63.7 ± 16.1 (n=10)
Number of fractions, mean ± SD	27.2 ± 4.6 (n=10)
Years since radiation treatment, median (IQR)	5 (2-16)
Duration of GI-symptoms, years, median (IQR)	5 (2-10)
Grade of damage in small bowel, n: 1, 2, 3, 4, 5	2, 8, 1, 0, 0
Diarrhea, n (VAS mean ± SD)	10 (64.4 ± 19.8)
Abdominal cramps, n (VAS mean ± SD)	8 (46.5 ± 20.8)
Rectal mucus, n (VAS mean ± SD)	7 (41.1 ± 15.9)
Rectal bleeding, n (VAS mean ± SD)	3 (30.1 ± 21.6)
Constipation, n	3
Fecal incontinence, n (times/week mean ± SD)	10 (5.1± 2.8)
IBS subtype, n	
IBS-diarrhea	8
IBS-constipation	1
IBS-mixed	2
IBS-SSS severity score, n	
Remission (0-75)	-
Mild (75-175)	-
Moderate (175-300)	4
Severe (>300**)**	7

Data are presented in n, mean ± SD and median with IQR, SD; Standard deviation, IQR; Interquartile range

3.2.1 Cancer history, radiation damage and duration of GI symptoms

The majority of subjects had former cervix cancer (n= 9), one had vulva cancer and one had ovarian cancer (Table 1). Number of years since finishing RT was at median 5, ranging from 0.6 to 39. In all but two participants the onset of the GI symptoms was during or right after RT and the duration since RISBD affliction onset hence had a median of 5 years. The majority had radiation damage grade 2, according to RTOG/EORTC scoring scheme. Seven participants had IBS-SSS total score equivalent to IBS-severe (>300), which also can reflect the grade of damage in the GI tract. The mean total received radiation dosage was 64 Gy, with a mean of 27 fractions. All participants fulfilled the Rome III criteria for IBS, and eight had the subtype IBS-diarrhea.

3.3 Dietary intervention

The mean baseline FODMAP intake was 22 g/day and the FODMAP group contributing most to the total was the disaccharide lactose (mean 10 g/day) (Table 2, Figure 6). The mean overall self-reported adherence to the diet was 94.8%.

Table 2: Daily dietary intakes at baseline and at 4 weeks of intervention

Mean ± SD	Baseline	4 weeks	p-value
Energy, kcal	1841 ± 636	1407 ± 448.5	0.004**
Body weight, kg	77.4 ± 19.0	75.9 ± 18.7	0.006**
Carbohydrates incl. fiber, g	215.9 ± 94.6	152.9 ± 78.2	0.001**
Fat, g,	72.3 ± 28.1	57.9 ± 23.1	0.092
Protein, g	74.4 ± 25.3	64.3 ± 18.2	0.225
Carbohydrates, E%	46.5 ± 7.6	42.0 ± 11.0	0.134
Fat, E%	36.8 ± 6.4	38.4 ± 9.6	0.508
Protein, E%	17.4 ± 3.6	19.3 ± 4.1	0.250
Dietary fiber, g	18.8 ± 8.4	13.9 ± 5.4	0.025*
Calcium, mg	672.5 ± 205.5	576.8 ± 240.3	0.332
Total FODMAP, g	22.0 ± 11.9	Not calculated	
Lactose, g	9.9 ± 4.1	Not calculated	
Compliance, %		94.8 ± 8.3	

Data are presented in mean ± SD, SD; standard deviation, E%; energy percentage, P-value from unpaired t-test *: p≤ 0.05, **: p≤ 0.01

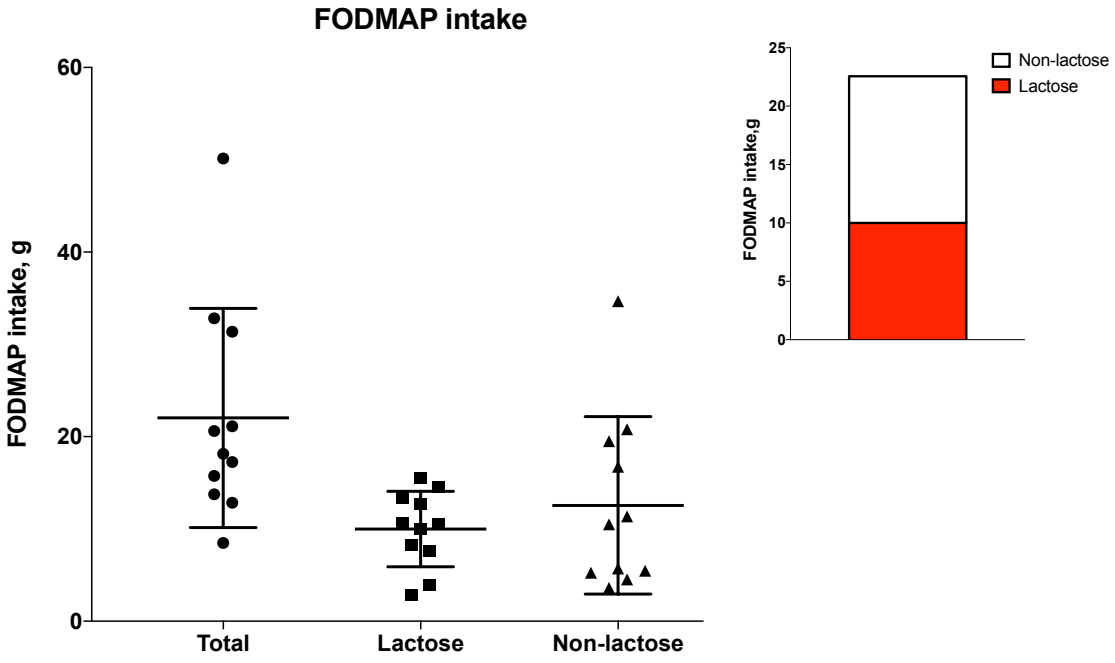

Figure 6: FODMAP intake, and consumed amount of lactose/non-lactose FODMAPs at baseline

From the food records at baseline and at 4 weeks, intakes of specific dietary components were estimated (Table 2). The mean total energy intake per day was significantly reduced with about 450 kcal from baseline to end of diet period (p=0.004)(Figure 7).

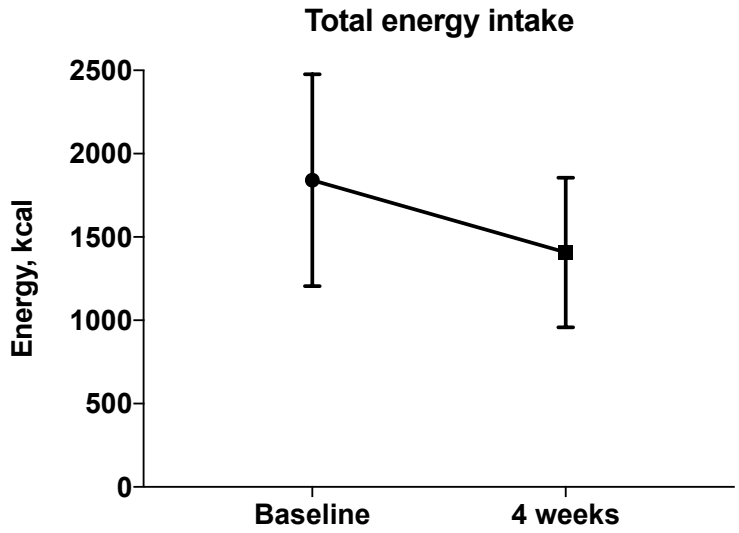

Figure 7: Mean total energy intake at baseline and at 4 weeks

Body weight was registered both before and after the diet intervention, and results are shown in Table 2. The mean change was a weight reduction of 1.6 kg (p=0.006)(Figure 8). The highest weight loss was 5 kg, and only one participant gained weight (1 kg) during the 4 weeks.

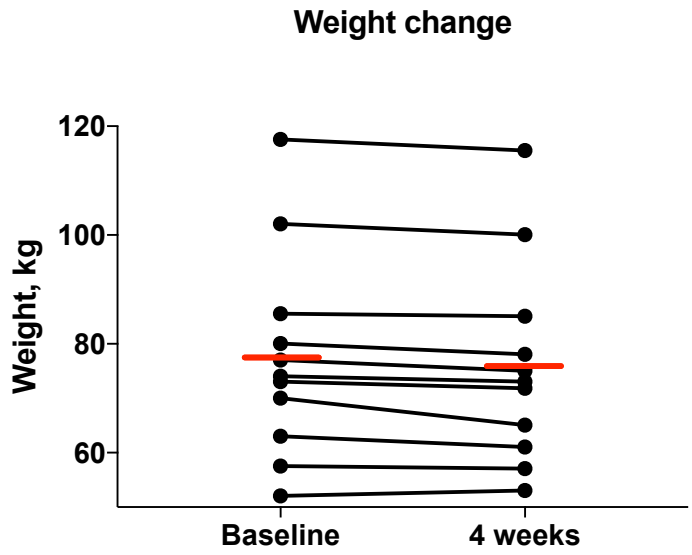

Figure 8: Individual and mean change in weight for the study population
Red line = mean

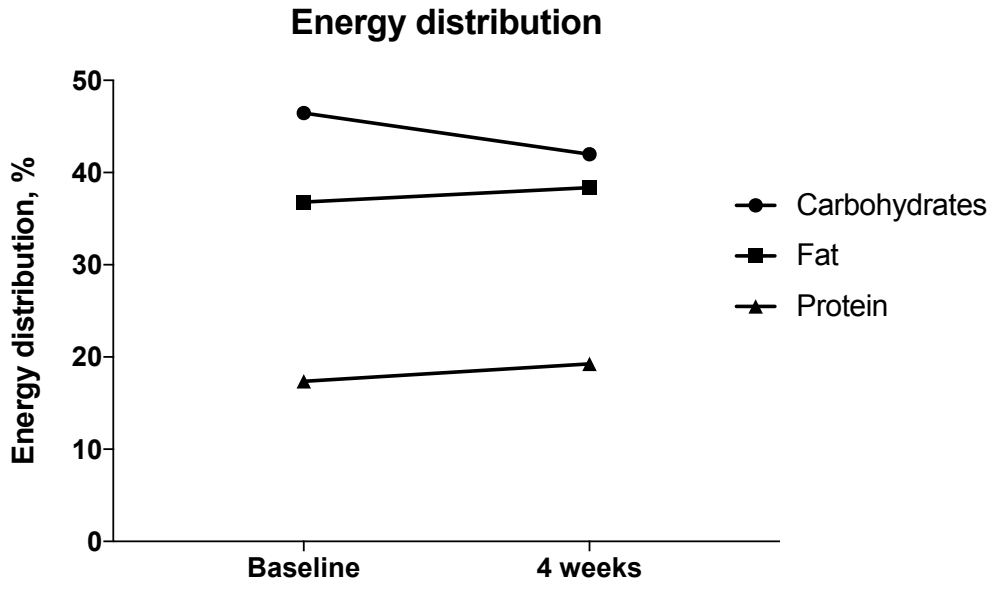

Figure 9: Distribution between the three main energy sources at baseline and at 4 weeks
Total energy intake = 100%

A detailed overview over the dietary intake is presented in Table 2. During the diet period, the participants changed their intake of macronutrients (Figure 9). A significant reduction was seen in carbohydrate intake, which decreased from mean 215.9 g/day to 152.9 g/day (Figure 10A), and the reduction in carbohydrate energy contribution was from a mean of 46.5 E% to 42 E% during intervention (p=0.134). The mean fiber intake at baseline was 18.8 g/day and decreased significantly to 13.9 g/day after 4 weeks on LFD (p=0.025)(Figure 10B). The intake of fat decreased from a mean of 72.3 g/day to 57.9 g/day (Figure 10C). This change was borderline significant (p=0.092). Despite this, the relative contribution from fat as an energy source increased due to changes in intake of other macronutrients (carbohydrate and protein). Energy provided by fat increased from 36.8 E% to 38.4 E% (p=0.508). Protein intake and contribution to total calories changed in a non-significant manner through the intervention. The amount of protein eaten fell from mean 74.4 g/day to 64.3 g/day (Figure 10D) and the mean protein contribution to total energy intake increased from 17.4 E% to 19.3 E%. Some participants consumed more calcium, but most of them consumed less at 4 weeks compared to baseline. The mean change in calcium intake was a decrease from 672.5 mg to 576.8 mg (p=0.332).

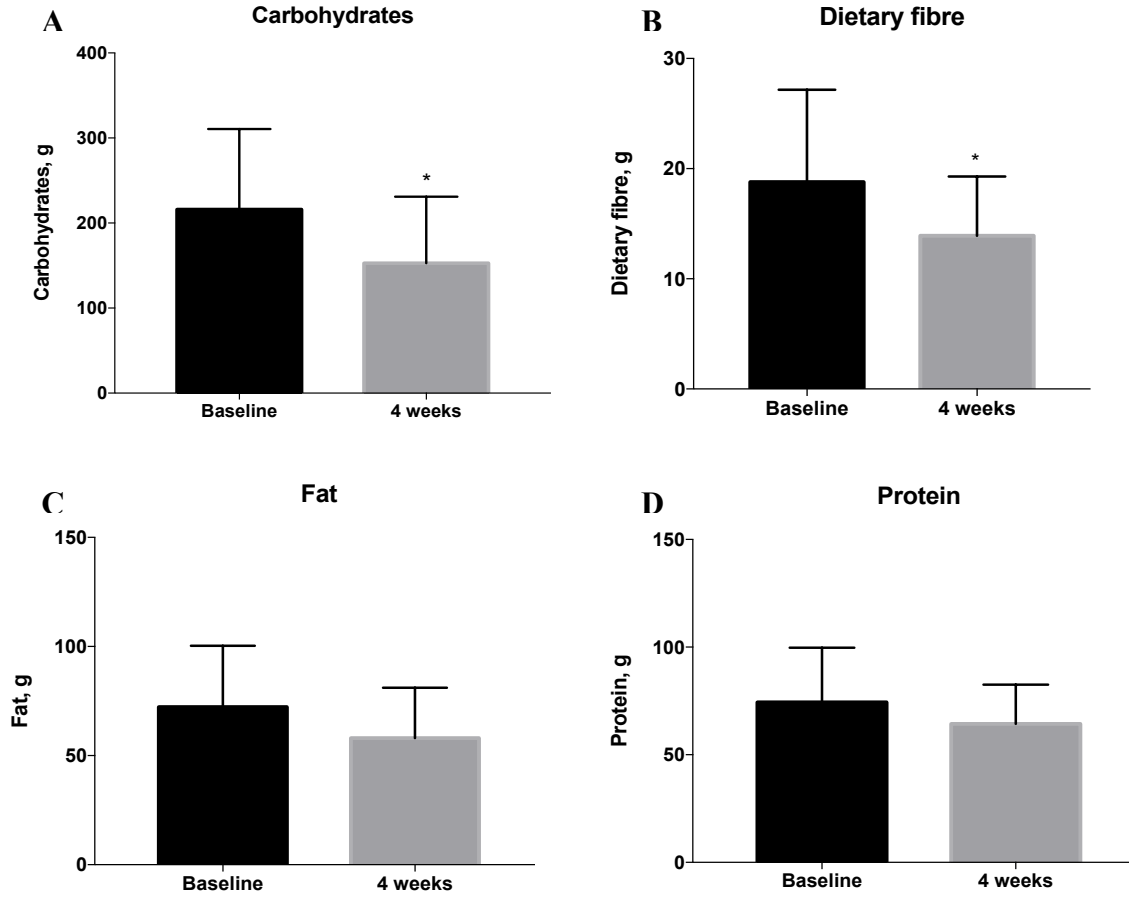

Figure 10: Mean intake of carbohydrates (A), dietary fiber (B), fat (C) and protein (D) at baseline and at 4 weeks, *: p≤ 0.05

3.4 Baseline vs. 4 weeks – Symptoms

3.4.1 IBS-SSS

Table 3 presents the results from the IBS-SSS questionnaire. All individual symptom scores dropped during the diet, but statistically significance was only reached for "abdominal pain", "abdominal distention", "dissatisfaction with bowel habits" and "interference with life in general" (p=0.006, p=0.0005, p=0.009, p=0.042, respectively)(Figure 11A). The IBS-SSS total score is a sum score of the five main questions in the questionnaire. This score decreased significantly from baseline 310.2 to 171.4 at 4 weeks (Figure 11B). For most participants the IBS-severity grade was reduced from baseline to 4 weeks, and two of them achieved remission (score <75)(Table 3).

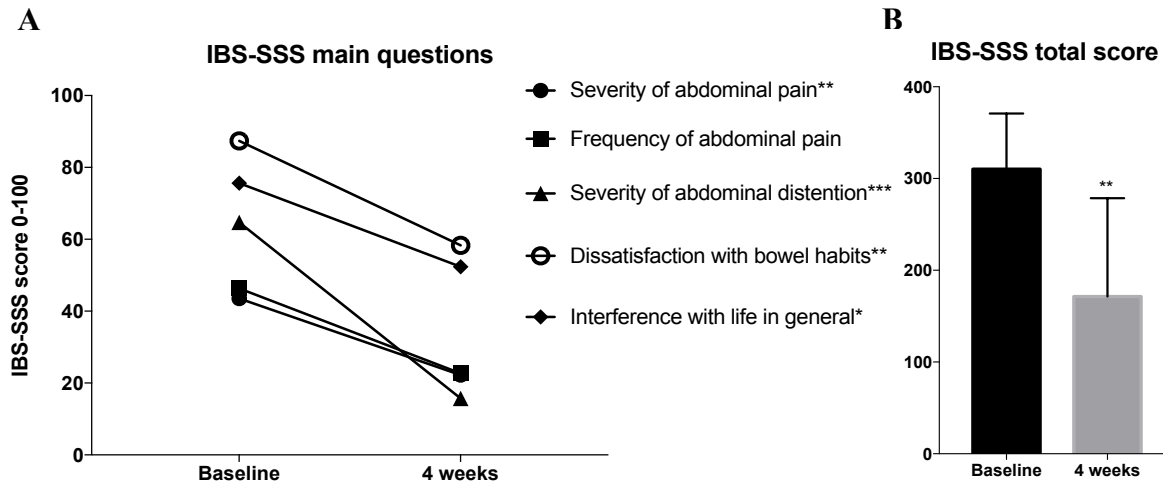

Figure 11: IBS-SSS individual score of main questions (A) and total score (B) at baseline and at 4 weeks, *: p≤ 0.05, **: p≤ 0.01, ***: p≤ 0.001

Table 3: IBS-SSS: Total, individual and additional GI complaints scores at baseline and at 4 weeks

	Baseline	4 weeks	p-value
IBS-SSS total score, mean ± SD	310.2 ± 60.7	171.4 ± 107.2	0.001**
Main questions, mean ± SD			
Severity of abdominal pain	43.5 ± 19.8	22.2 ± 25.2	0.006**
Frequency of abdominal pain	46.4 ± 30.4	22.7 ± 25.7	0.073
Severity of abdominal distention	64.7 ± 19.7	15.8 ± 26.7	0.0005***
Dissatisfaction with bowel habits	87.4 ± 12.8	58.3 ± 28.0	0.009**
Interference with life in general	75.6 ± 23.0	52.4 ± 33.4	0.042*
Additional questions, mean ± SD			
Total score	414.5 ± 111.9	263.7 ± 164.9	0.002**
Nausea and/or vomiting	25.7 ± 23.4	15.0 ± 18.5	0.022*
Difficulty in finishing meals	45.6 ± 20.2	24.1 ± 23.9	0.001**
Headache	29.8 ± 23.0	18.4 ± 22.6	0.072
Backache	47.3 ± 38.5	25.7 ± 31.2	0.006**
Fatigue	72.0 ± 23.4	50.3 ± 29.9	0.015*
Belching and/or passing gas	62.0 ± 34.7	34.4 ± 27.5	0.036*
Heartburn	18.8 ± 31.5	12.4 ± 24.6	0.061
Frequent/sudden urge to urinate	45.6 ± 37.7	44.9 ± 33.2	0.944
Pain in the thighs	27.3 ± 35.2	7.6 ± 14.8	0.038*
Pain in muscles and joints	42.1 ± 23.4	31.0 ± 26.2	0.087
IBS-severity, n			
Remission (<75)	-	2 subjects	
Mild (75-175)	-	4 subjects	
Moderate (175-300)	4 subjects	3 subjects	
Severe (>300)	7 subjects	2 subjects	
Total IBS severity grade	Severe	Mild	0.001**

Data are presented in n or mean ± SD for IBS-SSS total scores (0-500), individual scores (0-100) and scores of additional GI complaints (0-1000 and 0-10), P-value from unpaired t-test
*: p≤ 0.05, **: p≤ 0.01, ***: p≤ 0.001

3.4.2 IBS-SSS Additional GI complaints and comorbidity symptoms score

The total score of the additional questions in IBS-SSS showed a statistically significant reduction from 414.5 to 263.7 (p=0.002), reflecting improvement of symptoms (Table 3, Figure 12). The individual scores with a significant reduction were "nausea" (p=0.02), "early satiety/difficulty in finishing meals" (p=0.001), "backache" (p=0.006), "fatigue" (p=0.02), "belching and/or passing gas" (p=0.04) and "pain in the thighs" (p=0.04) (Figure 12). "Headache", "heartburn" and "pain in muscles and joints" were improved as well, but with borderline significance only (Table 3).

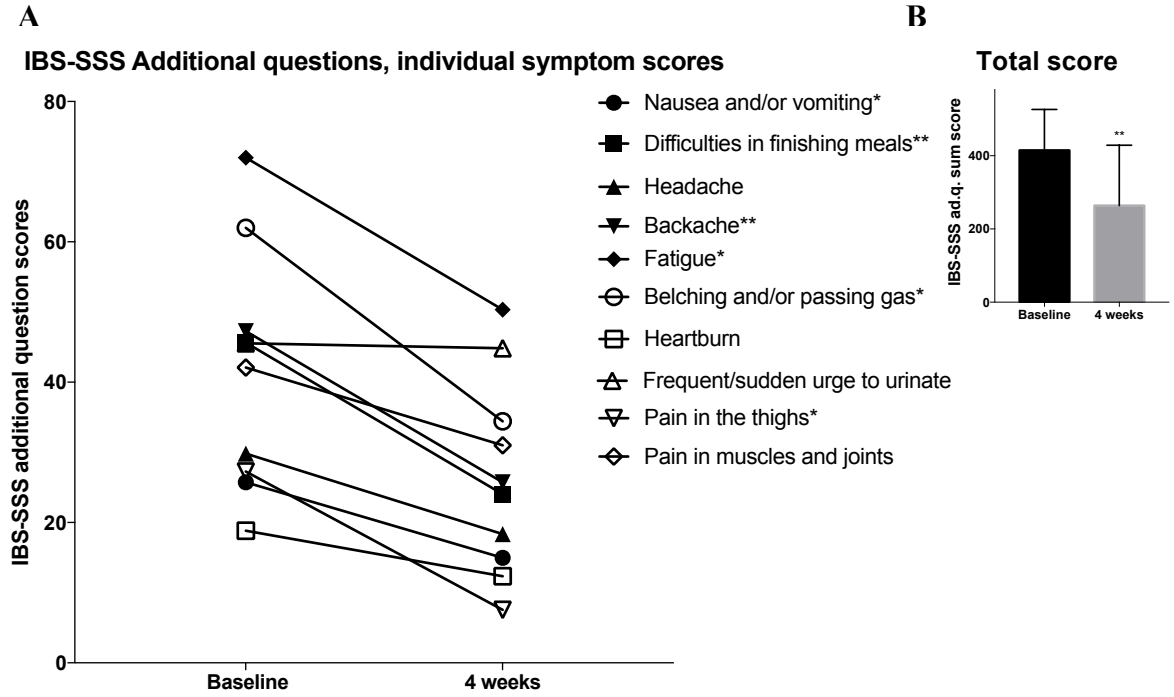

Figure 12: IBS-SSS additional questions individual scores (A) and total score (B) at baseline and after 4 weeks. Range of total score is 0-1000, range of individual scores are 0-100, *: p≤ 0.05, **: p≤ 0.01

3.4.3 IBS-SQ Grading of symptoms

Table 4 presents the results from IBS-SQ questionnaire. The mean total score was reduced significantly from 27.4 to 15.7 (p=0.002) reflecting improvement of symptoms after converting to LFD (Figure 13). The individual symptoms with a significant decrease were "bloating", "abdominal pain", "constipation" and "diarrhea", while the decrease in "nausea" was borderline significant only (Figure 13).

Table 4: IBS-SQ: Total score and individual symptom scores at baseline and at 4 weeks

	Baseline	**4 weeks**	**p-value**
IBS-SQ total score, mean ± SD	27.4 ± 4.1	15.7 ± 10.1	0.002**
IBS-SQ individual question scores			
Nausea	3.7 ± 3.3	2.7 ± 3.4	0.076
Bloating	7.2 ± 2.0	4.2 ± 3.1	0.006**
Abdominal pain	5.4 ± 1.5	2.8 ± 3.1	0.006**
Constipation	3.0 ± 1.8	1.4 ± 1.6	0.034*
Diarrhea	6.7 ± 2.8	4.1 ± 3.1	0.012*
Anorexia	1.4 ± 1.7	0.6 ± 0.8	0.158

Data are presented in mean ± SD for IBS-SQ total score (0-60) and individual scores (0-10).
P-value from unpaired t-test *: p≤ 0.05, **: p≤ 0.01

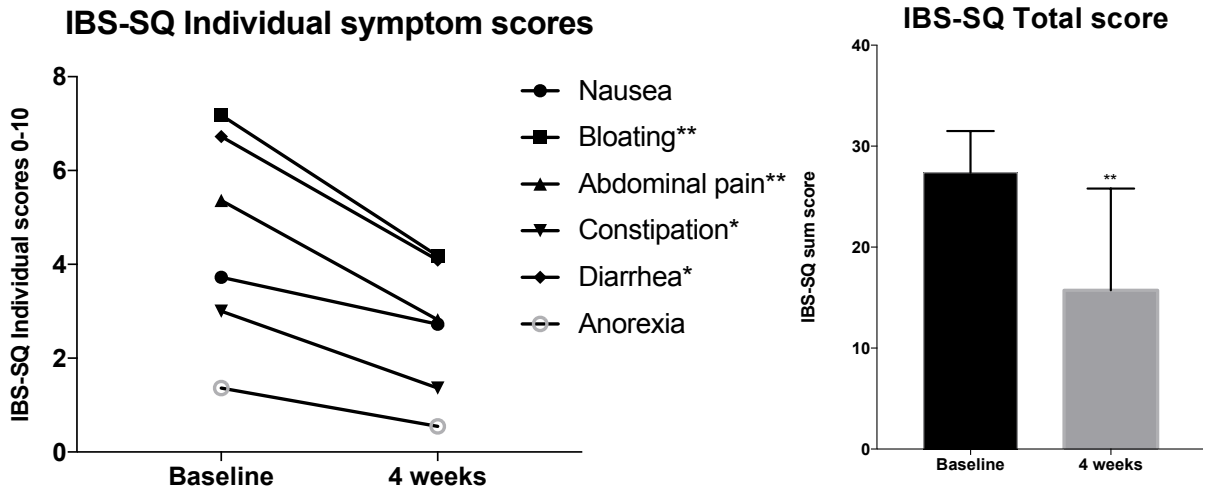

Figure 13: IBS-SQ individual symptom scores and total score at baseline and at 4 weeks
Range of total score is 0-60, range of individual scores are 0-10, *: p≤ 0.05, **: p≤ 0.01

3.4.4 Ad hoc questionnaire for grading of radiation injury based on RTOG

Only 10 participants completed the Ad hoc questionnaire both before and after intervention. Results from the VAS graded symptoms in the scheme are presented in Table 5. All the typical RISBD complaints were reduced from baseline, but the improvement was only significant for "diarrhea", and borderline significant for "Fecal incontinence" (Figure 14).

Table 5: VAS symptom scores from Ad hoc questionnaire for grading of radiation damage at baseline and at 4 weeks

	Baseline	**4 weeks**	**p-value**
Abdominal cramps, mean ± SD (n)	46.5 ± 20.8 (8)	32.3 ± 30.7 (6)	0.146
Rectal mucus, mean ± SD (n)	44.6 ± 14.1 (6)	22.8 ± 30.7 (4)	0.125
Rectal bleeding, mean ± SD (n)	30.1 ± 21.6 (3)	20.2 ± 30.2 (3)	0.193
Diarrhea, mean ± SD (n)	62.2 ± 19.7 (9)	20.2 ± 29.8 (4)	0.005**
Constipation, n	2	1	0.343
Fecal incontinence, times per week	5.1 ± 2.8	2.2 ± 3.5	0.053

Data are presented in mean ± SD for VAS scores (0-100) and for times per week (0-10) for fecal incontinence. P-value from unpaired t-test *: p≤ 0.05, **: p≤ 0.01

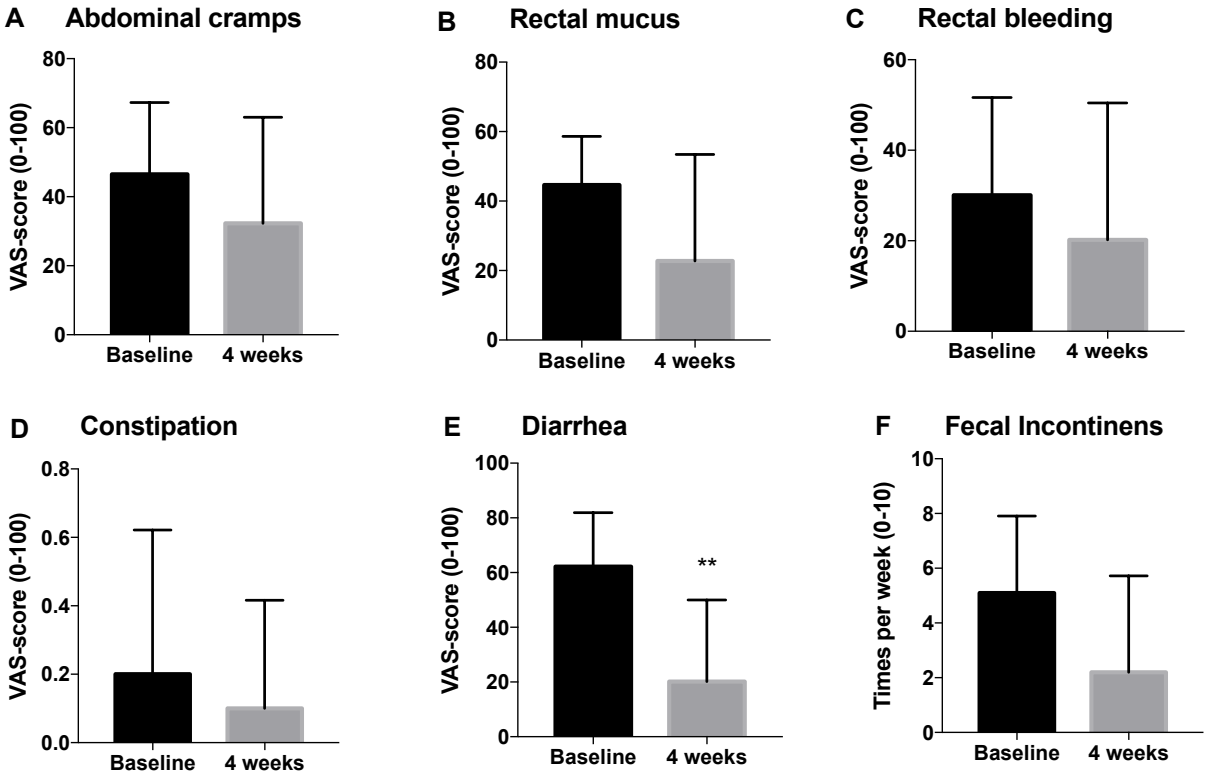

Figure 14: VAS symptom scores from Ad hoc questionnaire for RT damage grading
Showing change in scores of abdominal pain (A), rectal mucus (B), rectal bleeding (C), constipation (D), diarrhea (E) and fecal incontinence frequency (F) at baseline and at 4 weeks
*: p≤ 0.05, **: p≤ 0.01

3.4.5 Use of pharmaceuticals

The self-reported use of medications was registered. The most frequent used medication was Imodium® (Loperamide), an antidiarrheal drug that reduces peristaltic movement in the GI (84). Seven of the included participants used this drug during RT to diminish the acute symptoms of RISBD. Five have been using Imodium® after completing RT, either regularly (n=2) or only in periods when needed. Of the two participants that reported regularly usage of Imodium®, one used 2 mg daily and the other used 2 mg 2-3 times daily. The first-mentioned also reported daily use of the supplement Lectinect®, which is supposed to improve various GI-symptoms by the effect of the active herbal ingredient elderflower (85). During the LFD intervention she experimentally discontinued both drugs without reoccurrence of symptoms. The second participant tried to lower the dose to once daily, but without successful outcome.

3.5 Baseline vs. 4 weeks – Health related quality of life

3.5.1 SF-NDI

Table 6: SF-NDI Total score and subscale scores at baseline and at 4 weeks

	Baseline	**4 weeks**	**p-value**
Total score, mean ± SD	30.5 ± 9.4	18.3 ± 8.2	0.001**
Subscale scores			
Tension	3.2 ± 1.1	1.7 ± 0.8	0.001***
Interference with daily activity	3.2 ± 1.3	1.7 ± 1.1	0.004**
Eating/Drinking	3.5 ± 1.3	2.1 ± 1.2	0.011*
Knowledge/Control	2.6 ± 0.6	2.0 ± 0.8	0.038*
Work/study	2.7 ± 1.4	1.6 ± 1.2	0.009**

Data are presented in mean ± SD for total score (0-60) for subscale scores (0-10)
P-value from unpaired t-test *: p≤ 0.05, **: p≤ 0.01, ***: p≤ 0.001

Table 6 presents the change in HRQOL scores based on the completion of SF-NDI. The mean total score was 18.3 after 4 weeks intervention compared to 30.5 at baseline (p=0.001). This reduction reflects a significant improvement of perceived quality of life. A significant reduction, *i.e.* improvement of HRQOL, was achieved in all five of the subscale scores (Figure 15).

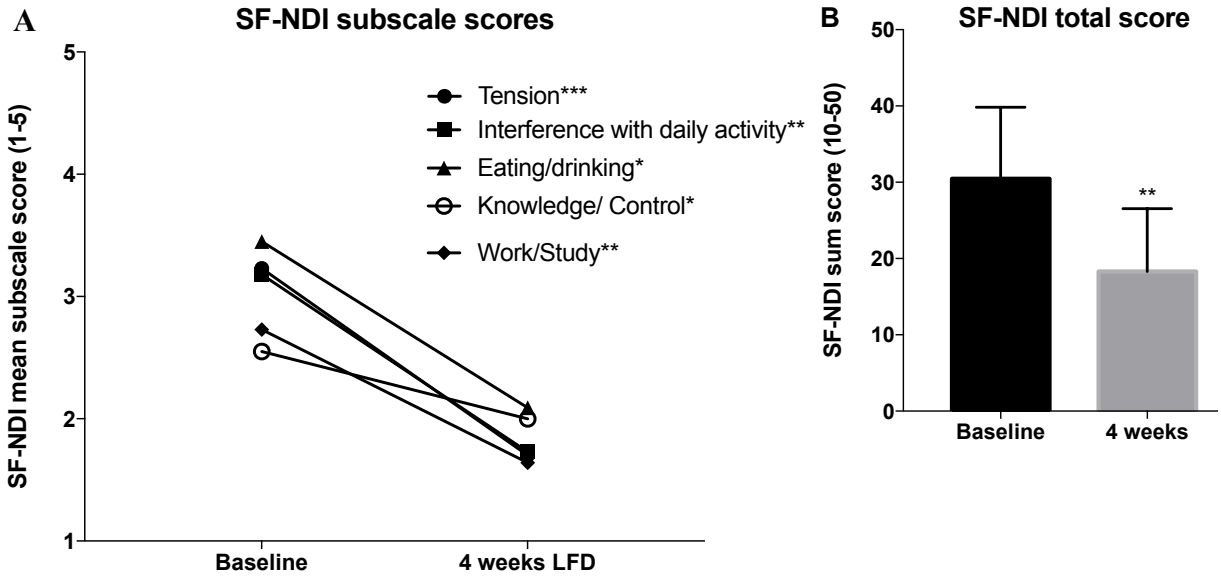

Figure 15: SF-NDI subscale scores (A) and total score (B) at baseline and at 4 weeks
*: p≤ 0.05, **: p≤ 0.01, ***: p≤ 0.001

3.5.2 SF-12

The responder results of SF-12 at baseline and at 4 weeks compose eight domain scores, which together determine a PCS score and a MCS score (Table 7). The domain scores that improved significantly were "role physical", "bodily pain", "general health", "vitality" and "role emotional", while the improvement of "social functioning" and "mental health" were borderline significant (Figure 16). At baseline the mean score for physical health (PCS) was 44.1 and increased to 48.8 after 4 weeks (p=0.134). The mean score for mental health (MCS) showed a significant increase from 45.9 to 55.1 at 4 weeks (p=0.047)(Figure 16). The increase in the scores reflects improvements in perceived HRQOL.

Table 7: SF-12: PCS scores, MCS scores and domain scores at baseline and at 4 weeks

	Baseline	4 weeks	p-value
Physical component summary, mean ± SD	44.1 ± 9.0	48.8 ± 7.9	0.134
Mental component summary, mean ± SD	45.9 ± 12.8	55.1 ± 5.1	0.047*
8 domain scores, mean ± SD			
Physical function (PF)	70.5 ± 29.2	79.6 ± 27.0	0.267
Role physical (RP)	65.9 ± 21.0	81.8 ± 15.2	0.031*
Bodily pain (BP)	65.9 ± 25.7	88.6 ± 13.1	0.033*
General health (GH)	35.5 ± 32.1	57.3 ± 33.9	0.024*
Vitality (VT)	27.3 ± 26.1	50.0 ± 22.4	0.016*
Social functioning (SF)	72.7 ± 26.1	90.9 ± 16.9	0.070
Role emotional (RE)	78.4 ± 26.9	97.7 ± 5.1	0.033*
Mental health (MH)	62.5 ± 28.5	80.7 ± 13.0	0.070

Data are presented in mean ± SD for PCM (0-100), MCS (0-100) and domain scores (0-100)
P-value from unpaired t-test *: p≤ 0.05

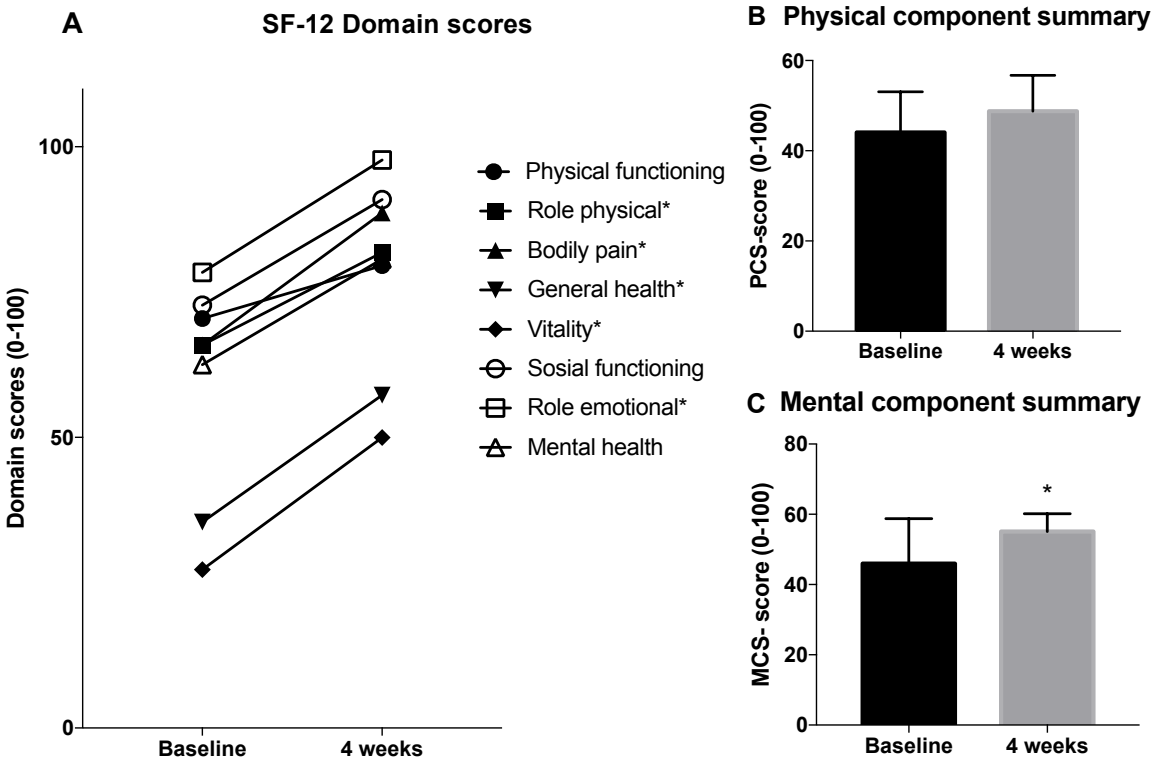

Figure 16: SF-12: Domain scores (A), physical (B) and mental component score (C) at baseline and at 4 weeks, *: p≤ 0.05

3.6 Compliance

3.6.1 Adherence during the intervention

The participants seemed satisfied with the effects of the diet, and had high adherence based on the self-reported compliance form filled after 4 weeks, despite the fact that they reported the diet to be relatively challenging (Table 8). The adherence to the diet was for all but one participant higher than 75% and the remaining one reported a compliance of 72%.

Table 8: VAS scores for adherence, satisfaction and level of difficulty following LFD

	Mean	**SD**
Range of adherence to LFD through 4 weeks (0-100)	94.8	8.3
Satisfaction with LFD on symptom relief (0-100)	89.4	16.5
Level of difficulty in following LFD (0-100)	51.9	24.3

Data are presented as mean and SD for VAS scores (0-100)

3.6.2 The low FODMAP diet

On the question regarding if they wanted to continue on the diet, eight replied “yes”, two replied “maybe”, and one replied “only with continuous counseling”. Deviations from the diet was reported as “4-6 times a week” by one, “1-5 times during 4 weeks” by seven, and three participants reported to have had no deviations. The amount of non-LFD foods eaten was for two “a whole meal”, for four “2-5 mouthfuls” and for two “one mouthful”. Most of those who made exceptions from the diet, reported that it happened by accident or lack of knowledge of ingredients (n=5). Two deviated because of lack of alternatives available during restaurant visit and one had craving for something else. Fructans in form of onion/garlic and fructose were the most frequent FODMAP groups in diet deviation. All patients were pleased with the information given about the diet, with two being “satisfied”, and nine being “very satisfied”.

3.6.3 Adherence to the diet 4-6 weeks after completing intervention

All participants filled and returned a second compliance form 4-6 weeks after the study period and the self-reported results from this are presented in Table 9.

Table 9: VAS scores for adherence and reintroduction phase difficulty 4-6 weeks after completing the intervention

	Mean	**SD**
Level of maintaining adherent to LFD (0-100)	65.8	27.8
Level of difficulty in reintroducing FODMAPs (0-100)(n=9)	51.5	21.2

Data are presented in mean and SD for VAS scores (0-100)

Not all participants continued to follow LFD. Reasons for going back to their habitual diet were that "the diet did not give enough effect to make the effort worthy" (n=3), "there are only some foodstuffs that promote symptoms"(n=3), "privation for too many foodstuffs" (n=2) or "lack of self-discipline" (n=1). Four participants did a systematic reintroduction of FODMAP groups, five tried to systematic reintroduce some FODMAPs, and two went back to habitual diet without trying to reintroduce. The most problematic FODMAP groups regarding symptom onset and symptom severity reported by the participants are presented in Figure 17.

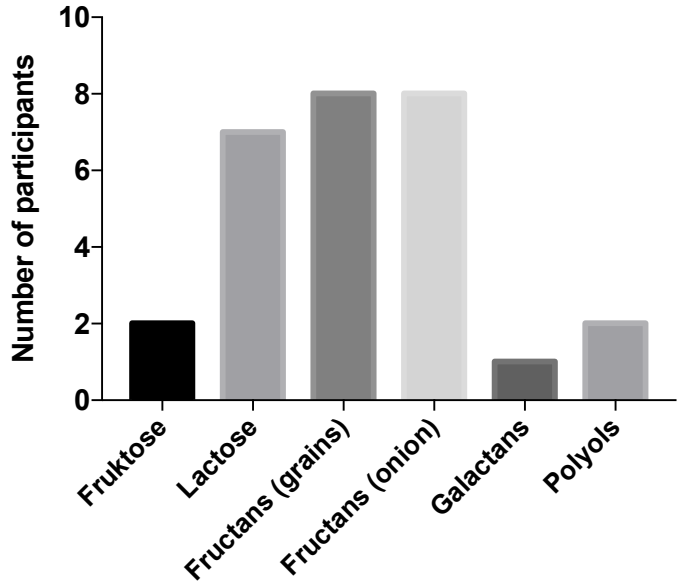

Figure 17: Most problematic FODMAPs reported 4-6 weeks after completing intervention
Shown in number of participants reporting the exact FODMAP group as symptom promoting

The reintroduction phase seems to be perceived relatively difficult, as the reported mean degree of difficulty was 51.5% whit the maximum score of 100% being equivalent to "very challenging". The reported difficulties with this phase was "to know that they most probably would get symptoms from the food item", "to know whether the symptoms came from that specific food item" and "to differentiate between normally occurring symptoms and symptoms arising from that specific food item". Four answered "yes" on the question regarding if they were to continue on the diet, and seven answered "partially".

3.7 Correlations

Correlation analyses revealed no statistically significant correlations between symptoms and the other variables measured; HRQOL, baseline FODMAP intake and radiation dosage (Table 10). Only a borderline significant correlation was seen between the baseline score of IBS-SSS and SF-NDI.

Table 10: Correlation analyses of FODMAP intake, symptoms and quality of life

Pearson r analysis	r	r^2	p-value
IBS-SSS vs. SF-NDI baseline	0.576	0.332	0.064
IBS-SSS vs. SF-NDI 4 weeks	0.467	0.218	0.148
IBS-SQ vs. SF-NDI baseline	-0.116	0.013	0.735
IBS-SQ vs. SF NDI 4 weeks	0.156	0.024	0.646
FODMAP vs. IBS-SSS	-0.317	0.100	0.343
IBS-SSS vs. Dosage	0.094	0.009	0.796

Data are presented in Pearson correlation coefficient (r) and r-squared. P-value from Pearson correlation test

4. DISCUSSION

4.1 Main findings

We conducted an open quantitative, prospective pilot study to examine the effect of a low FODMAP diet on patients with RISBD developed after pelvic radiation treatment against cancer. The intervention group consisted of 11 participants who followed LFD for 4 weeks. There was no control group. Dietary intake, RISBD-related symptoms and HRQOL were registered before and after the diet period to reveal and quantify changes.

The intervention was successful in form of reduction of FODMAP intake, shown by a 3-day food record, together with a self-reported compliance scheme (mean adherence 94.8%). In addition to FODMAP intake, the subjects significantly lowered their daily total energy intake, their carbohydrate intake and their fiber intake ($p=0.004$, $p=0.001$ and $p=0.03$, respectively). The absolute intake of fat and protein (g/day) was reduced compatible with the reduction in total amount of energy consumed, but their relative contribution to the total calorie intake (E%) increased. The LFD accordingly seems to make a shift to less carbohydrate and more fat and protein in the diet. Based on self-reported weight, the populations mean change in body mass was -1.6 kg ($p=0.006$).

GI-symptoms improved considerably during the intervention. The total IBS-SSS score decreased from mean 310.2 to 171.4 from baseline to end of intervention ($p=0.001$). The mean score was reduced for all the individual main IBS-SSS questions and this change was significant for “severity of abdominal pain”, “severity of abdominal distention”, “dissatisfaction with bowel habits” and “interference with life in general”. For the 10 additional questions in the IBS-SSS questionnaire, the total score (mean 414.5 vs. 263.7), and the individual question scores for “nausea and/or vomiting”, “difficulties in finishing meals”, “backache”, “fatigue”, “belching” and “pain in thighs” were significantly lower after 4 weeks LFD compared to baseline. Significant symptom improvement was also documented by the IBS-SQ questionnaire (mean total score 27.4 vs. 15.7). Reported scores of bloating, abdominal pain, constipation and diarrhea were significantly improved on the diet.

LFD seems also to enhance HRQOL for RISBD patients based on this study. The mean total score of the SF-NDI questionnaire decreased from 30.5 to 18.3 ($p=0.001$), corresponding to improved perceived quality of life. The improvement in scores was significant for the

subscales “tension”, “interference with daily activity”, “eating/drinking”, “knowledge/control”, and “work/study”. Results from SF-12 showed a significant increase of the mental (MCS) score (45.9 vs. 55.1), and a non-significant increase of the physical (PCS) score (44.1 vs. 48.8). Significant improvements were achieved for the domains “role physical”, “bodily pain”, “general health”, “vitality” and “role emotional”. Non-significant improvements were observed for “physical functioning”, “social functioning” and “mental health”.

4.2 Discussion of findings

4.2.1 Dietary intake

From the study results, LFD seems to cause a shift to less carbohydrate and more fat and protein in the diet, and this tendency is also reported from previous LFD trials (86). This is an expected consequence because all FODMAPs are carbohydrates, but not a wanted outcome. The aim of the dietary counseling is to provide good information about food alternatives to keep the distribution between the main energy sources unchanged. The increased energy contribution from protein is not considered problematic, but an increased fat intake could be. This is based on the established opinion that excessive intake of fat, especially saturated fat, implies a potential negative risk for lifestyle diseases (87). In addition, RISBD patients may have a lower absorption capacity for fat due to bile acid malabsorption, which can lead to increased GI symptoms when increasing fat intake (4, 16, 88). The recommended distribution of energy sources is 45-60 E% from carbohydrate, 25-40 E% from fat, and 10-20 E% from protein (87). In the conducted study the baseline E% of fat was 36.8 and this increased to 38.4 at 4 weeks. Carbohydrate changed from 46.5 E% to 42 E% and protein from 17.4 E% to 19.3 E%. This shows that despite the increase in energy proportion from fat, the distribution is still in line with the general recommendation. Based on the amount in gram, the fat intake was not at all excessive, nor risk promoting, during LFD.

Besides being the largest contributor to energy, carbohydrates have other important roles in the diet. In the traditional Norwegian eating habits, most meals are based on this source in form of different variants of bread, cereals and also as a side dish for supper. Foods high in carbohydrates have a good filling capability and provide fiber to the diet. Fiber should be included in a healthy diet because it promotes healthy bowel function and also serves as nutriment for a favorable microbiota. Based on this, the Norwegian Directorate of Health has

set a daily recommendation for dietary fiber intake of 25-35 g/day (87). This is above both the reported baseline and at 4 weeks mean intake of fiber in the study population, which was 18.8 g/day and 13.9 g/day, respectively. Regarding the effect LFD has on microbiota, this is currently a research topic of high interest. No firm conclusions are made, but it seems as if the diet could have a negative long-term effect on the composition and function of microbiota (55, 56, 61, 64, 65, 89).

The amount of calcium was registered from the food records before and after intervention. The reason for this interest is that dairy products, which are the main diet source for calcium, often contain lactose that needs to be excluded on LFD. Therefore, there is a possible risk for a decreased and inadequate intake of this micronutrient. The recommended daily intake is 800 mg/day for the study populations sex and age group (87). According to the food records, the mean intake of calcium was below this recommendation both at baseline and during the diet intervention. While the mean intake decreased with about 100 mg/day ($p=0.332$), the majority of the participants ($n=6$) actually increased their intake of calcium on LFD. The reason why the calcium intake overall remained relatively stable, is probably the wide selection of lactose free and lactose reduced dairy products on the Norwegian marked.

The mean change of weight during four weeks on LFD was a reduction of about 1.6 kg. About all subjects lost weight, and only one gained 1 kg, from baseline to end of intervention. This is consistent with the reduction in mean energy intake and is reported also from other LFD studies (90, 91). An interesting observation was that the only subject who increased the intake of calories was also the one who lost most body mass (5 kg). Simultaneously, the only participant who gained weight still had decreased her daily energy intake (about 100 kcal). The explanation for these findings is most likely that the food records filled during only three days did not capture a representative picture of the actual dietary intake for the whole period of four weeks. This is a known weakness of methods assessing dietary intake (67, 92). An alternative possible explanation could be that the reduced intake of energy (and also FODMAP), lead to less symptoms and less diarrhea, promoting an improvement in uptake and utilization of the calories consumed.
The participants reported their body mass themselves by writing both weight and height on the first page of the food records. This limits the reliability of the registration, as self-reported weight implies a high bias risk (93). There was no assurance that the written weight was the subjects' actual weight, and that it was measured recently not only a report of what they use

to weigh. If the values actually are correct, the resulting mean weight loss is an interesting but undesirable effect of LFD. The wanted effect is a relief in symptoms and improved HRQOL, not a reduction in weight. The diet should provide good alternatives so that adequate amounts of energy, macro- and micronutrients are consumed. This emphasizes the importance of comprehensive counseling by preferably a registered dietitian (94). Noteworthy, some of the participant expressed a want for a weight reduction, and may have used the diet for this purpose in addition to the IBS symptom response. The negative noted side effects on intake of energy, dietary fiber and weight change, denotes skepticism about the safety of eating LFD over time. The diet is possibly not accurate to meet the basic dietary needs, neither in line with a diet that diminishes the risk for lifestyle diseases and promotes a healthy GI bacterial flora.

4.2.2 FODMAP intake

The study only included patients who were not already following the low FODMAP diet. Yet, some participants had heard of it, and some had already excluded various foodstuffs and drinks based on self-experienced correlation between food intake and symptom onset. Many of these foodstuffs were FODMAP containing (such as wheat, dairy products and onion). All subjects were encouraged to eat a "regular" diet from recruitment until start of diet period, and hence include the problematic food they had excluded. This was necessary to diminish the risk that restrictions at baseline could mask the effect of the intervention. Based on the baseline food records, it seems like the participants did re-include problematic foods in prior to the start of the diet period.

The participants mean intake of FODMAP at baseline was 22 g/day. The mean FODMAP intake in the Norwegian population in general is unknown, but in a recent study the FODMAP content of a regular Australian diet was found to contain 23.7 g/day (95). Magge et al. defined 9 g of FODMAP per day as low, and 50 g/day as high (96). Former similar studies conducted by master students at UiB reported baseline daily FODMAP intakes for their study populations of 19.2 g, 13 g and 6.3 g, respectively (the last one being a gluten free diet) (65, 97, 98). In the original description of LFD, a food item is high in FODMAP if it contains >3 g fructose per meal, >0.2 g fructans + galactans per meal or >0.5 g polyols per meal (54). Based on this, the baseline FODMAP intake in the present study seems relatively normal, being neither extraordinary high, nor low. The FODMAP group that contributed most to the total amount was the disaccharide lactose, whit a baseline mean of 10 g/day. The threshold value per meal for this FODMAP group is not given in the description.

Interestingly Suarez et al. found that up to two cups of milk (equals around 16 g lactose) per day can be tolerated by lactose intolerant individuals if it is divided over several meals (99). The prevalence of lactose malabsorption in the western population is low, and not found to be more prominent in IBS patients (100). The participant with the lowest reported adherence to LFD also had minimal improvements in symptoms (260 to 235 points in IBS-SSS score). Her FODMAP intake at 4 weeks was 9.2 g/day, which is an amount just above what is defined as low FODMAP (<9g). Her intake of lactose was 6.7 g/day, which is a notable but not a very high amount if it is spread over several meals, based on the findings from Suarez et al. Her lack of symptom improvement could thus be due to her LFD deviations, but this is not unambiguous.

No significant correlation was found between the baseline intake of FODMAP and the severity of IBS symptoms (IBS-SSS total score) based on Pearson r two-tailed correlation analysis ($p=0.340$). The participant that had the highest amount of FODMAP intake (50 g/day) also had one of the lowest IBS-SSS total scores at baseline (258 points). The one with the highest score on IBS-SSS (420 points) had a FODMAP intake around the average for the study population (21.1 g/day). This reflects the multifactorial situation in the symptom picture of this disease. It can also be a result of a large intra-individual variation of FODMAP intake and symptom severity from day to day. Neither a 3-day food record, nor the registration of symptoms at only two time points is enough to uncover this variation.

4.2.3 Symptoms

Information about the received RT was obtained from the participant's medical record at the respective hospitals, for 10 of the 11 participants. Mean dosage received was 63.7 Gy. During the diagnostically evaluation of a new cancer case, a FIGO stadium (The International Federation of Gynecology and Obstetrics) is determined. Stadium I is often treated only with surgery, while stadium II-IV are treated with radiation with or without combined chemotherapy (13). In the study population four had stadium I, four had stadium II, one had stadium IV and for the last two these data were not found. There was no correlation between radiation dosage and severity of IBS symptoms at baseline (based on IBS-SSS). However, the low number of patients, variable radiation dosages and co-treatments, as well as uncertainties about disease stages, limit the reliability of correlation analyses. Multiple factors influence the development of chronic RISBD, and longitudinal studies of larger and homogenous patent groups are required.

The mean decrease of IBS-SSS of about 139 is far above the cut-off value of 50 points that is considered successful treatment response, and the change is equivalent to an improvement of mean IBS-grade from severe to mild. Based on the severity grading of IBS, two participants achieved remission of their GI symptoms (IBS-SSS score <75) (75). The improvements seen in "diarrhea", "abdominal pain" and "dissatisfaction of bowel habits" is not surprising. These symptoms are all part of the diagnostic criteria for IBS, and because of LFD's known effect for IBS, the improvement could be anticipated. But in the two symptom-questionnaires all symptoms were reduced, including comorbidity symptoms. This includes "nausea", "vomiting", "early satiety", "headache", "backache", "tiredness", "heartburn", "urge to urinate" and "pain in tights and muscles". Some of these can indirectly be linked to IBS-criteria symptoms, but some are unrelated to them. The reason for the result on non-GI and upper-GI symptoms is not known, but similar observations have been seen in studies on the effect of LFD for IBS (65, 101, 102).

The two questionnaires used to register symptoms were overlapping as they both graded abdominal pain, bloating and nausea (either as a VAS-score or as a numeric scale from 1 to 10). The first two of these symptoms were significantly reduced according to both IBS-SSS and IBS-SQ, but that was not the case for nausea. Both schemes registered a reduction in nausea (mean 25.7 to 15.0 and 3.7 to 2.7), but this was only significant in IBS-SSS. Because of these not throughout significant findings, it is difficult to make a conclusion on the effect LFD has on the severity of nausea. This inconsistent finding between the questionnaires used in the study, can also elucidate a reason for doubt on the suitability of using these exact questionnaires for this purpose. On the other hand, nausea is not the most prominent symptom in this patient group, having a mean of 25.7 of 100 and 3.7 of 10 at baseline, and therefore is less sensitive for change. The low number of participants, the wording of the questions asked, and also the scales used, probably affects the results. Therefor, a lack of significant reduction based on SF-SQ is maybe not that substantial.

4.2.4 Responders vs. non-responders

Three study participants had a lower decrease in IBS-SSS total score than 50 points, and this defines them as non-responders based on this questionnaire. Published papers on LFD suggest that non-responders should be investigated on the basis of adherence to the diet, and that possible "hidden sources" of FODMAPs in their diet should be revealed. If compliance to the diet was good, but symptoms still persist, the attention should be focused on other

factors in the diet that can provide the same complaints. This could be excessive intake of resistant starch, insoluble fiber, caffeine or fat, or an unfavorable meal size or rhythm (55).

Adherence to the diet during the 4 weeks of intervention is crucial to achieve an effect on both symptoms and HRQOL. The grade of compliance for the three non-respondents was relatively high, but varied. One of them reported an adherence of 100%, one of 90%, and the last one had an adherence of only 72%. The latter had a moderate intake of lactose during the LFD period in form of eating brown cheese almost daily for breakfast. This is possibly a contributing factor for her failing symptom relief. In addition to this she consumed both apple and orange juice during the intervention period resulting in a estimated mean FODMAP intake at 4 weeks of 9.2 g/day (*e.g.* above the limit of 9 g/day) (96). This participant also had the lowest intake of calories, which was as low as 958 kcal/day at baseline and surprisingly low, 504 kcal/day on LFD. This amount is far below the recommended intake for her age and gender of about 2000 kcal/day based on estimations from *Kostholdsplanleggeren.no*. Based on these findings, this particular patient should perhaps be considered an extraordinary case, which presents with dissimilarities to the other included participants. Statistical analyses excluding data from this patient should perhaps have been done.

If the subjects still consume high amounts of fiber, this may explain the lacking/insufficient effect of LFD. Coia et al. suggests that a low-residue diet can limit the symptoms (53, 103). The low FODMAP diet is not necessary in accordance with that. The Norwegian recommendation for daily fiber intake is 25-35 g/day. The study populations mean daily intake at baseline was 18.8 g, and was reduced to 13.9 g during the LFD period. The group's intake of fiber was accordingly beneath the recommended amount both before and after the intervention. The individual intakes for the subjects who did not have successful symptom reduction, showed no correlation with the fiber intake. The three subjects in this group had baseline daily fiber intake of 14.3 g, 27.5 g and 17.3 g, respectively. They all reduced their intake to 12.2 g, 14.7 g and 5.4 g, respectively.

Fat intake can be related to response effect in symptoms. The traditional advises given to patients at risk for RISBD include reduction and distribution of the daily fat intake. This recommendation is based on the fact that bile acid absorption can be affected after small bowel damage and that this can provoke diarrhea if the fat load to GI is high (4, 88). It is expected that the intake of fat could increase on LFD because of the restriction in

carbohydrates. Again looking at the three non-respondents, their fat intake at baseline contributed to 28%, 32% and 29% of their total energy intake. This is for all of them in line with the government's recommendation of 25-40% of energy coming from fat (87). Their intake changed respectively to 27 E%, 30 E% and 38% on the LFD. The absolute change in fat intake in grams for these three participants was from 41.2 to 35.2, from 70 to 62.7 and from 31.3 to 21.6, respectively. The fat load to the GI lumen accordingly decreased rather than increased when looking at the absolute amount consumed. Based on these numbers, intake of fat is most likely not the cause of the lacking symptom relief.

4.2.5 Health related quality of life

Based on SF-NDI and SF-12 the participants' perceived HRQOL improved. These findings are highly important to report, since RISBD is known as a disease that strongly affects quality of life (2). Independent of which kind of symptoms that alleviate, the fact that the life quality for patients improved is an effect that is highly appreciated. Fecal incontinence is considered to be the symptom that most prominently influences RISBD patients quality of life (11). This was supported by the results of this study. The three patients with the strongest reduction in total score of SF-NDI (reductions of 22-25 points) all had scored their frequency of fecal incontinence to zero times per week at the study endpoint (baseline scores was 5, 6 and 7 times of maximal score of 10).

4.2.6 Relationship between symptom relief and improvement in quality of life

A significant improvement was found in both RISBD-related symptoms and perceived quality of life. These findings suggest that GI symptoms affect HRQOL and/or visa versa. Still, this does not prove that these two variables are directly correlated. For example, the participant with the highest score in SF-NDI (*i.e.* worse HRQOL) at baseline (45 points) had only the sixth highest score in IBS-SSS (339 points). Simultaneously the one with highest total score in IBS-SSS (420 points) had only the sixth highest score in SF-NDI. The same was seen at 4 weeks where the one with the highest score in SF-NDI had the third highest in IBS-SSS, and the highest in IBS-SSS had the third highest in SF-NDI. This trend is supported by correlation analyses conducted, which did not show significant results, neither at baseline nor at 4 weeks. An explanation for this discrepancy between symptom relief and improvement in HRQOL is perhaps that many other factors affect quality of life, and that these are expected to change during a period of 4 weeks.

4.2.7 Patient experiences

The participants found it quite challenging to follow LFD. The mean level of difficulty score was about 52 of maximum 100. This score varied considerably between the participants, as the lowest score was 9.5 and the highest was 79. Looking at the individual scores, it seems as those who found the diet undemanding, were the same ones who had larger difference in IBS-SSS scores between baseline and 4 weeks. The four subjects that found the diet most difficult (over 60%) also had the lowest difference in IBS-SSS score (around 100 or less). This relation was supported by a significant correlation analysis between "level of difficulty following LFD" and the difference in IBS-SSS total score (from baseline to 4 weeks) with a Pearson r of -0.7 ($p=0.018$)(results not shown). The cause/effect relation between these two variables is not known. It could be that those finding the diet easy to follow consequently have better adherence, which gives better effect. It could also be that those who feel symptom relief get higher motivation and therefore find it easier to follow the strict diet.

In addition to the measurable effects presented, the participants' overall satisfaction communicated orally is very pleasing. Some of the subjects have described the diet as "life-changing" for them, and that adapting to LFD has opened new possibilities for them. Many subjects felt isolated and homebound because of their need of always having a toilet within reach, because of incontrollable fecal urge. The master student experienced examples of this when participants were forced to hang up on the phone suddenly during the diet counseling to find the nearest toilet. Many have reported more control over this problem after implementing LFD. One patient, who earlier had to quit her job, was one month after the end of study back working full time. Some also report that they to a greater extent dare to join social events than before implementing LFD. On the other hand, others found social events more challenging to attend on the diet, especially during the first weeks of the strict diet period. Reason for this is that they were uncertain of what to eat and not to eat, and the need to pre-plan meals away from home. The feeling of being a burden to the one inviting them for a meal is also not unusual. This corresponds to the lack of significant improvement of the SF-12 domain "social functioning". This aspect of LFD being both an advantage and a disadvantage in social settings is probably varying over time. When the participant gradually are becoming more certain of what they can eat and not, and get known with their tolerable limits of foodstuffs, hopefully the diet becomes more an advantage.

Another challenge reported during the study, was to eat enough and the feeling of hunger. Some subjects contacted the master student during the first weeks, because they needed

extended counseling and help finding low FODMAP alternatives. Most of them struggled with finding good alternatives for between-meal-snacks, but also alternatives to bread and crisp bread.
Noteworthy, the registration of weight change did not differentiate between intended and unintended weight loss, and several participants expressed satisfaction with having lost some kilos.

4.3 Study limitations

4.3.1 Recruitment

The methods for recruiting patients to the study present some possible risks of bias. First of all there is a limitation in the fact that the study was open and that a lot of the participants contacted the master student by their own initiative through information shared on Internet. This presents a risk for the group of participants to be more motivated to follow a diet like LFD, and that the type or severity of symptoms differs from the patient group in general. This method of recruitment only reaches out to patients that are active on Internet and social media, and therefore looses the ones that don't seek these platforms. Internet activity is also most likely related to age and gender.
Secondly, the fact that the recruitment of most of the participants did not go through referral from clinicians either at HMU, the Department of Medicine or the Department of Gynecology, as we initially intended, makes the information about the extent and type of radiation damage limited. Although we ensured that all participant had received pelvic RT in the past and that the symptoms arised in aftermath, it is possible that some of them suffered from regular IBS not related to their cancer treatment. This bias could have been diminished if the inclusion criteria had required that a full gastroenterological examination needed to have been conducted before recruitment. Still, this would have made the recruitment more challenging, more resource demanding and beyond the scale of this project.

Pre-inclusion efforts to adapt to the low FODMAP diet did not lead to exclusion from the study and some participants reported to have tried the diet before. Individuals in this situation may have had a better understanding and motivation to adapt to LFD, and therefore have been more likely to comply with the diet and consequently respond positively. This risk is especially present if the former attempt was by own initiative.

The recruitment process could have been better planned and more systematically carried out. The way of getting in touch with the patient group was in many ways generated concurrent with the recruitment. New channels to spread the information came up during the entire recruitment period, also after suggestions from already included participants. As a result, some potentially valuable sources for new participants were discovered too late regarding the limited duration of the recruitment phase. By protocol, the desirable number of subjects was 18. This number was set based on the number of patients with GI-complaints referred to the HMU the past years, combined with the number of patients needed for statistical power of the hypothesis tests. Still, we did not want more than 18 subjects because of the fact that the study was a pilot study. It would have been unethical to include a high sample size when the diet is known to be demanding and the effects unclear. The resulting number of 11 subjects is lower than wanted, but was still sufficient to draw statistically conclusions on the effect of the diet on symptoms and HRQOL.

4.3.2 Demography

The study only included female subjects. In the literature, RISBD is described as a prominent late effect also after treatment of prostate cancer (10), and we expected to include some male participants. Still there were almost exclusively women that expressed interest to join the study. In the recruitment phase, there was only one male patient that made contact and requested more information about the study. In addition, two male candidates were contacted through the waiting list at HMU. After receiving a brief description of the diet, all three considered it too demanding and therefor abstained from joining the study. Because they were referred to HBO, which is known to be a successful treatment, the motivation to try a new and strict diet in prior to their planned treatment, might have been diminished.
The explanation for the gender discrepancy in interest for the study is probably multifactorial. First of all, the recruitment method using web pages and Facebook may have reached out to more female patients, as they might be more active on these platforms. Second, the fact that the intervention was a diet can attract more females based on a hypothesis that women are more interested and engaged in nutrition and food. Third, and the desirable true reason, is that more women suffer RISBD than men after pelvic RT. This could be a fact because the location of prostate cancer is more proximal to the small bowel than gynecological cancers, and because of the new methods used to radiate prostate cancer tumors. The new methods are

considered to be more precise and consequently affect the surrounding normal tissue in a lesser extent, presenting lower risks of RISBD (104, 105).

The mean BMI was 27.7 kg/m^2, ranging from 19.6 to 39.7. BMI is a measure used to categorize individuals as underweight (<18 kg/m^2), normal weight (18,5-25 kg/m^2), overweight (25-30 kg/m^2) or obese (>30 kg/m^2) (106). The study population's mean BMI corresponds to overweight, five individuals had normal weight and none of the subjects was underweight. Based on former published papers describing RISBD, it was expected to have a study population with an overall lower BMI (39). The fact that most participants were in the upper stratum of BMI could be an indication of having an unrepresentative patient-selection in the study. Having some kilos in excess can also make the participants more likely to join a project that involves a diet.

4.3.3 Data collection

4.3.3.1 Food records and calculation of FODMAP intake

Food intake was registered both in prior to and during the LFD period, using a self-administered 3-day food record continuously filled by the participants. This is a validated and frequently used method, but can be vulnerable for both over- and under reporting of intake (67). The fact that one participant who gained weight simultaneously seemed to have decreased her energy intake exemplifies this.

The method used to calculate the consumed amount of FODMAP at baseline also implies a number of bias risks. Many foodstuffs are registered as FODMAP sources in the *Dietist Net* database, but not all. Therefore, for several meals/foods the FODMAP content had to be estimated from the ingredient list and by use of published analysis, databases and knowledge. This may have been imprecise, and could also have contributed to relatively large variations in the estimated baseline FODMAP intakes. In addition, the participants were included continuously and the calculation of their baseline FODMAP intake was not performed all at the same time. During the months the inclusion lasted, the master student may have improved the skills in identifying and calculating FODMAP contents. Therefore, there is a possibility that the intake was measured more accurate for the last participant, then the first.

4.3.3.2 Effect measurement

The effects of the study were without exception measured by questionnaires. This presents a response bias, as the completion of questionnaires can be affected by many factors (107). The method is also very subjective and vulnerable to affection from the placebo effect. Participants may think they know the wanted outcome of the study, and answer the questionnaires thereafter. Other factors that can vary substantially and therefore affect the outcome are the time allocated to fill the questionnaire, participants memory, the order of different questionnaires (response fatigue), the opportunity to ask follow-up questions, embarrassment, the wish to succeed and the mood of the subject (107). The fact that it was a pilot study provides additional risk of response bias. Most participants made contact unprompted, and seemed very pleased to have the opportunity to join the study. This can have lead to patients feeling indebted to the master student, and consequently completed the forms in a way that favored a positive outcome.

Two different questionnaires were used both to measure symptoms (IBS-SSS and IBS-SQ) and HRQOL (SF-NDI and SF-12). The reason for using both schemes was the uncertainty of which one of those was most suitable to reveal the effect for this exact patient group. The questionnaires are in many ways overlapping, but still measure some different aspects of GI symptoms and quality of life. Correlation analyses were done for IBS-SSS vs. IBS-SQ and for SF-NDI vs. SF-12 both at baseline and at 4 weeks. The symptom questionnaires had a positive correlation at 4 weeks ($p=0.004$), but no further correlations were found. This indicates that the questionnaires have limited overlap and their combination may be useful to capture a wider aspect of the symptom picture and HRQOL.

4.3.4 Diet counseling

Low response in the recruitment phase, lead to inclusion of participants from all parts of Norway. This resulted in that most of the diet counseling was done by phone, which made the standardization of the information given challenging. When not being able to use body language, pictures etc., the phoned counseling possibly held a lower quality then the ones given face-to-face. In addition, the participants were included and set to start the diet period in a continuing manner as they got in touch with the study coordinator. This can have led to a development in the way of providing the information over time, so that the first participants received the counseling in a different way compared to the last ones.

Some participants got their counseling only one or a few days before the diet was to be implemented. This is a short time to prepare for a quite complicated diet. The time between counseling and diet start was attempted to be held constant, normally getting information on Thursday and starting the diet period on Monday. This was not always possible to overhold. However, as the symptoms were not measured until 4 weeks later, needing some days to get used to the diet should not influence the results notably.

4.3.5 Compliance

During the study compliance was only registered at the end of the diet period. This presents a limitation, as bad compliance could not be corrected by the study coordinator in form of providing additional counseling and motivation for better adherence to the diet. On the other hand, in an actual clinical situation, close monitoring of patients is usually not possible. Therefore the results of the study are possible to generalize to a realistic setting.

Being part of a clinical study, with a need to fill out forms and food records can give a false effect of the LFD caused by higher motivation and adherence. The expectations of improvement may also be greater in a scientific situation compared to a clinical setting after only one consultation. This can result in a significant placebo effect on improvement of symptom control and HRQOL. Since the study did not include a control group, the placebo effect cannot be assessed closer. This is a major weakness of the study, especially because this effect is known to be prominent in IBS patients on LFD. A meta-analysis with 45 placebo-controlled RCT's reported a placebo response of 40.2% (108).

4.3.6 Safety

Since most of the participants made contact by own initiative, and lived far away from the study center, no medical examinations was conducted. Only two participants lived close enough to meet in person. According to the Royal Marsden Hospital (RMH) algorithm all RISBD-patients with prominent GI symptoms should have a holistic assessment to exclude recurrent cancer and other treatable causes for their symptoms. This is especially important if the symptom picture includes bleeding and/or has major impact on quality of life (29, 109). In the conducted pilot study, no examinations like endoscopy, ultrasound, blood test or breath test were conducted. The study itself did thus not ensure optimized care beyond what was already established for the individuals.

It seems as LFD poses a risk for inadequate intake of energy, fiber, macro- and micronutrients, and can possibly change the composition and functioning of the GI bacteria flora over time. These factors contribute to the fact that the conduction of this study was not completely without safety concerns.

4.4 Future aspects

To define this patient group by providing an understanding of the pathophysiology, identify criteria for dietary intervention, and develop suitable diets, requires further investigation. The relation between RISBD and IBS is intriguing both clinically and scientifically.

Based on the positive results of this small-scaled pilot study, more investigation on the effect of LFD for this patient group should be conducted. There is a need for controlled studies including patients with an ensured diagnosis of RISBD, preferably after endoscopic and histological examinations. Objective measurement should also be conducted before and after implementing LFD to reveal effects on symptoms and HRQOL. As a gold standard in clinical research, randomized double-blinded placebo-controlled studies are required for final conclusion about the effect of LFD intervention. This is a challenging approach when it comes to dietetic interventions. A possible approach would be to give a supplement of either high FODMAP or no FODMAP to two groups already following LFD. This has been conducted on IBS patients and can uncover if the reported effects are merely due to the placebo effect (65). There is also a need for studies with higher sample size to improve statistical power, as well as studies including both genders.

It is not known which of the FODMAP components are most symptom promoting for this group of patients. Further knowledge about this could simplify the dietary advises.

Finally, longitudinal studies are needed because of the safety concerns related to following a strict LFD over time. Insufficient consumption of energy or micronutrients, and reduced amount of prebiotical substances are risk factors. Baseline status and the influence of LFD on intestinal microbiota, mucosal microstructure and motility as well as safety and feasibility should be investigated. Such studies should include a substantially higher number of patients, ass well as a more structured and multidisciplinary approach.

5. CONCLUSION

Our findings establish that the low FODMAP diet seems effective in alleviating IBS symptoms in patients with RISBD, and that it improves their HRQOL. Typical IBS symptoms (*e.g.* diarrhea, constipation, bloating and abdominal pain) improved significantly after 4 weeks of LFD, and several comorbidities (*e.g.* nausea, early satiety, headache, backache, fatigue and muscle pain) were also alleviated. Clinical complaints typical for RISBD patients improved in a consistently but non-significantly manner. The participants reported improved perceived quality of life after converting to the diet. This seemed to be more prominent for mental aspects of HRQOL, then of physical aspects.

Our results also suggest that high compliance to LFD is possible with adequate diet counseling and continuous guidance. Despite finding it challenging to follow, the majority of participants was adherent to the strict diet. They also reported to be content during the intervention and most of them wanted to continue after ending the trial.

There are some concerns in following a strict LFD over time, because of a possible reduction in weight, energy intake, intake of important micronutrients and the unknown effect on microbiota. More research in form of controlled studies with larger samples is needed so that clinicians can consider implementation of the LFD as an efficacious management strategy for patients with chronic RISBD.

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7. APPENDIX

Appendix 1: REC Approval

Appendix 2: Study information and consent form

Appendix 3: 3-day food record registration

Appendix 4: FODMAP booklet

Appendix 5: FODMAP lists

Appendix 6: Compliance questionnaire for low FODMAP diet during 4 weeks

Appendix 7: Compliance questionnaire for low FODMAP diet 4-6 weeks after intervention

Appendix 8: FODMAP Reintroduction phase

Appendix 9: Baseline characteristic questionnaire

Appendix 10: Questionnaire for grading of radiation injury based on RTOG

Appendix 11: Rome III criteria

Appendix 12: IBS-SSS

Appendix 13: IBS-SQ

Appendix 14: SF-NDI

Appendix 15: SF-12

Appendix 16: Study protocol

Appendix 1: REC Approval

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK vest	Øyvind Straume	55978496	11.05.2016	2016/567/REK vest
			Deres dato:	**Deres referanse:**
			09.05.2016	

Vår referanse må oppgis ved alle henvendelser

Trygve Hausken
Gastroenterologisk seksjon

2016/567 Effekt av lav FODMAP-diett ved stråleskadet tarm

Forskningsansvarlig: Helse Bergen HF
Prosjektleder: Trygve Hausken

Vi viser til søknad om prosjektendring datert 09.05.2016 for ovennevnte forskningsprosjekt. Søknaden er behandlet av sekretariatet ved REK vest på fullmakt, med hjemmel i helseforskningsloven § 11.

Vurdering
Ønsket endring
Prosjektendringen innebærer revisjon av informasjonsskriv.

REK vest ved sekretariatet vurderte saken.

Vurdering
REK vest har ingen innvendinger til ønsket endring.

Vedtak
REK vest godkjenner prosjektendringen i samsvar med forelagt søknad.

Klageadgang
Du kan klage på komiteens vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes til REK vest. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK vest, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Med vennlig hilsen

Øyvind Straume
sekretariatsleder

Kopi til: *postmottak@helse-bergen.no*

Appendix 2: Study information and consent form

FORESPØRSEL OM DELTAKELSE I FORSKNINGSPROSJEKTET

EFFEKT AV LAV FODMAP-DIETT VED STRÅLESKADET TARM

Det er kjent at pasienter som har vært utsatt for stråleterapi mot kreft i mageregionen kan utvikle mage-tarm symptomer som følge av akutt eller kronisk stråleskade. Dette er et spørsmål til deg om å delta i et forskningsprosjekt for å undersøke om en FODMAP-redusert diett kan ha symptomlindrende effekt for denne pasientgruppen. Vi vil også se på om dietten kan forbedre opplevd livskvalitet. Deltakerne i studien vil motta grundig veiledning i hvordan FODMAP-redusert kost gjennomføres. Studien er en pilotstudie og vil derfor ikke ha noen kontrollgruppe som mottar en annen, sammenliknende behandling.

Tekst

FODMAP er en forkortelse for fermenterbare oligosakkarider, disakkarider, monosakkarider og polyoler. Dette er karbohydrater som er tunge å fordøye og som gir næring til bakterier i tarmen. Dette kan hos enkelte med såkalt irritabel tarm forårsake mageplager som diaré, forstoppelse, magesmerter og oppblåsthet. Matvarer som inneholder FODMAP er blant annet hvete, rug, visse melkeprodukter, løk, bønner, brokkoli, epler, mango, plommer og søtstoffer. FODMAP-redusert diett går ut på å unngå å spise matvarer med høyt innhold av FODMAP.

Du er valgt ut til å få tilbud om å delta i studien fordi du er i alderen 18-70 år, og har vært i kontakt med Kvinneklinikken eller Medisinsk Avdeling ved Haukeland Universitetssykehus, andre instanser eller sett min annonse, på grunn av mage-tarm plager som følge av tidligere stråleterapi mot kreft. Det finnes forskning som viser at lav FODMAP-diett kan lindre symptomer hos pasienter med irritabel tarmsykdom (IBS). Det er imidlertid ikke forsket på om dietten kan være nyttig også for pasienter med irritabel tarm som følge av stråleskade. Derfor spør vi om du vil være med i denne studien som kan vise om FODMAP-restriksjon kan gi effektiv symptomlindring for pasienter som deg.

Studien er en åpen pilotstudie utført av en masterstudent i klinisk ernæringsfysiologi, veiledet av overlege/professor ved Universitetet i Bergen/Haukeland Universitetssykehus og klinisk ernæringsfysiolog ved Haukeland Universitetssykehus, som ansvarlige for prosjektet.

HVA INNEBÆRER PROSJEKTET?

Studien innebærer at du over en periode på 4 uker spiser en kost som inneholder lite FODMAP. Alle deltakerne i studien vil få samme veiledning og spise den samme kosten hele studieperioden. Du vil få en detaljert oversikt over matvarer du ikke kan spise, og en liste med alternativer til de matvarene du må kutte ut. Dersom du velger å delta i studien vil du bli invitert til en avtalt telefonsamtale der du får utdypende forklaring om hva som skal skje i studien, samt mer informasjon om lav FODMAP-dietten. Dersom du bor i nærheten av Bergen, kan denne informasjonen og veiledningen gis via et personlig møte med studieholder på Haukeland Universitetssykehus. Underveis i studien vil det også være mulighet til å ta kontakt med studieholder for spørsmål og ytterligere veiledning. To ganger i løpet av studien skal du fylle ut spørreskjemaer og fylle ut en kostregistrering for 3 dager. Dette gjøres før oppstart av studien og etter 4 uker når studien avsluttes. I tillegg vil du bli kontaktet i løpet av de 6 ukene som følger etter avsluttet studie for å fylle ut et ytterligere spørreskjema.

Studieresultatet vil bare basere seg på evaluering av spørreskjemaer, ingen blodprøver, avføringsprøver og lignende vil bli tatt.

Om du velger å delta i studien vil dette på ingen måte påvirke den øvrige medisinske behandlingen du eventuelt mottar.

I prosjektet vil vi innhente og registrere opplysninger om deg. Dette innebærer informasjon som henvisningsårsak til Helse-Bergen og informasjon om hvilke mage-tarmrelaterte symptomer du har opplevd.

MULIGE FORDELER OG ULEMPER

Mulige fordeler
Fordelen ved å delta er en mulig bedring i mage-tarm symptomene. Det betyr mulig mindre diaré, mindre forstoppelse, mindre magesmerter og/eller mindre oppblåsthet. En bedring av symptomer fra tarmen vil ofte også medføre en bedring i livskvalitet.

Mulige ulemper
Det er lite sannsynlig at studien kan medføre bivirkninger eller ubehag. Det kan skje at du ikke får noen bedring av dietten. Utover dette er det ingen risiko forbundet med studien. Du må være tilgjengelig for avtalt telefonsamtale og fylle ut skjemaer som skal sendes i posten/e-post, noe som kan oppleves som belastende og/eller tidskrevende for enkelte.
Dietten du skal følge fører også til at du sannsynligvis må kutte ut en del matvarer som du vanligvis spiser, noe som kan oppleves som vanskelig for noen. Det kan også være en utfordring å gå på diett i sosiale sammenhenger.

FRIVILLIG DELTAKELSE OG MULIGHET FOR Å TREKKE SITT SAMTYKKE

Det er frivillig å delta i prosjektet. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke. Dette vil ikke få konsekvenser for din videre behandling. Dersom du trekker deg fra prosjektet, kan du kreve å få slettet innsamlede opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner. Dersom du senere ønsker å trekke deg eller har spørsmål til prosjektet, kan du kontakte Trine Larsen (telefon: 97013209, e-post: trine.L@student.uib.no). Eventuelt kan ansvarlig lege Trygve Hausken kontaktes på e-post (trygve.hausken@helse-bergen.no).

HVA SKJER MED INFORMASJONEN OM DEG?

Informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Du har rett til innsyn i hvilke opplysninger som er registrert om deg og rett til å få korrigert eventuelle feil i de opplysningene som er registrert.

Alle opplysningene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger gjennom en navneliste.

Prosjektleder har ansvar for den daglige driften av forskningsprosjektet og at opplysninger om deg blir behandlet på en sikker måte. Informasjon om deg vil bli anonymisert eller slettet senest fem år etter prosjektslutt.

FORSIKRING

Forsikringsordningen som gjelder er pasientskadeerstatning, idet du som deltaker er under behandling ved Haukeland Universitetssykehus.

OPPFØLGINGSPROSJEKT

Som deltaker vil du kunne bli kontaktet i løpet av 6 uker etter endt studie, for å besvare et spørreskjema. Dette omhandler spørsmål om hvorvidt du i noen grad har holdt på kostendringene en FODMAP-reduksjon innebærer. Dette vil skje over telefon eller ved personlig møte ved Haukeland Universitetssykehus.

ØKONOMI

Studien er finansiert gjennom forskningsmidler fra gastroenterologisk seksjon ved Klinisk Institutt 1 ved Universitetet i Bergen. Det er ingen mulige interessekonflikter.

Deltakere som bor i Bergens-området og som har mulighet til å stille til personlig møte ved Haukeland Universitetssykehus, vil få erstattet utgifter som måtte følge i forbindelse med offentlig transport (buss/tog) og parkering.

GODKJENNING

Prosjektet er godkjent av Regional komite for medisinsk og helsefaglig forskningsetikk, (2016/567).

KONTAKT

Dersom du ønsker å delta i studien kan du kontakte masterstudent i klinisk ernæringsfysiologi Trine Larsen.

Telefon: 97013209
E-post: trine.L@student.uib.no

UTDYPENDE INFORMASJON OM HVA STUDIEN INNEBÆRER

Kriterier for deltakelse
Du er valgt ut til å få tilbud om å delta i studien fordi du er i alderen 18-70 år, og har vært i kontakt med Kvinneklinikken eller Medisinsk Avdeling ved Haukeland Universitetssykehus, eller andre instanser, på grunn av mage-tarm plager som følge av tidligere stråleterapi mot kreft. Du har scoret på ROMA III-kriteriene for IBS, og har dermed symptomer på "irritabel tarm".

Bakgrunnsinformasjon om studien
Det e kjent at pasienter som har vært utsatt for stråleterapi mot kreft i mageregionen i etterkant lider av mage-tarm symptomer som følge av akutt eller kronisk stråleskade. Dette er et forskningsprosjekt for å undersøke om en FODMAP-redusert diett kan ha symptomlindrende effekt i denne pasientgruppen. Vi vil også se på om dietten kan bedre opplevd livskvalitet. Deltakerne vil motta grundig veiledning i hvordan FODMAP-redusert kost gjennomføres. Studien er en pilotstudie og vil derfor ikke ha noen kontrollgruppe som får annen behandling.

Gynekologisk, gastrointenstinal og urologisk kreft blir ofte behandlet med stråleterapi mot buken. Dagens metoder innen strålebehandling gir behandling sentrert mot krefttumoren, men skade i omkringliggende organer skjer. På grunn av vevsskaden dette kan gi rapporteres det om

symptomer som magesmerter- og ubehag, oppblåsthet, diaré, forstoppelse, kvalme, hyppig trang for tarmtømming, appetittnedsettelse, malabsorpsjon og rektale blødninger. De fleste av disse symptomene sees også hos pasienter med diagnosen irritabel tarmsykdom (IBS), diagnostisert vha. Roma III-kriteriene. Hos disse pasientene kan man ikke påvise noen vevsforandringer i mage-tarmkanalen eller være helt sikker på årsaken til plagene, men symptomene er altså like.

FODMAP er en forkortelse for fermenterbare oligosakkarider, disakkarider, monosakkarider og polyoler. Matvarer som inneholder mye FODMAP kan gi plager fra mage- tarm området, særlig hos de med irritabel tarm. Mat som inneholder FODMAP blir fermentert i tykktarmen. Det betyr at bakterier i tykktarmen omdanner ufordøyd mat til gass og til energi (korte fettsyrer). Dette er en normal og viktig prosess, og det er blant annet essensielt for tarmcellenes helse. Fermentering er noe som i ulik grad skjer hos alle mennesker, men de med irritabel tarm får antageligvis mer plager av dette enn friske.

Ved irritabel tarm skjer det en unormal respons i mage- tarm kanalen som kan skyldes overfølsomhet i tarmen. Det kan også skyldes en unormal respons fra nervesystemet i tarmen, en forstyrrelse i bakteriefloraen, motilitetsforstyrrelse (unormal bevegelse av tarminnholdet) eller smerter fra gassdannelse fordi det blir en utvidelse av tarmen. Dette kan gi de typiske symptomene på irritabel tarm, som oppblåsthet, magesmerter, gassdannelse, diaré og/eller forstoppelse. Tanken ved lav-FODMAP diett er å redusere inntak av mat som kan fermenteres av bakterier slik at det blir mindre fermentering i tarmen, og dermed mindre plager.

Matvarer som inneholder FODMAP er blant annet hvete, rug, visse melkeprodukter, løk, bønner, søtstoffer, epler, mango, brokkoli og plommer. FODMAP-redusert diett går ut på å unngå å spise matvarer med høyt innhold av FODMAP. Det finnes forskning som viser at lav FODMAP-diett kan lindre symptomer hos pasienter med irritabel tarm. Det er imidlertid ikke forsket på om dietten kan være nyttig for pasienter med irritabel tarm som følge av stråleskade. Det er nærliggende å tro at denne dietten kan ha effekt også i denne pasientgruppen siden det er likheter i symptomene og bakgrunnen for plagene.

Spørreskjemaer og kostregistrering

Du skal svare på noen spørreskjemaer før oppstart av studien, og avslutningsvis etter fire uker. Disse skjemaene er et RTOG-basert spørreskjema som graderer stråleskader, Roma III (kriterier for irritabel tarm), IBS-SSS (symptomer på irritabel tarm), Roma III og Kane (graderte symptomer på irritabel tarm), SF-NDI (kartlegging av livskvalitet) og SF-12 (kartlegging av livskvalitet). Studieholder vil også innhente noe, samt stille noen spørsmål angående strålekuren du har vært igjennom. I tillegg skal du utføre en 3-dagers kostregistrering på de samme tidspunktene. I kostregistreringen skal du notere alt du spiser og drikker i løpet av tre sammenhengende dager, som inkluderer en helgedag (søndag-tirsdag eller torsdag-lørdag). Du skal estimere mengder av inntatt mat så nøyaktig som mulig, aller helst med bruk gramvekt. Noter også spesifikasjoner som matvaremerker, lettprodukter osv. I tillegg til dette vil du måtte besvare et skjema som anslår ettergivenheten (complience) til dietten. Dette skal utfylles ved studiens avslutning, samt i løpet av de påfølgende seks ukene etter studien.

Tidsskjema – hva skjer og når skjer det?

Du har blitt kontaktet og blitt forespurt om å delta i studien. Dersom du er villig til å være med i studien, signerer du samtykkeskjemaet bakerst i dette skrivet. Dette skal sendes via post, til adressen lengre ned på siden. I tillegg vil du etter hvert bli kontaktet over telefon for å bekrefte deltakelse.

Du vil også få utdelt skriftlig informasjon og spørreskjemaer. Skjemaene RTOG, Roma III, IBS-SSS, Roma III og Kane SF-12 og SF-NDI angir hvor plaget du er av irritabel tarm og hvordan det påvirker din livskvalitet. Disse skal fylles ut. Du skal også gjøre en 3 dagers prospektiv

kostregistrering der du noterer ned alt du spiser. Etter at du har registrert kosten din i 3 dager, sender du registreringen, signert samtykkeskjema og utfylte spørreskjemaer så fort som mulig i posten til postadresse:

Trygve Hausken
v/Trine Larsen
Medisinsk avdeling
Haukeland universitetssjukehus
5021 Bergen

For deltakere som holder til i Bergensområdet kan kostregistreringen tas med til møtet, og skjemaene blir utdelt og utfylt under møtet.
Detaljert oversikt og informasjon om hvilke matvarer som inneholder FODMAPs og som ikke kan spises under studien vil bli utdelt/tilsendt. I tillegg vil deltakerne motta en liste med alternativer til de matvarene som må kuttes ut. Det vil for dem som ikke har mulighet til å møte personlig, bli avtalt en avsatt tid for telefonsamtale der innføring i FODMAP-dietten vil bli gitt og eventuelle spørsmål besvart av student i klinisk ernæringsfysiologi.

Etter to uker med dietten vil deltakerne bli kontaktet via telefon for å få mulighet til å motta oppklarende informasjon, diskutere problemer og stille spørsmål angående dietten. Deltakerne kan også underveis i de fire ukene når som helst ta kontakt med Trine Larsen (telefon: 97013209, e-post: trine.L@student.uib.no), om det skulle være usikkerhet i forhold til dietten.

Etter fire uker avtales det et personlig møte eller telefonmøte med studieholder. I forkant av dette møtet skal det på ny fylles ut en 3 dagers kostregistrering som skal tas med til eller være sendt før møtet. I tillegg skal det under møtet fylles ut nye skjemaer av SF-12, SF-NDI, IBS-SSS og Roma III og Kane, samt ettergivenhetsskjema. Deltakerne vil under dette møtet også bli tilbydd en veiledning i hvordan matvarer med FODMAP kan reintroduseres, slik at man kan kartlegge hvilke av FODMAPene man reagerer på (ulike personer reagerer på ulikt antall og typer FODMAPs),

Alternative prosedyrer dersom du velger å ikke delta i studien:
Dersom du ikke ønsker å delta i studien vil det ikke få noen konsekvenser for din videre behandling. Dersom du underveis i studien ønsker å trekke deg kan du ta kontakt når som helst. Da vil du bli invitert til en samtale, og eventuelle problemer vil bli diskutert. Du har selvfølgelig fortsatt rett til å slutte i studien når som helst uten å oppgi grunn.

Studiedeltakerens ansvar:
Som deltaker i denne studien ber vi om at du setter deg inn i informasjonen og følger diettene så godt som mulig. Tid og dato for møter skal avtales slik at det passer for begge parter. Du må for personlige møter stille opp til avtalt tid, eller eventuelt ringe i god tid hvis timen ikke passer. Under den første samtale med studenten vil du få mer nøyaktig informasjon enn det som står i dette skrivet.

Endringer i planen:
Dersom det skjer en endring i planen, eller en tidligere avslutning av dietten, vil du bli informert så raskt som mulig. Du vil også bli orientert dersom ny informasjon blir tilgjengelig som kan føre til at du ikke lenger vil delta i studien. Dersom det oppstår en uforutsett hendelse som gjør at studien må avsluttes vil du bli kontaktet snarest mulig.

Utgifter
Som deltaker vil du ikke motta godtgjørelse for deltakelse eller tilskudd til diett.

Pasienter som har mulighet til å stille til personlig møte ved Haukeland Universitetssykehus, vil få erstattet utgifter som måtte følge i forbindelse med offentlig transport (buss/tog) og parkering.

SAMTYKKE TIL DELTAKELSE I PROSJEKTET

JEG ER VILLIG TIL Å DELTA I PROSJEKTET

Sted og dato

Deltakers signatur

Deltakers navn med trykte bokstaver

Jeg bekrefter å ha gitt informasjon om prosjektet

Sted og dato

Signatur

Rolle i prosjektet

Appendix 3: 3-day food record registration

HELSE BERGEN - ALT HANDLAR OM MENNESKE
Haukeland universitetssjukehus

KOSTREGISTRERING

NAVN _____

ADRESSE _____

_____

FØDSELSNR _____

HØYDE _____

VEKT _____

Skjemaet returneres i utfylt stand til:

Trygve Hausken
v/ Trine Larsen
Medisinsk avdeling
Haukeland Universitetssykehus
5021 Bergen

Slik går du frem:

For at vi skal kunne beregne næringsstoffinntaket ditt så nøyaktig som mulig, er det nødvendig at du noterer *alt* du spiser og drikker i løpet av en 3 dagers sammenhengende periode. Perioden torsdag til lørdag (evt. søndag til tirsdag) er best, for da får du med én helgedag.

Det er vesentlig at du spiser slik som du pleier i registreringsperioden.

- Angi klokkeslett for hver gang du spiser eller drikker noe.

- Beskriv mat og drikke så nøyaktig som mulig
  - *Brød*: Type, navn, grovhet, tykkelse på skiver, antall skiver. Ev. rundstykke, knekkebrød..
  - *Fett på brødet:* Type, navn, mengde, lett eller vanlig
  - *Pålegg:* Type, mengde, produktnavn, lett eller vanlig
  - *Middag:* Type kjøtt, fisk, kjøttfarse-/fiskeprodukt. Produktnavn. Fettprosent.
  - *Frukt og grønnsaker:* Rå, kokt eller hermetisk.

- Beskriv hvordan maten er tilberedt.
  - Kokt, bakt, stekt, grillet eller varmet i mikrobølgeovn
  - Er maten er renset for skinn og/eller fett?

- Hjemmelagede matretter beskrives i detalj, gjerne ved å skrive ned oppskriften bak på arket.

- Notér alt tilbehør, som saus, pickles, rømme, dressing eller krem, med navn/produsent. Oppgi også om du bruker sukker på gryn, grøt eller i te.

- Få med alle mellommåltider, samt tilfeldig spising og drikke utenom de faste måltidene.

- Kosttilskudd, som tran, vitamintabletter o.l. skal også noteres, med navn, produsent og mengde.

- Mengder kan beskrives på følgende måte:
  - aller helst skal du veie maten og føre mengden opp i gram
  - hvis du ikke kan veie, kan du angi mengder i husholdningsmål, som spiseskje, glass, desiliter eller antall, alt ettersom hva som er hensiktsmessig
  - oppgi størrelse på glassene du bruker i dl

Eksempel:

Kl	*Tirs* **dag** *14 / 1 / 11*	**Produktnavn/Produsent**	**Vekt**
0730	*1 butikkskåret skive kneip*	*Bakers*	*30g*
	m/ skrapet lag margarin	*Soft Soya*	
	3 høvelskiver hvitost, 16% fett	*Norvegia, Tine*	
	1 stor grapefrukt		*200g*
	1 stort glass lettmelk (Stort glass = 2 dl)	*Tine*	
1100	*1 beger fruktyoghurt*	*Yoplait Dobbel 0%, mango*	*125g*
	1 melkesjokolade	*Freia*	*100g*
	1 kopp svart kaffe		*150g*
1500	*kokt torsk*		*140g*
	3 små potete, kokt		*150g*
	3 toppede ss revet gulrot		
	1 ss remulade	*Idun*	
	2 store glass saft	*Lerum uten tilsatt sukker*	

Kl	..... dag ... / ... / ...	Produktnavn/Produsent	Vekt

HELSE BERGEN
Haukeland universitetssjukehus
Avdeling for klinisk ernæring

Kl	..... dag ... / ... / ...	Produktnavn/Produsent	Vekt

HELSE BERGEN
Haukeland universitetssjukehus
Avdeling for klinisk ernæring

Kl	..... dag ... / ... / ...	Produktnavn/Produsent	Vekt

HELSE BERGEN
Haukeland universitetssjukehus
Avdeling for klinisk ernæring

FODMAP-redusert kost

En kostveiledning i forbindelse med diettstudie for pasienter med stråleskadet tarm

Først og fremst en stor takk til deg som ønsker å delta i studien "Effekt av lav FODMAP-diett ved stråleskadet tarm". Dette er et informasjonsskriv til deg bestående av litt teoretisk bakgrunn kombinert med en beskrivelse av hvordan dietten utføres i praksis og en matvareliste. Ikke nøl med å ta kontakt på mail eller telefon dersom du har spørsmål!

Trine Larsen – Masterstudent i klinisk ernæring
E-post: trine.L@student.uib.no
Telefon: 970 13 209

IRRITABEL TARM ETTER STRÅLESKADE

Irritabel tarm, eller irritable bowel syndrome (IBS), er ikke en sykdom, men en tilstand som kan medføre ulike plager i mage og tarm. Man kan oppleve symptomer som kvalme, mageknip, magesmerter, magekramper, oppblåsthet, utspilt mage, luft/gass og rumling i tarmen. Man kan også ha avføringsforstyrrelser som akutt avføringstrang, diaré, forstoppelse og vekslende løs/hard avføring. Som regel er det ikke kjent hva som er årsaken til disse symptomene, men IBS-symptomer har vist seg å være en vanlig akutt og kronisk bivirkning av strålebehandling mot kreft i buk-regionen. Årsaken til dette er at vevsforandringer etter strålebehandlingen kan medføre at tarmen får svekket opptak av næringsstoff, blir overfølsom for gass og utvidelse, får endret tarmbakterieflora og/eller endret bevegelsesmønster i tarmveggen. For noen kan plagene utløses eller forverres av mat eller drikkke. Å endre på kosten kan være en god symptomlindrende behandling når man har stråleskadet tarm, men vil ikke fjerne *årsaken* til symptomene (vevsforandringen i tarmveggen).

Generelle råd ved stråleskadet tarm

Siden tarmveggen er skadet av strålebehandlingen vil dette kunne føre til at absorpsjonen (opptaket) av næringsstoffer i tarmen reduseres. Dette påvirker noen næringsstoffer mer enn andre. De generelle kostrådene ved stråleskadet tarm er basert på prinsipper om å redusere inntak av laktose, fett, gassdannende matvarer, sterkt krydder, hard stekeskorpe, samt å spise små, hyppige og regelmessige måltider. Disse rådene er generelle og passer kanskje for noen, men ikke for alle. Prinsippene har noen likhetstrekk i det man ser i en FODMAP-redusert kost, men ”tillater” mange matvarer som inneholder FODMAPs. Det er en erfaring hos kliniske ernæringsfysiologer at lavFODMAP-dietten kan gi symptomlindring hos pasienter med stråleskadet tarm.

HVA ER FODMAP?

FODMAP er en forkortelse for **f**ermenterbare **o**ligosakkarider, **d**isakkarider, **m**onosakkarider og (**a**nd) **p**olyoler. Dette er karbohydrater som regnes som *tungtfordøyelige* siden tynntarmen kan ha vanskeligheter med å bryte ned og absorbere dem. De havner derfor ufordøyd i tykktarmen hvor de tiltrekker væske (fra blodet til tarmen) og fermenteres (gjæres) av bakterier. Fermentering betyr at bakterier omdanner ufordøyd mat til gass og til energi (korte fettsyrer). Et stort inntak av tungtfordøyelige karbohydrater vil altså gi økt mengde væske, gass og fettsyrer i tarmen Dette er en normal og viktig prosess, og det er blant annet essensielt for tarmcellenes helse. Fermentering er noe som i ulik grad skjer hos alle mennesker, men de med irritabel tarm får mer uttalte plager og plager ved mindre mengder FODMAPs enn andre. Tanken ved lav-FODMAP dietten er å redusere inntak av karbohydrater som kan fermenteres i tarmen, og på den måten minske plagene. Dietten er utarbeidet av australske forskere (Peter Gibson og Sue Shepherd) ved Monash Universitet, og den er utprøvd i mange store studier, med positive resultater.

Hvorfor reagerer noen mer på FODMAPs enn andre?

Mange av de tungtfordøyelige karbohydratene absorberes dårlig av alle mennesker, men folk flest tåler likevel FODMAP godt. Grunnen til at personer med irritabel tarm som følge av strålebehandling får plager av FODMAP kan være følgende:

Tarmoverfølsomhet for gassproduksjon

Ved irritabel tarm er tarmen mer følsom for gassen som blir produsert, og den trykkøkningen i tarmen som gassen forårsaker oppleves mer smertefull og ubehagelig.

Bakteriell overvekst i tynntarmen

Bakterier som normalt sett er lokalisert i tykktarmen, beveger seg over i tynntarm. Når FODMAP gjæres av bakterier i tynntarm, vil gassen som dannes øke trykket i et smalt parti i tarmen som gir smerte og ubehag.

SLIK GÅR DU FREM

Når man skal prøve ut FODMAP-redusert diett snakker man om to faser. Den første fasen er *restriksjonsfasen* hvor man unngår/begrenser inntaket av matvarer med høyt FODMAP-innhold i 4 uker. Om man ikke merker bedring etter disse 4 ukene, er det ingen hensikt i å fortsette med dietten. Om plagene blir mindre, derimot, kan man gå videre til den ande fasen som kalles *reintroduksjonsfasen*. I denne fasen forsøker man på en systematisk måte å reintrodusere de matvarene man har fjernet fra kosten. Man innfører en og en av undergruppene av FODMAP og registrerer symptomer. Denne fasen tar sikte på å "skreddersy" et kosthold tilpasset hver enkels individuelle toleranse for type og mengde FODMAP. Dette resulterer i at man kan spise et variert kosthold uten mage- og tarmplager, som samtidig ikke er mer begrenset enn det behøver å være. Alle som deltar i studien vil i etterkant bli tilbydd veiledning i reintroduksjon. Informasjon om hvordan man går frem vil da bli tilsendt.

Restriksjonsfasen

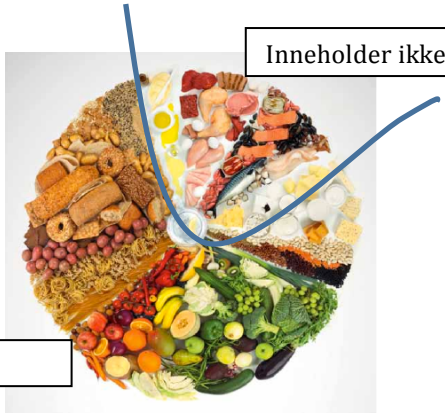
Tre sentrale spørsmål må besvares når man skal starte med FODMAP-redusert diett

1. Hvor i kosten finner man *karbohydrater?*
2. Hvilke karbohydrater er *tungtfordøyelige?*
3. Hvilke matvarer har et *høyt innhold* av tungtfordøyelige karbohydrater?

1. Hvor i kosten finner man karbohydrater?

Karbohydrater er en av de tre hovednæringsstoffene som gir energi til kroppen, i tillegg til fett og proteiner. Karbohydrater finnes i de fleste matvarer med unntak av i rent matfett (smør, margarin, olje) og i rene animalske matvarer som rent kjøtt, fjærkre, fisk, skalldyr og egg. Nevnte matvarer kan derfor spises ubegrenset på dietten. Vær oppmerksom når disse varene er smaksatt, marinerte eller i form av blandingsprodukter (pølser, farse osv.), da de kan inneholde bl.a. løk, hvitløk, melk og hvete. Matvarer som inneholder karbohydrater og som derfor *potensielt* kan inneholde FODMAPs, er følgende:

- korn, kornprodukter, nøtter og frø
- grønnsaker, frukt, bær og belgfrukter
- poteter, ris og pasta
- melk og meieriprodukter
- blandingsprodukter, godteri og snacks



Bilde: Redigert kostholdssirkel Helsedirektoratet.

2. Hvilke type karbohydrater er tungtfordøyelige?

Det er mange måter å kategorisere ulike typer karbohydrater på, slik som ”raske og langsomme” eller ”sukker, stivelse og fiber”. FODMAP-karbohydrater er gruppert etter *antall sukkerenheter*. Nedenfor er en oversikt, men det er ikke nødvendig å kjenne alle disse navnene.

GRUPPE	Antall sukkerenheter	Potensiell FODMAP
Monosakkarid	1	*Fruktose*
Disakkarid	2	*Laktose*
Oligosakkarid	3-10	*Fruktaner* (FOS: Frukto-oligosakkarider og inulin) *Galaktaner* (GOS: Galakto-oligosakkarider)
Polysakkarid	>10	**Ingen**
Polyoler		Sukkeralkoholer og søtstoff som ender på ”-ol" *Sorbitol, xylitol, mannitol, maltitol, isomalt, lactitol*

3. Hvilke matvarer har et høyt innhold av tungtfordøyelige karbohydrater?

Å følge en FODMAP-redusert diett innebærer ikke at man skal ekskludere alle matvarer som inneholder karbohydrater, men å begrense de matvarene som har et høyt innhold av *tungtfordøyelige karbohydrater.* En oversikt over slike matvarer og hvilke matvarer som har lavt innhold er fremstilt i tabellene i det vedlagte heftet. Disse er kategorisert etter matvaregrupper. Det er viktig å beholde karbohydrater i kosten mat da matvarer med små mengder FODMAPs både kan og bør inngå i en sunt og variert kosthold. Karbohydrater uten FODMAP er:

- Glukose (druesukker) i frukt og bær
- Sukrose (vanlig sukker) som bør begrensen av hensyn til generell helse
- Stivelse (lange glukosekjeder) i poteter, korn, pasta, ris og rotgrønnsaker
- Kostfiber (lange ufordøyelige kjeder) i grove kornprodukt, frukt og grønnsaker.

NB! Toleranse av kostfiber vil være individuelt. Kostfiber er i likhet med FODMAPs også tungtfordøyelige karbohydrater, men forekommer som større forbindelser. Man skiller mellom vannløselige og ikke- vannløselige, og de førstnevnte er gunstige.

FODMAP-redusert kost er ikke det samme som lavkarbo eller glutenfri kost!

Utfordringen ved å gå på en FODMAP-redusert diett er å lære seg hvilke matvarer som inneholder de tungtfordøyelige karbohydratene og å kunne finne disse i varedeklarasjoner og innholdslister. I starten kan det virke overveldende og komplisert, men etter hvert lærer man seg hva man skal se etter, og man vil bli mindre avhengig av å slå opp i listene.

I det vedlagte heftet er det tabeller over matvarer som har *lavt* innhold av FODMAPs og kan spises fritt, har *høyt* innhold av FODMAPs og bør unngås, og varer med *moderat* innhold av FODMAPs som kan spises i begrensede mengder. Porsjonsmengden i gram som er oppgitt gjelder mengder en ikke bør overskride innenfor et måltid. Det er viktig å påpeke at selv om man holder seg innenfor de anbefalte mengdene av en matvare, må man samtidig passe på at man ikke inntar mange ulike matvarer med moderat innhold i ett og samme måltid. Da kan den totale mengden FODMAPs overskride toleransegrensen. Dette gjelder også om man inntar veldig store mengder av varene i lav FODMAP- kategorien. Derfor er det lurt å holde seg innenfor de anbefalte og "normale" porsjonsstørrelsene, samt å fordele karbohydratinntaket over flere måltider. Det er viktig å huske på at listene er ment som oppslagsverk, hvor man kan sjekke innholdet i de varene man bruker selv. Listene inneholder mange matvarer som mange aldri bruker, eller har kjennskap til i det hele tatt.

Tabellene er basert på matvarelistene til Julianne Lyngstad, som har utarbeidet dem ved hjelp av mobilapplikasjonen "The Monash Uni Low FODMAP Diet". Om du har en smarttelefon er det anbefalt å kjøpe denne applikasjonen. Vi vil refundere kostnadene for denne om det er ønskelig, bare spør etter et refusjonsskjema. Det finnes også en nyutviklet norsk applikasjon som heter Mollyosa. Denne er detaljert og fin, men vi kan ikke garantere at all info der stemmer.
Det anbefales å bruke facebook gruppen "Low FODMAP-norsk gruppe" for å motta og dele erfaringer, oppskrifter og utfordringer med andre. Det er også gitt ut mange norske bøker om dietten, som er å finne hos bokhandleren. Det finnes utallige nettsteder med informasjon om dietten, og det er viktig å ikke lese ukritisk overalt, da dette kan være mer forvirrende enn oppklarende. Om du skulle ha spørsmål, ta heller kontakt med studieholder.
Andre nyttige linker:

- Nasjonal kompetansetjeneste for Funksjonelle Mage-tarm sykdommer www.helse-bergen.no/nkfm
- www.lowfodmapnorskgruppe.blogspot.no (bloggen til facebook-gruppen)
- www.friskforlag.no/lavfodmap-lister/
- www.lyngstadernaering.no

PRAKTISKE RÅD VED FODMAP-REDUSERT KOST

Frokost/Lunsj/Kvelds

- 2 skiver surdeigsbrød av spelt eller glutenfritt brød/knekkebrød/rundstykker med pålegg
- Havregrøt på laktosefri melk, med bringebær, jordbær, blåbær eller banan
- Havregryn eller cornflakes med laktosefri melk/biola/yoghurt/kesam
- Hjemmelaget müsli av havregryn, rosiner og nøtter
- Omelett (med eks. skinke, hvitost, potet, paprika, brokkoli, squash, oliven)
- Salat
    - Grønn salat, tomat, agurk, paprika, vårløkblader, oliven, melon
    - Glutenfri pasta
    - Kylling/kjøtt/egg/fisk/sjømat
    - 1 ss Pinjekjerner eller gresskarkjerner

Middag

- Rene produkter av kjøtt, egg, fisk og sjømat
- Blandingsprodukter av kjøtt/fisk – les innholdslisten nøye!
- Poteter, ris, glutenfri pasta, risnudler, quinoa
- Eggeretter
- Pannekaker med havremel, glutenfritt mel og laktosefri melk
- Pizza med glutenfri bunn og FODMAP-redusert pizzafyll
- Nachos (tortillachips) med kjøttdeig, hvitost og grønnsaker
- Hjemmelaget suppe med grønnsaker, kjøtt osv.
- Stekte grønnsaker/ wok
- *Tilsett:* oljer, sitronsaft, laktosefri rømme/kesam, friske urter, chili, ingefær, lønnesirup, salt og pepper, hvitløksolje (la hvitløksfedd trekke i olje en uke, fjern så hvitløksbitene, eventuelt frese hvitløk i olje for så å plukke ut bitene – obs. dette fungerer ikke om det kokes i vann)
  Thousand Island dressing (Idun), selskapsdressing (Salatmesteren).

Pålegg

- Rene kjøttpålegg
- Egg
- Reker og annen sjømat (stabburet makrell i tomat)
- Rene fiskepålegg (røkelaks, tunfisk)
- Kaviar, majones
- Avokado (noen spiseskjeer)
- Ost: hvitost, brie, cottage cheese (noen spiseskjeer), cheddar, edamer, mozarella, camembert, fetaost
- Syltetøy: jordbær, bringebær, blåbær
- Peanøttsmør
- Banan
- Agurk, tomat, paprika, salat

Mellommåltider

- Lav-FODMAP frukt eller grønnsaker
- En liten neve nøtter (peanøtter, paranøtter, valnøtter, hasselnøtter, mandler)
- Laktosefri mager kesam eller laktosefri yoghurt med lav-FODMAP frukt/bær
- Riskaker med pålegg
- Müslibar (oppskrift på lyngstadernæring.no)
- Matmuffins av egg og tilbehør
-

Snacks

- Sorbet-is, vannis (av eks. Fun-light med lav-FODMAP frukt/bær)
- 1 lite glass moothie av lav-FODMAP frukt/bær, banan, laktosefri yoghurt
- Fruktsalat med laktosefri meieriprodukt
- Glutenfrie kjeks og kaker – les innholdslisten nøye!
- Havrekjeks med nøtter og mørk sjokolade
- Pannekaker/vafler av spelt/glutenfritt mel og laktosefri melk
- Riskaker (naturell eller salt) med eks, banan/peanøttsmør
- Tortillachips, popcorn,potetchips (salt)
- Nøtter
- Mørk sjokolade (70% kakao), Non-stop
- Mentos mint, Ahlgrens biler, Nidar lakrisbåter, vepsebol, Haribo stjernemix, vingummi, smågodt uten FODMAPs,
- Av tyggis og pastiller/drops er de sukkerholdige trygge

Obs!

- Ikke alle glutenfrie produkter er lav-FODMAP (se etter inulin, fruktose, eplefiber, epleekstrakt, betefiber, roefiber, honning, soyamel, løk osv.)
- Konsentrert fruktjuice (eple/pære) brukes i blant som søtning
- Dipp og dressing inneholder ofte løk og hvitløk
- Smaksatt vann kan inneholde fruktose
- Yoghurt kan være tilsatt fruktose
- Inulin kan finnes i yoghurt, brød og müsli (som fiber eller prebiotikum)
- Dersom du reagerer på mye kostfiber, begrens matvarer med mye fiber, og velg heller fine produkter enn grove. En gradvis økning av fiber kan bedre toleransen.

På **varedeklarasjonen** skal alle ingrediensene oppgis i rekkefølge etter vekt. Den ingrediensen det er mest av nevnes først, og den det er minst av til sist. Bruk denne kunnskapen når du skal vurdere om en matvare kan inngå i kostholdet ditt. Små mengder FODMAP går som regel bra. Står for eksempel hvete listet opp sent i ingredienslisten inneholder matvaren så lite at de aller fleste tåler det.
Unntak: Søtstoffene som ender på –ol (Tabell 3), løk og hvitløk bør unngås selv i små mengder i eksklusjonsperioden.

ET LITE UTVALG OPPSKRIFTER

Grove hjemmelagde knekkebrød (to brett)

- 3 dl havregryn/havremel (evt. rismel, bokhvetemel, hirseflak, glutenfri melblanding)
- 1 dl gresskarkjerner
- 1 dl sesamfrø
- 1 dl solsikkefrø
- 1 dl linfrø
- 3 ss havrekli
- 2 ss fiberhusk
- 1 ts salt
- 4-5 dl vann

Slik gjør du:
Bland sammen alle ingrediensens og la røren svelle i 10 minutter. Fordel deigen med en slikkepott over 2 stekebrett dekket med bakepapir (bruk gjerne flergangsbruk bakepapir). Stek på 165°C i ca. 35 minutter. Ta brettene ut og skjær opp ruter med et pizzahjul. Bytt plass på brettene og stek i ytterligere 35 minutter. Temperatur og steketid varierer fra ovn til ovn, pass på underveis og ha på varmluft eller ha en liten glippe i ovnsdøra.

Grovt brød (1 stykk)

- 850 g melblanding av Toro lys glutenfri melblanding, eller en blanding av eks.:
    - rismel
    - bokhvetemel
    - tapiokamel
    - potetmel
    - havregryn
    - hirseflak
- 2 ts. bakepulver
- 1 ts. sukker
- 1 pk tørrgjær
- 1 ss linfrø
- 1-2 ss olje (kan sløyfes)
- 1 egg
- 5 dl lunkent vann

Slik gjør du:
Ha tørrgjær og sukker i det lunkne vannet og bland godt. Tilsett resten av ingrediensene og kna deigen. La den heve på et lunt sted i minst 50 minutter, til dobbel størrelse. Ha deigen i en brødform (1 liter) og la den etterheve i 15 minutter. Stekes på 200°C i 40-50 minutter på nederste rille i ovnen.

Banan-og havregrynspannekaker
Slik gjør du:
Mos ½-1 banan, 1-2 egg og ½-1 dl havregryn med en stavmikser. Fordel røren på 3-4 mellomstore pannekaker/lapper i en stekepanne og stek dem på middels varme i ca. 1 min på hver side.

Pannekaker og vafler generelt: ta utgangspunkt i vanlig oppskrift og bytt ut hvetemel med ca 2/3 glutenfritt mel og 1/3 havremel. Melken erstattes med laktosefri melk.

Lav-FODMAP, glutenfri gjærdeig (til pizza, pitabrød eller rundstykker)

- 150 ml laktosefri melk
- 150 g laktosefri kesam
- 190 g Toro lys glutenfri melblanding + 50 g til utbaking
- 30 g smeltet smør
- ½ pk. tørrgjær
- 1 ts. sukker
- 2 ts. fiberhusk
- 1/3 ts. hjortetakksalt (viktig!)

Slik gjør du:
Varm opp melk, kesam og smør til ca. 38-40°C. Tilsett sukkeret og tørrgjæren og visp til det er løst opp. Bland sammen resten av det tørre, og tilsett væsken. Rør godt. Deigen er ganske løs, og det skal den være. La den så heve i ca. 1 time.
Kna så deigen godt med en god del mel på bordet.
For rundstykker og pitabrød: form deigen og etterhev 45 min før du steker på 220-250°C i 8-15 minutter.
For pizza: forstek deigen på 250°C i 4-8 min, ha på fyll og stek til osten er gyllen

Scones (8-10 stk.)

- 145 g Toro lys, glutenfri melblanding
- 40 g havremel
- 1 ts bakepulver
- 1 ts salt
- 1 ts sukker
- 60 g smør
- 40 g parmesan-ost (kan sløyfes)
- 100 g cottage cheese (kan byttes med laktosefri melk/yoghurt)
- 1 dl laktosefri melk
- 1 egg

Slik gjør du:
Bland alt det tørre og smuldre smøret inn. Bland melk og cottage cheese og bruk en stavmikser for å jevne ut cottage cheesen. Tilsett egget i blandingen og bland godt. Bland det våte med det tørre raskt. Her skal du ikke elte, kna og røre, deigen skal ikke bli seig. Settes på bakepapir med skje.
Stekes på 200 grader i 10-12 min.
(denne oppskriften kan også brukes til hamburgerbrød, pølsebrød osv.

Havrekjeks med nøtter og sjokolade (ca. 40 stk.)

200 g smør/margarin
2 dl brunt sukker + 2 dl hvitt sukker
1 ts vaniljesukker
2 egg
3 dl glutenfri melblanding
½ ts salt
1 ts bakepulver
6 1/2 dl havregryn
ca. 100 g mørk sjokolade, grovhakket
ca. 80 g mandler, grovhakket

Slik gjør du:
Rør smør, sukker og vaniljesukker til det blir en porøs smørkrem. Tilsett eggene, ett om gangen, og rør godt. Bland i mel, salt og bakepulver og rør godt. Tilsett til slutt havregryn og hakkete mandler og sjokolade. Sett kjeksene med skje på stekeplate dekket med bakepapir, og ha litt god avstand mellom kakene. Stekes ved 150°C i ca. 15 minutter og avkjøles på rist.

MATVARELISTE FODMAP

Siden FODMAP er mange ulike undergrupper av karbohydrater er det slik at det er individuelt hvilke typer FODMAP en tåler og ikke tåler. Derfor er det i matvarelistene oppgitt forkortelser for hvilke undergrupper av FODMAP matvaren inneholder. Dette er relevant informasjon mest i etterkant av fase 2 – reintroduksjon av FODMAPs.
OF = Oligosakkarider (Fruktaner)
OG = Oligosakkarider (Galaktaner)
D = Disakkarid (laktose)
M = Monosakkarid (Fruktoseoverskudd)
PM = Polyoler (Mannitol)
PS = Polyoler (Sorbitol)

GRØNNSAKER OG BELGFRUKTER

LAV FODMAP (SPIS)	MODERAT FODMAP (BEGRENS)	HØY FODMAP (UTELUKK)
Agurk	Artisjokk, hermetisert: 56 g (OF, M)	Artisjokk (OF, M)
Alfalfaspirer	Avocado: 20-40 g (PS)	Asparges (M)
Aspargesbønner	Flaskegresskar: 60 g (OG, PM)	Blomkål (PM)
Aubergine	Fermentert rødkål: 140 g (OF)	Kassava (OG)
Bambusskudd	Gresskar, hermetisert: 120 g(OF, OG)	Hvitløk (OF)
Bladbete/sølvbete	Selleristilk: 19 g (PM)	Jordskokk (OF)
Bok choy/Pak Choy	Soltørket tomater: 16 g (M)	Løk, gul (OF)
Bønnespirer		Løk, rød (OF)
Chili, grønn/rød	**BELGFRUKTER**	Mais (OG, PS)
Choy sum	Chana dal, kokte: 46 g (OG)	Portobello sopp (PM)
Galangarot	Grønne linser, kokte: 46 g (OF, OG)	Purreløk, hvit del (OF)
Gresskar	Kikerter, hermetiserte: 44 g (OG)	Rødbeter (OF, OG)
Gressløk	Linser, hermetiserte: 46 g (OG)	Salatløk (OF)
Grønnkål	Røde linser, kokte: 46 g (OG)	Sauerkraut, fermentert (PM)
Gulrot	Urid dal, kokte: 46 g (OG)	Savoykål (OF)
Ingefær		Shiitake sopp (PM)
Nepe	*Brokkoli: 47 g (OF, OG, PS)	Sjalottløk (OF)
Nori (sjøgress)	*Fennikel: 49 g (OF, PM)	Sjampinjong + sopp (OF, PM)
Okra	*Kål: 94 g (PS)	Søtpotet (PM)
Oliven	*Kålrabi: 65 g (PS)	Taro (M)
Paprika (alle farger)	*Rosenkål: 38 g (OF, PS)	Vårløk, hvit del (OF)
Pastinakk	*Rødkål: 89 g (6 stk.) (PS)	
Poteter		**BELGFRUKTER**
Purreløk (det grønne)	*Listet som lav av Monash University,	Bondebønner (OG)
Reddik	men bør begrenses pga. moderat	Borlottibønner (OG)
Ruccola	innhold av FODMAPs	Delikatessebønner (OG)
Salater		Favabønner (M)
Sellerirot		Grønne erter (OG)
Sikoriblader (endive)		Kidneybønner (OF, OG)
Sitrongress		Kikerter (OG)
Sjampinjong, hermetisert		Limabønner (OF, OG)
Spinat		Mungbønner (OF, OG)
Squash		Soyabønner (OF, OG)
Tomat		Splitterter (OF, OG), flate (OF,
Vannkastanjer		OG, PM)
Vårløk (det grønne)		Sukkererter, runde (M)
Yam		Tomatbønner (OF, OG, M)

* Løk og hvitløk: Disse blir ofte brukt i pulverform og kan skjule seg bak ”krydder” i ingredienslisten

FRUKT OG BÆR

LAV FODMAP (SPIS)	MODERAT FODMAP (BEGRENS)	HØY FODMAP (UTELUKK)
FRUKT Ananas Appelsin Banan Banan, tørket (20 g) Cumquats Dragefrukt Druer Durian Fikenkaktus Guava, moden Kaktusfiken Kiwi Klementin, mandarin Kokebanan Lime Melon, Cantaloupe Melon, Honning Papaya Pasjonsfrukt Rabarbra Sitron, sitronsaft Stjernefrukt **BÆR** Blåbær Bringebær Jordbær Tyttebær *Begrens inntaket frukt og bær til 2-3 à 100 gram selv av lav-FODMAP typer	**FRUKT** Avocado: 40 g (PS) Banan, moden: 3⁄4 banan (M) Granateple: 0,5 dl frø (OF) Kokosnøtt: 96 g (PS) Kokos, tørket: 37 g (PS) Longan: 10 stk (PS) Rambutan: 4 stk (OF) **TØRKET FRUKT** Tranebær, tørket: 26 g (OF) Pasjonsfrukt, tørket: 5 g Kokos * Uansett type (lav/moderat/høy) vil visse former frukt være høy FODMAP: - Fruktjuice - Større porsjoner av frisk frukt/smoothie - Hermetisk frukt i egen juice - Det meste av tørket frukt/bær	**FRUKT** Aprikos (OF, PS) Eple (M, PS) Fersken (PS) Fiken (M) Grapefrukt (OF) Granateple (OF) Guava, umoden (M) Litchi, Lychee (PS) Mango (M) Nektarin (OF, PS) Persimmon (sharon) (OF) Plomme (OF, PS) Pære (M, PS) Tamarillo (M) Vannmelon (M, OF, PM) **BÆR** Bjørnebær (PS) Boysenbær (M) Kirsebær (M, PS) Solbær (OF) Tindved **TØRKET FRUKT** Dadler (OF) Korinter Rosiner (OF) Svisker (OF, PS) Tørket ananas (OF) Tørket aprikos (OF, PS) Tørket eple (M, PS) Tørket fiken (OF) Tørket gojibær (OF) Tørket mango (OF) Tørket papaya (OF) Tørket pære (M, PS)

NØTTER OG FRØ

LAV FODMAP (SPIS)		MODERAT FODMAP (BEGRENS)	HØY FODMAP (UTELUKK)
NØTTER*	**FRØ**	**NØTTER**	**NØTTER**
Kastanjenøtter	Chiafrø	Hasselnøtter - 10 stk (OF, OG)	Cashew (OF, OG)
Makademia	Gresskarkjerner	Mandler - 10 stk (OF, OG)	Pistasjnøtter (OF, OG)
Paranøtter	Linfrø		
Pekan	Sesamfrø		
Peanøtter	Solsikkefrø		
Pinjekjerner	Valmuefrø		
Valnøtter			
*En håndfull per måltid			

MEL, KORN OG PASTA

LAV FODMAP (SPIS)	MODERAT FODMAP (BEGRENS)	HØY FODMAP (UTELUKK)
MEL OG KORN Bokhvetemel Bokhveteflak Hirse Hirseflak Hirsemel Maismel Maisenna (maisstivelse) Polenta Potetstivelse Quinoamel Quinoaflak Quinoa Ris, brun Ris, fullkorn Ris, hvit Ris, vill Risflak Rismel Sorghum Surdeigsbrød av 100% spelt* Tapiokastivelse Teff **PASTA OG NUDLER** Glutenfri pasta** Risnudler Rispasta Sobanudler (av bokhvete) Quinoa-pasta Glutenfri pasta produseres av eks. Schar, Semper og Barilla *Inneholder mindre enn rug og hvete, men bør unngås i restriksjonsfase. Ved surdeigsbakt speltbrød har gjæringsprosessen brutt ned noe FODMAP ** Obs. noen inneholder soya	**MEL OG KORN** Bokhvete, hel: 54 g (OF) Havregryn: 47 g (OF, OG) Havrekli: 2 ss (OF, OG) Havremel: 47 g (OF, OG) Riskli: 2 ss (OF) **CEREALER** Cornflakes: 30 g (OF) Puffet ris: 30 g (OF)	**MEL OG KORN** Amarant (OF) Bulgur (OF) Bygg (OF, OG) Couscous av hvete (OF) Couscous av ris og mais (OF) Durumhvete (OF) Emmer (OF) Enkorn (OF) Ertemel (OG) Grahamsmel Hvete (OF) ** Kamut (OF) Kikertmel (OG) Kruskakli/hvetekli (OF) Linsemel Lupin (OF) Mandelmel (OF) Rug (OF, OG) Soyaflak (OG) Soyamel (OG) Spelt (OF) Triticale (Rughvete) (OF, OG) Fiberrike glutenfrie mel-blandinger (OF)* **PASTA** Glutenfri fiberrik pasta (OF)* Hvetenudler (OF, M) Gnocci (OF) Pasta/spagetti av hvete (OF) Speltpasta (OF) *Les ingredienslisten: Kan inneholde soyamel, inulin, sikorirot eller roefiber. **Kan oppgis med navnene: durum, spelt, semule, bulgur, coscous og gluten

* Cornflakes: kan ha malt, maltekstrakt og honning. Den glutenfrie fra Schar er lav-FODMAP
* Havre: trenger ikke være glutenfri med mindre cøliaki er påvist. Mengdene oppgitt er basert på australsk havre og mengder opp mot 100 g av norsk havre skal vise seg tolerabelt. Vurder egen inntaksgrense
* Glutenfritt: gluten er et protein som pasienter med cøliaki reagerer på, og trengs ikke unngås i FODMAP-redusert diett. Grunnen til at mange glutenfrie produkter er egnet, er at de er laget av alternative kornsorter som også er lavFODMAP. Selv om glutenfrie produkter er laget av lavFODMAP kornsorter kan de likevel være tilsatt høyFODMAP ingredienser som eplefiber, inulin, epleekstrakt, fruktose, honning, løk, betefiber og roefiber.

MELK, MEIERIPRODUKTER OG ALTERNATIV TIL MELK

LAV FODMAP (SPIS)	MODERAT FODMAP (BEGRENS)	HØY FODMAP (UTELUKK)
MELK OG MEIERIPRODUKTER Laktosefri gresk yoghurt Laktosefri kremfløte Laktosefri lettrømme Laktosefri mager kesam Laktosefri matfløte Laktosefri melk Laktoseredusert melk Laktosefri yoghurt naturell Laktosefri yoghurt blåbær/vanilje Litago, lettere sjokolade Margarin Meierismør Sorbet-is av lav-FODMAP frukt/bær Tine yoghurt fyldig naturell/vanlilje **OST** Brie Blåmuggost Camembert Cheddar Chevre Cottage cheese (4 ss) Edamer Emmentaler Fetaost (i blokk) Havartiost Hvit geitost Hvitost (norvegia, synnøve osv.) Mozarella Parmesan Pecorino Pultost Sveitserost Smøreost, kavli **ALTERNATIV TIL MELK** Hempmelk Kokosmelk Mandelmelk	**OST** Haloumi: 100 g (D) Kremost: 81 g (D) Ricotta: 80 g (D) Rismelk: 2 dl	**MELK OG MEIERIPRODUKTER** Fløteis (D) Geitemelk (D) Kefir (D) Kesam (D) Kremfløte (D) Kumelk (og fra andre pattedyr) (D) Matfløte (D) Rømme (D) Soyayoghurt (OG) Vikingmelk (D) Yoghurt (D) **OST** Brunost (D) Fetaost i marinade (OF) Geitost (D) Prim (D) **ALTERNATIV TIL MELK** Havremelk (OG) Soyamelk (OG)* *Laget av soyabønner.

VARM OG KALD DRIKKE

LAV FODMAP (SPIS)	MODERAT FODMAP (BEGRENS)	HØY FODMAP (UTELUKK)
KAFFE*	**JUICE**	**KAFFE**
Espresso	Appelsinjuice, ferskpresset: 100 ml	Kaffe med laktoseholdig melk (D)
Kaffe, koffeinfri, svart	Smoothie av lavFODMAP ingredienser	Kaffe med soyamelk (OG)
Kaffe, svart	Tranebærjuice: 250 ml	
Kakao (laktosefri)	Tomatbasert grønnsakjuice: 210 ml	**TE**
Litago, lettere sjokolade		Fennikel-te (OF)
Pulverkaffe		Kamille-te (OF)
Traktekaffe		Løvetann-te (OF)
TE*		Oolong-te (OF)
Peppermyntete		Roibos (OF)
Te, grønn		Urte-te med sikorirot (OF)
Te, hvit		*Sterk te kan generelt gi plager
Te, svart		
		ALKOHOL
*Koffein i kaffe og te kan trigge symptomer		Cider (M)
		Dessertvin (M)
ALKOHOL*		Rom (M)
1 enhet pr. dag er lavFODMAP		**LESKEDRIKK**
Gin		Appelsinjuice fra konsentrat (M) Brus, sukkerfri med fruktjuicekonsentrat (M)
Musserende vin (brut nature)		Brus, sukkerholdig med fruktjuicekonsentrat (M)
Rødvin		Eplebaserte juicer (M, PS)
Tørr hvitvin		Eplejuice (M, PS)
Vodka		Kokosvann (OF, PS)
Whisky		Tropisk juice (M, PS)
Øl		
*Alkohol kan trigge symptomer		
LESKEDRIKK		
Brus, sukkerfri uten fruktjuicekonsentrat	* Brus: vær obs. på at kullsyre kan gi oppblåsthet.	
Brus, sukkerholdig uten fruktjuicekonsentrat	* Pulverkaffe: kan inneholde mye fiber	
Fun light saft		
Sprudlevann, farris		
Zeroh saft		

VEGAN/VEGETAR – SOYAPRODUKTER

Ost fra Wilmersburger	Chana dal, kokte: 46 g (OG)	Silketofu (OG)
Tempeh	Grønne linser, kokte: 46 g (OG, OF)	Soyamelk (OG)
Tofu	Kikerter, hermetiserte: 44 g (OG)	Soyayoghurt (OG)
Tofutti ost	Linser, hermetiserte: 46 g (OG)	
Quorn	Røde linser, kokte: 46 g (OG)	**Tips:** Er produktet laget av hele soyabønner er det høyFODMAP.
	Urid dal, kokte: 46 g (OG)	
Tips: Er produktet laget av soyaproteiner er det lavFODMAP.		

SNACKS, DROPS OG SØTSAKER

LAV FODMAP (SPIS)	MODERAT FODMAP (BEGRENS)	HØY FODMAP (UTELUKK)
Drops, sukkerholdige Laktosefri fløteis Melkefri/laktosefri melkesjokolade Mørk sjokolade (over 70 % kakao) Potetgull, salt Popcorn Riskaker, salt Tacoskjell Tortillachips, salt	Hvit sjokolade: 30 g (D) Melkesjokolade: 30 g (D)	Fløtekarameller (D) Iskrem (D) Potetgull, krydret (OF) Saftis, fruktjuicekonsentrat (M) Sukkerfrie drops (PS) Sukkerfritt godteri (PS) Sukkerfrie halslinser (PS) Sukkerfrie halslinser med honning (PS, M) Sukkerfri tyggegummi (PS)

SUKKER OG SØTSTOFF

LAV FODMAP	HØY FODMAP
SUKKER Lønnesirup Melis Rismalt sirup Sukker, brunt Sukker, hvitt Sukker, palme Sukker, rårør Vaniljesukker **SØTSTOFF** Acesulfat K Aspartam Erythritol (sukrin) *omdiskutert - begrens Sakkarin Stevia Sukralose *1-2 ss sukker per måltid. Kan sammen med frukt og bær gi symptomer	**SUKKER** Agavesirup (M) Bjørkesøt Fruktose (M) High fructose corn sirup (M) Honning (M) Maissirup Molasse (M) Sukrin, GOLD Yaconsirup (OF) **SØTSTOFF** Isomalt – E953 Laktitol – E966 Maltitol – E965 Mannitol – E421 Polydextrose – E1200 Sorbitol – E420 Xylitol – E967

ANNET

LAV FODMAP (SPIS)		MODERAT FODMAP (BEGRENS)	HØY FODMAP (UTELUKK)
Acacia gum Aspartam Bakepulver Byggmalt Dextrose Fiberhusk Gelatin Glukose Glukosesirup Gjær Guar gum Hvetestivelse	Kakaopulver Maltekstrakt Maltodextrin Maltose Natron Pektin Soya lecithin Soyaolje Tapioca Whey protein-isolat Xanthan-gummi	Johannesbrødkjernemel (carob powder) – 1 ts (OF) Eplesyre - ikke testet men sannsynligvis lav	Chikorirot ekstrakt (OF) Eplefiber (OF) Epleekstrakt (OF) Fruktjuicekonsentrat (M) Fruktooligosakkarider/FOS (OF) Galaktooligosakkarider/GOS (OG) Fruktose (M) High fructose corn sirup (M) Inulin (OF) Isomalto-oligosakkarider (OF) Laktitol (D) Laktulose (D) Sukkerroefiber/betefiber/roefiber (OF)

KRYDDER, URTER, SMAKSTILSETNINGER OG FERDIGSAUSER

LAV FODMAP

FRISKE OG TØRKEDE URTER
Basilikum
Dill
Gressløk
Kaffirlime blader
Koriander
Mynte
Oregano
Persille
Rosmarin
Salvie
Sitrongress
Sitronmelisse
Timian

TØRKET KRYDDER OG KRYDDERBLANDINGER
Asafoetida
Chilipulver**
Fennikelfrø
Garam masala
Gurkemeie
Karri
Kajennepepper
Kanel
Kardemomme
Korianderfrø
Muskat
Nellik
Paprikapulver
Pepper
Safran
Salt
Sennepsfrø
Spisskummen
Stjerneanis
Vaniljepulver

SMAKSTILSETNING/ FERDIGSAUS
Balsamikoeddik
Eplesidereddik
Fiskesaus
Fond Cups Kylling (Maggi)
Fond Cups Okse (Maggi)
Glutenfri brun saus (Toro)
Glutenfri hvit saus (Toro)
Grønn pesto (Helios)
Hvitvinseddik
Kapers
Ketchup (idun)*
Kyllingfond (touch of taste)
Oksefond (touch of taste)
Kalvefond (touch of taste)
Fiskefond (touch of taste)
Majones
Oljer m/u smak
Riseddik
Sambal oelek
Sennep
Soyasaus
Teryakisaus
Tomatpure
Wasabi
Worcestershiresaus
Østerssaus

Vær obs på at produsentene kan gjøre endringer i produktene sine. Les derfor alltid ingredienslisten når du velger et ferdigprodukt.
** En del ketchup inneholder løkpulver*
*** Chili og rød paprika inneholder kapsikum som for noen gir mageplager*

HØY FODMAP

KRYDDERBLANDINGER
Currypaste
Grillkrydder
Hot curry
Sitronpepper
Hvitløkspulver

SAUSER
Ketchup (Heinz)
Mangochutney
Tahini (sesampasta)

FERDIGMAT*
Buljong
Blandingskrydder
Dressinger
Ferdigsaus
Fond
Gryteretter
Halvfabrikata
Kraft
Salsasaus
Tacokryddermiks

*Les ingredienslisten

Noen påleggsvarianter

LAV FODMAP (SPIS)	MODERAT FODMAP (BEGRENS)	HØY FODMAP (UTELUKK)
Baconost (Kavli) Banan Banos Egg Hvitost Kaviar (Mills) Kyllingfilet naturell (Solvinge) Laktosefri kremost naturell Laks, gravet Laks, røkt Makrell i tomat (Stabburet) Makrell, skinnfri (King Oscar) Magerost (Kavli) Majones Majones, lett Peanøttsmør Peppermakrell (Stabburet) Reker Rekeost (Kavli) Rekesalat (Delikat) Roastbiff (Gilde) Skinke, kokt (Gilde) Skinkeost (Kavli) Skinke, speket Strandamør Syltetøy, blåbær Syltetøy, bringebær Syltetøy, jordbær Sjokade Våssafår (Stabburet) Ikke glem lavFODMAP-grønnsaker på brødskiva!	Kremost: 4 ss (D)	Brunost (D) Krydderost (OF)* Leverpostei (OF, D)* Nugatti (OF, OG, D) Prim (D) Salami (OF)* Syltetøy av høyFODMAP frukt og bær. Syltetøy, solbær (OF) Syltetøy, sukkerfritt** *Inneholder ofte løk- og hvitløkspulver. Les ingredienslisten. **Kan være laget med isomalt, les ingredienslisten.

Noen glutenfri melblandinger/hurtigløsninger

BAKEMIKSER

(Må lages med lavFODMAP-alternativer til melk, kefir, kesam osv.)

Det glutenfrie verksted (meny, spar, allergimat.no)

- Brød, Fiberbrød, Knekkebrød, Loff, Rundstykker uten gjær
- Boller, Vafler, Pannekaker
- Brownies, Cookies
- Pizzabunn, Paibunn
- Rundstykker uten gjær

MELBLANDINGER

Fin Mix	(Semper)
Lys glutenfri melblanding	(Toro)
Lys glutenfri melblanding, kaker	(Toro)
Glutenfri pizzabunn	(Villa Paradiso – allergimat.no)
Grov og halvgrov melblanding	(Cornells alternativ – allergimat.no og helsekostbutikker)
Havremel	(AXA, Møllerens) – Eventuelt kan man lage selv ved å male havregryn med stavmikser eller blender Husk mengdebegrensning på ca. 47 g per måltid.

FERDIGE BRØD/KNEKKEBRØD

Havreknäcke	(Semper)
Rosmarinknäcke	(Semper)
Havrerundstykker, glutenfrie	(Hatting)
Havrebrød, glutenfritt	(Hatting)
Chiabrød	(Meny)
Surdeigsbrød av 100 % spelt	- hos bakeren (eks. Godt Brød)
Speltlomper	(Aulie Speltlomper med havre (Kiwi) - innhold av spelt er så lavt at et par lomper regnes som lav/moderat FODMA (begrens til maks 2 per dag)
Maisbrød	Ymse slag, sjekk ingredienslisten for krydder ol.
Riskaker	Salt (uten krydder)


PRODUKTER MED HØYT FODMAP-INNHOLD (kan ikke brukes i streng fase)

MELBLANDINGER (Høy FODMAP)

Grov Glutenfri Mix	(Semper) (sukkerroefiber)
Glutenfri mix	(Semper) (melk)
Grov glutenfri melblanding	(Toro) (roefiber)

FERDIGE BRØD/KNEKKEBRØD (Høy FODMAP)

Gluten- og laktosefri knekkebrød (OF)	(Wasa, Schar, Toro 1-2-3)
Superknäcke Chia	(Semper)
Mørkt glutenfritt brød (ferskt)	(Coop)

*Vær obs på fiberrike glutenfrie brød/melblandinger: De kan ofte inneholde et fiber kalt sukkerroefiber/betefiber/roefiber/sukkerbetefiber som kan trigge symptomer hos IBS-pasienter. Produktene kan også inneholde andre FODMAPs som inulin, løk, hvitløk, epleekstrakt, fruktose og honning.

Appendix 6: Compliance questionnaire for low FODMAP diet during 4 weeks

Overholdelse av lav-FODMAP dietten gjennom 4 uker

Hvor fornøyd er du med lav-FODMAP dietten som symptomlindring?

Svært fornøyd Svært misfornøyd

0% _____ 100%

Kan du tenke deg å fortsette på dietten:

- O Ja
- O Kanskje
- O Nei
- O Kun dersom jeg får videre veiledning

Hvis nei, hvorfor:

- O For tidkrevende
- O Savner for mange matvarer
- O Ble ikke bedre
- O For dyrt

Hvor nøye har du fulgt lav-FODMAP dietten gjennom de 4 ukene?

Ikke fulgt den i det hele tatt Kun spist lav-FODMAP mat

0% _____ 100%

Hvor ofte hadde du avvik fra dietten løpet av de 4 ukene:

- O Ingen ganger
- O 1-5 ganger i løpet av de 4 ukene
- O 1-3 ganger i uken
- O 4-6 ganger i uken

Hvor store mengder FODMAPs inntok du ved avvik fra dietten?

- O En munnfull
- O 2-5 munnfull
- O Et helt måltid
- O Alle måltidene i løpet av dagen

Hvor lenge gikk du på dietten før du spiste matvarer med FODMAPs :

- O Ingen dager
- O 1-3 dager
- O 4-7 dager
- O 2-3 uker
- O 3-4 uker

Hvilken matvarer inneholdt avvik fra dietten:

- O **Fruktose**holdige matvarer som eple, pære, honning, juice, tørket frukt (rosiner, svisker, aprikos), asparges
- O **Laktose**holdige matvarer som melk/fløte/yoghurt og matvarer med laktose (vafler, boller, kaker, is etc.), melkesjokolade.
- O **Fruktan**holdige matvarer som inneholder hvete, rug og bygg som for eksempel brød, boller, vafler, kjeks, middagsmat med hvetemel.
- O **Fruktan**holdige matvarer som inneholder løk eller hvitløk, f.eks middagsmat, krydder, ferdigretter.
- O **Galaktan**holdige matvarer som bønner, linser, kikerter eller pistasjnøtter.
- O **Polyoler** som man finner i sukkerfrie pastiller eller tyggis.
- O **Polyoler** som man finner i avokado, aprikos, blomkål, plomme, sopp, vannmelon.

Hvordan synes du det var å følge dietten:

Veldig lett Veldig utfordrende

0% 100%

Hvorfor spiste du matvarer som inneholdt FODMAPs:

- O Spiste kun lav-FODMAP mat
- O Ikke tilgang på lav-FODMAP mat på restaurant/gatekjøkken
- O For tidkrevende å lage lav-FODMAP mat
- O Hadde lyst på mat med FODMAP
- O Lav-FODMAP mat var for dyr
- O Visste ikke at matvaren inneholdt FODMAPs

Hvor fornøyd er du med informasjonen du fikk om dietten:

- O Meget fornøyd
- O Fornøyd
- O Ok
- O Misfornøyd
- O Meget misfornøyd

Appendix 7: Compliance questionnaire for low FODMAP diet 4-6 weeks after intervention

Overholdelse av lav-FODMAP dietten én måned etter diettslutt

Har du fulgt dietten de siste 4 ukene?

- O Ja
- O Litt
- O Innimellom
- O Nei

Hvor godt har du oppretthold lav-FODMAP dietten etter 1 mnd.?

Gått tilbake til
Mitt normale kosthold — Kun spist lav-FODMAP

0% ——————————— 100%

Hva er grunnen til at du ikke spiser 100 % lav-FODMAP lenger?

- O Ikke aktuelt, følger fortsatt dietten for fullt
- O Merket ikke noe effekt av dietten
- O Merket ikke god nok effekt til å ofre mitt vanlige kosthold
- O Det er kun noen matvarer jeg reagerer på
- O Savnet for mange matvarer

Dersom du har fulgt dietten, har du reintrodusert noen FODMAPs?

- O Ja
- O Nei
- O Kun noen matvarer
- O Prøvd, men ble dårlig av alt

Hvordan synes du det var å reintrodusere matvarer til dietten?

Veldig lett — Meget vanskelig

0% ——————————— 100%

Hva var utfordrende med reintrodusering av matvarer:

- O Visste ikke hvordan jeg skulle gjøre det
- O At jeg mest sannsynligvis kom til å få symptomer av den matvaren
- O Vanskelig å skille «normale symptomer» med strikt diett (jeg ble ikke helt frisk med dietten) og symptomer jeg evt får når jeg innfører ulike FODMAPs igjen
- O Vanskelig å vite om jeg fikk symptomer fra akkurat den matvaren
- O Hadde ikke problemer med re-introdusering
- O Ville ikke reintrodusere noen matvarer

Hva var det du prøvde å reintrodusere først?

- O **Fruktose**holdige matvarer som eple, pære, honning, juice, tørket frukt (rosiner, svisker, aprikos), asparges
- O **Laktose**holdige matvarer som melk/fløte/yoghurt og matvarer med laktose (vafler, boller, kaker, is etc.), melkesjokolade.
- O **Fruktan**holdige matvarer som inneholder hvete, rug og bygg som for eksempel brød, boller, vafler, kjeks, middagsmat med hvetemel.
- O **Fruktan**holdige matvarer som inneholder løk eller hvitløk, f.eks middagsmat, krydder, ferdigretter.
- O **Galaktan**holdige matvarer som bønner, linser, kikerter eller pistasjnøtter.
- O **Polyoler** som man finner i sukkerfrie pastiller, tyggis, avokado, aprikos, blomkål, plomme, sopp og vannmelon.

Kommer du til å fortsette på lav- FODMAP dietten fremover?

- O Ja, 100 %
- O Delvis
- O Nei
- O Kanskje

Hvilken type FODMAP tror du at du ikke tåler? Flere kan krysses av.

- O Tåler alle
- O Tåler ingen
- O **Fruktose**holdige matvarer som eple, pære, honning, juice, tørket frukt (rosiner, svisker, aprikos), asparges
- O **Laktose**holdige matvarer som melk/fløte/yoghurt og matvarer med laktose (vafler, boller, kaker, is etc.), melkesjokolade.
- O **Fruktan**holdige matvarer som inneholder hvete, rug og bygg som for eksempel brød, boller, vafler, kjeks, middagsmat med hvetemel.
- O **Fruktan**holdige matvarer som inneholder løk eller hvitløk, f.eks middagsmat, krydder, ferdigretter.
- O **Galaktan**holdige matvarer som bønner, linser, kikerter eller pistasjnøtter.
- O **Polyoler** som man finner i sukkerfrie pastiller, tyggis, avokado, aprikos, blomkål, plomme, sopp og vannmelon.

REINTRODUKSJONSFASEN

Etter å ha har fulgt en FODMAP-redusert kost i 4 uker, og oppnådd symptomlindring, er det på tide å introdusere mat du har unngått i restriksjonsperioden.

Først litt mer om undergruppene av FODMAPs:

- Fruktose (fruktsukker) finnes i frukt, fruktjuice, bær og honning, ofte sammen med glukose. Fruktose absorberes godt sammen med like store mengder glukose, men 30-40% av befolkningen absorberer ikke overskuddet av fruktose. Inntak av mat som har mer fruktose enn glukose kan derfor skape problemer hos de med irritabel tarm.
- Laktose (melkesukker) finnes i melk og meieriprodukter. Det er et disakkarid hvor glukose og galaktose er bundet sammen. Under fordøyelse spaltes disse fra hverandre vha. enzymet laktase som produseres i tarmslimhinnen. Genetisk laktasemangel er vanlig i store deler av verden og blant innvandrere, men sjeldent blant etnisk norske. Tarminfeksjon og skader i tarmen kan gi midlertidig eller varig laktasemangel.
- Polyoler (sukkeralkoholer) er sorbitol og andre søtstoff som ender på –ol. Disse absorberes ikke fullstendig i tarmen og kan forårsake diare og luftplager hos alle. Ved irritabel tarm kan også mindre inntak gi symptomer. Polyoler finnes naturlig i visse typer frukt og grønnsaker, og brukes i sukkerfri tyggegummi, drops og pastiller.
- Fruktaner er korte kjeder av fruktose og finnes i blant annet løk, hvete og rug. Galaktaner er også oligosakkarider og finnes i blant annet belgfrukter. Disse stoffene brytes ikke ned av enzymene i tynntarmen, men blir i stedet mat for tykktarmsbakterier som produserer gass.

Eksempler på matvarer innenfor de ulike FODMAP-gruppene

Fruktaner/galaktaner	**Laktose**	**Fruktose**	**Polyoler**
Frukt: Plomme, nektarin, granateple, vannmelon **Grønnsaker:** Artisjokk, bønner, brokkoli, erter, hvitløk, løk, kikerter, kål, linser, purre, rosenkål	**Melk:** Yoghurt Fløte Rømme Kesam	**Frukt:** eple, mango, pære, vannmelon **Grønnsaker:** sukkererter (runde)	**Frukt og bær:** Aprikos, bjørnebær, eple, fersken, kirsebær, mango, moreller, nektarin, plommer, pære, svisker
Korn: Hvete, spelt, rug og bygg (Som hovedingrediens i brød/bakverk, pasta, grøt, müsli)	**Ost:** Brunost Ferske og myke hvite oster	**Søtstoff:** Fruktose, honning, høy-fruktose-maissirrup	**Grønnsaker:** Avokado, blomkål, sopp, sukkererter (flate), stangselleri
Tilsetningsstoffer: FOS, GOS, oligogalaktose, oligofruktose, inulin	Iskrem	**Stor porsjon av:** Frukt, tørket frukt, fruktjuice	**Søtstoff:** Isomalt, laktitol, maltitol, mannitol, sorbitol, xylitol

Reintroduksjonsfasen

Hvorfor er reintroduksjonen viktig?

- Toleransen for FODMAP er individuell
- Reintroduksjonen kan avdekke hvor *mye* FODMAP du tåler og om noen FODMAP-grupper tåles bedre enn andre
- Noen FODMAP-holdige matvarer fremmer vekst av gode bakterier i tarm og det er trolig ikke ideelt å unngå prebiotiske fibre over lang tid
- Å følge streng lavFODMAP diett over lang tid kan svekke toleransen for FODMAP
- Streng lavFODMAP-diett kan være upraktisk og sosialt vanskelig å følge

Hva er målet med reintroduksjonen?

- Å kartlegge symptomtriggere hos deg
- Å få svar på hvilke og hvor mye FODMAP matvarer du kan spise uten symptom
- Å oppnå et kosthold med minst mulig restriksjoner og samtidig god symptomlindring

Forslag til reintroduksjon

Etter 4 uker på FODMAP-redusert kost gjeninnfører du FODMAP-gruppene én etter én. Start for eksempel med *fruktose*. Merker du ubehag/plager av dette, bør du gå på FODMAP-redusert kost til du blir bra igjen (utvaskingsperiode), før du prøver ut neste gruppe. Om du ikke merker ubehag ved den første gruppen etter tre dager med gradvis økende mengde, kan du gå videre til neste gruppe, for eksempel *laktose*, uten utvaskingsperiode. Prøv deg på den måten gjennom alle gruppene.

Følgende matvarer egner seg godt til uttesting fordi de inneholder mye av én FODMAP-type og lite eller ingenting av de øvrige .Start forsiktig og øk etter hvert til normale porsjonsstørrelser:

FODMAP	TESTMATVARE	Dag 1	Dag 2	Dag 3
Fruktose:	Mango Honning Asparges	¼ stk. 1 ts 1 stk.	½ stk. 2 ts 2 stk	2/3 stk. 3 ts 3 stk
Laktose:	Søtmelk Brunost	1 dl 1 skive	1,5 dl 1,5 skive	2 dl 2 skiver
Polyoler: *Sorbitol*	Bjørnebær Tyggis/ Pastiller (sukkerfri)	5 stk. 1 stk. 2 stk.	10 stk. 2 stk. 4 stk.	15 stk. 3 stk. 6 stk.
Polyoler: *Mannitol*	Sjampinjong Blomkål	2 stk. 1 bukett	3 stk. 2 buketter	4 stk. 3 buketter
Fruktaner:	Hvetebrød Løk Hvitløk	1 skive 1 ss 1 fedd	1,5 skive 2 ss 1,5 fedd	2 skiver 3 ss 2 fedd
Galaktaner:	Bønner Linser (kokt)	2 ss 2 ss	4 ss 4 ss	6 ss 6 ss

Slik går du frem:

- Start gjerne med den gruppen du har savnet mest
- Test en FODMAP-gruppe om gangen
- Start med en liten mengde og øk gradvis til en ”normal” porsjon
- Test den samme matvaren tre dager i løpet av en uke og øk mengden som foreslått. Noen velger å teste annenhver dag fordi det kan ta litt tid før man opplever symptomer
- Registrer symptomene hver dag under testukene. Bruk vedlagt skjema

Hvis du ikke får symptomer av i løpet av minst 3 dager, gjør du følgende:

- Øk mengden av FODMAP innenfor den hovedgruppen du tester for å kartlegge toleranse
- Noter ned mengden du tolererer
- Husk at det er ingen grunn til å teste større mengder enn du normalt ville spist
- Fortsett å spis matvaren (i tolerert mengde) og test neste FODMAP-gruppe

Hvis du får symptomer, kan du gjøre en eller flere av følgende:

- Avbryte testen og gå tilbake til å spise lavFODMAP til du oppnår symptomkontroll (ca. 2 dager)
- Test den samme matvaren du fikk symptom av, men reduser til halv mengde
- Anta at du ikke tolerer matvaren du testet og utelat den fra kosten videre
- Forsøk en annen matvare innenfor samme hovedgruppe, for eksempel hvetebrød i stede for løk.
- Test neste FODMAP-gruppe

Vi anbefaler at matvarer som har gitt symptomer testes igjen med jevne mellomrom (eks. etter 2-3 mnd.) da toleransegrensen kan endre seg over tid.

Mange finner ut at de kan ta tilbake flere høyFODMAP-matvarer til kostholdet sitt, men kanskje ikke i like store mengder og/eller innta dem like ofte som andre

Ved laktoseintoleranse
Dersom du gjennom utprøvingen finner ut at du tolererer laktose dårlig, kan du ha nytte av preparater med laktaenzym, som selges reseptfritt på apoteket. De finnes i flere varianter. *Kerutabs* og *Lactrase* fungerer ved at man tar 1-3 tabletter/kapsler i forbindelse med måltid som inneholder laktose. Disse kan være nyttige ved selskap, restaurantbesøk, ferie og lignende anledninger.

Appendix 9: Baseline characteristic questionnaire

Kartleggingsskjema pilotstudie

Deltaker nummer:

Fra når har du hatt mage-tarm problemer relatert til stråleskade?		
	Ja	**Nei**
Hadde du mage-tarmsymptomer under strålebehandlingen eller i ukene etter?		
Fikk du forebyggende tiltak for å begrense tarmskader?		
Tok du medikamenter mot mage-tarmproblemer under strålebehandlingen?		
Hvis ja, hvilke?		
Har du tatt medikamenter mot mage-tarmproblemene som har oppstått som sen-effekter?		
Hvis ja, hvilke?		
Har du innført noen kostrestriksjoner som følge av mage-tarmproblemene?		
Hvis ja, hvilke?		
Har du hørt om FODMAP-redusert diett tidligere?		
Har du prøvd ut FODMAP-redusert diett tidligere?		
Hvis ja, hadde det effekt og hvor lenge/når forsøkte du?		
Din vekt: Din høyde:		

Info om strålekuren:

Hvor lenge er det siden du ble strålebehandlet sist?	
Antall fraksjoner	
Antall kurer	
Dosestørrelse	
Innvendig, utvendig eller kombinert stråling?	
Fikk du cellegift samtidig? Fikk du hormonbehandling samtidig? Fikk du medikament mot bakteriell overvekst(antibiotika) samtidig? Fikk du andre medikamenter samtidig med stråling?	
Er du blitt operert i tarmen før strålebehandlingen? - Hvis ja, når og hvorfor?	
Røyker du? (eventuelt under behandlingen)	
Har du høyt blodtrykk?	
Har du diabetes?	
Har du hatt medisinsk undersøkelse av din tarm i etterkant av strålebehandling? (endoskopi)	

Appendix 10: Questionnaire for grading of radiation injury based on RTOG

Spørreskjema for gradering av stråleskader

Basert på RTOG – Late Radiation Morbidity Scoring Scheme

1. a) Er du for tiden plaget med diaré? **JA** **NEI**

   b) Hvis ja, hvor alvorlige er diaréplagene?
   (sett kryss på linje for beskrivelsen som passer best)

0% ——————————— **100%**

Mild diaré | Moderat diaré | Alvorlig diaré

   c) Anslå antall dager du har diaré i løpet av en 10 dagers periode: ☐

2. a) Er du for tiden plaget med magekramper?
   (smerter ved avføringstrang) **JA** **NEI**

   b) Hvis ja, hvor alvorlig er krampene?

0% ——————————— **100%**

Milde kramper | Moderate kramper | Alvorlige kramper

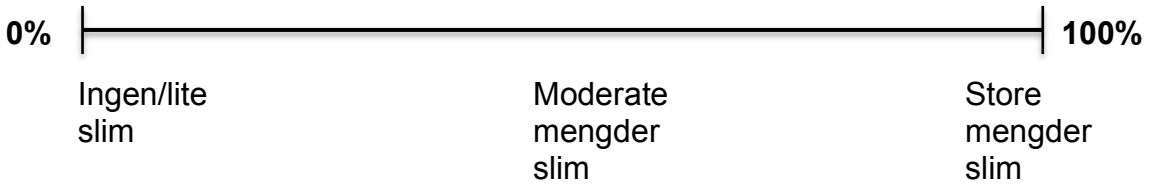
3. Anslå antall ganger du har avføring i løpet av et døgn

☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
1 eller færre	2	3	4	5	6	7	8	9	10	Flere enn 10

4.

a) Har du for tiden slim i avføringen? **JA** **NEI**

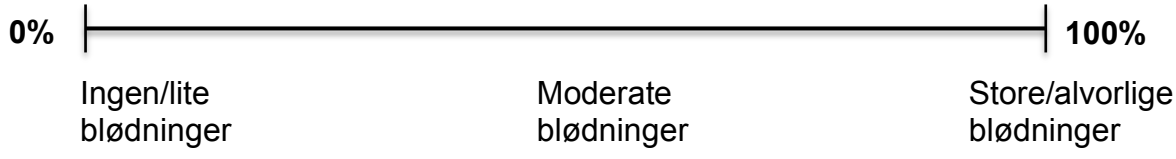
b) Hvis ja, anslå mengdene slim i avføringen



5.

a) Har du for tiden blod i avføringen? (rektale blødninger) **JA** **NEI**

b) Hvis ja, anslå hvor alvorlig blødningene er



6. Er du for tiden plaget med forstoppelse? **JA** **NEI**

7.

a) Har du blitt operert i tarmen som følge av dine stråleskader? **JA** **NEI**

b) Hvis ja, hva var årsaken og hva ble gjort?

_____

_____

_____

8.

a) Har du i den siste tiden hatt problemer med ukontrollerbar avføringstrang? (Opplevelse av å ikke kunne holde deg/behov for å måtte løpe på toalettet)

JA **NEI**

b) Hvis ja, omtrent hvor mange ganger i uken opplever du dette?

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

1 eller færre 2 3 4 5 6 7 8 9 10 eller flere

Appendix 11: Rome III criteria

ROME III SPØRRESKJEMA – MAGEPLAGER

13	I løpet av de siste 3 måneder, hvor ofte har du følt deg ubehagelig mett etter et vanlig stort måltid?	Aldri	Mindre enn 1 dag i måneden	En dag i måneden	2-3 dager i måneden	En dag i uka	Mer enn 1 dag i uka	Hver dag

14	Har du hatt denne ubehagelige metthetsfølelsen etter måltid i 6 måneder eller lenger?	Nei	Ja

15	I løpet av de siste 3 måneder, hvor ofte har du ikke kunnet fullføre et vanlig stort måltid?	Aldri	Mindre enn 1 dag i måneden	En dag i måneden	2-3 dager i måneden	En dag i uka	Mer enn 1 dag i uka	Hver dag

16	Har du hatt dette problemet med ikke å kunne fullføre et vanlig stort måltid i 6 måneder eller lenger?	Nei	Ja

17	I løpet av de siste 3 måneder, hvor ofte har du hatt smerter eller brenning midt i magen, over navlen, men ikke i brystet?	Aldri	Mindre enn 1 dag i måneden	En dag i måneden	2-3 dager i måneden	En dag i uka	Mer enn 1 dag i uka	Hver dag

18	Har du hatt denne smerten eller brenningen i 6 måneder eller lenger?	Nei	Ja			
19	Kom og forsvant denne smerten eller brenningen fullstendig i løpet av samme dag?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid
20	Hvor alvorlig var vanligvis smerten eller brenningen i midten av magen, over navlen?	Svært mild	Mild	Moderat	Sterk	Svært sterk
21	Ble denne smerten eller brenningen påvirket av spising?	Ikke påvirket av spising	Mer smerter etter spising	Mindre smerter etter spising		
22	Ble denne smerten eller brenningen lindret av å ta syrenøytraliserende midler?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid
23	Ble denne smerten eller brenningen vanligvis bedre eller forsvant den etter at du hadde hatt avføring eller luftavgang fra endetarmen?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid
24	Når denne smerten eller brenningen begynte, hadde du vanligvis endring i antall avføringer (enten hyppigere eller sjeldnere avføring)?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid
25	Når denne smerten eller brenningen begynte, hadde du vanligvis løsere eller hardere avføring?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid

26	I løpet av siste 3 måneder, hvor ofte har du hatt plagsom kvalme?	Aldri	Mindre enn 1 dag i måneden	En dag i måneden	2-3 dager i måneden	En dag i uka	Mer enn 1 dag i uka	Hver dag
41	I løpet av siste 3 måneder, hvor ofte har du hatt ubehag eller smerter noe sted i magen?	Aldri	Mindre enn 1 dag i måneden	En dag i måneden	2-3 dager i måneden	En dag i uka	Mer enn 1 dag i uka	Hver dag

42	Har du hatt kun smerter (ikke ubehag eller blanding av ubehag og smerter)?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid

43	For kvinner: Har du kun hatt dette ubehaget eller smerten i forbindelse med menstruasjonsblødning, og ikke til andre tider?	Nei	Ja	Ikke aktuelt fordi jeg ikke har menstruasjon			
44	Når du hadde denne smerten, hvor ofte hemmet eller begrenset den daglige gjøremål (for eksempel arbeid, gjøremål i hjemmet eller sosiale aktiviteter?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
45	Har du hatt dette ubehaget eller smerten i 6 måneder eller lenger?	Nei	Ja				
46	Hvor ofte ble ubehaget eller smerten i magen bedre eller forsvant etter at du hadde hatt avføring?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
47	Når dette ubehaget eller smerten begynte, hadde du hyppigere avføring?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
48	Når dette ubehaget eller smerten begynte, hadde du sjeldnere avføring?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
49	Når dette ubehaget eller smerten begynte, hadde du løsere avføring?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
50	Når dette ubehaget eller smerten begynte, hvor ofte hadde du hardere avføring?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
52	I løpet av de siste 3 måneder, hvor ofte har du hatt færre enn tre (0-2) avføringer hver uke?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
53	I løpet av de siste 3 måneder, hvor ofte har du hatt hard eller klumpete avføring?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
60	I løpet av de siste 3 måneder, hvor ofte har du hatt 4 eller flere avføringer i løpet av en dag?	Sjelden/aldri	Noen ganger (ca 25 % av tiden)	Ofte	Det meste av tiden	Alltid	
61	I løpet av de siste 3 måneder, hvor ofte har du hatt løs, grøtete eller vandig avføring?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
66	I løpet av de siste 3 måneder, hvor ofte har du vært oppblåst eller utspilt i magen?	Aldri	Mindre enn 1 dag i måneden	En dag i måneden	2-3 dager i måneden	En dag i uka	Mer enn 1 dag i uka	Hver dag
68	I løpet av de siste 3 måneder, hvor ofte har du hatt vedvarende smerter i midten eller på høyre side øverst i magen?	Aldri	Mindre enn 1 dag i måneden	En dag i måneden	2-3 dager i måneden	En dag i uka	Mer enn 1 dag i uka	Hver dag
69	Varte denne smerten 30 minutter eller lenger?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
70	Bygget denne smerten seg opp til en vedvarende, sterk smerte?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
71	Forsvant denne smerten fullstendig mellom hver gang den kom?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	
72	Hindret denne smerten deg i vanlige aktiviteter, eller førte den til at du øyeblikkelig oppsøkte lege eller legevakt?	Sjelden/aldri	Noen ganger	Ofte	Det meste av tiden	Alltid	

Appendix 12: IBS-SSS

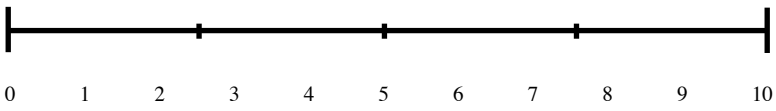
IBS-SSS

1. Har du hatt tilfredsstillende lindring av dine IBS-smerter/-ubehag de siste 7 dager? Sett en ring rundt svaret ditt. **JA** **NEI**

2. **a)** Har du magesmerter? Sett en ring rundt svaret ditt. **JA** **NEI**

b) Dersom ja, hvor sterke er magesmertene? (marker på linja)

0% 100 %



Ingen smerte Veldig mye smerte

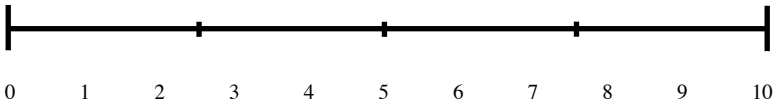
c) Oppgi antall dager du har kjent magesmerter i løpet av en 10 dagers periode. Dersom du f.eks. skriver 4 betyr det at du har smerte 4 av 10 dager. Om du har smerte hver dag, skriver du 10.

Antall dager med smerte: _____

3. **a)** Har du oppblåst og/eller spent mage? Sett en ring rundt svaret ditt. **JA** **NEI**

b) Dersom ja, hvor mye plaget er du? (marker på linja)

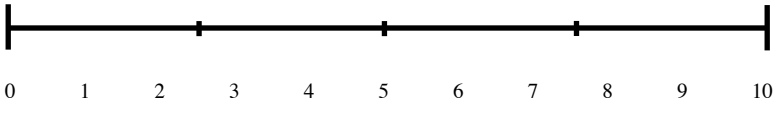
0% 100 %



Ingen plager Veldig mye plager

4. Hvor fornøyd er du med dine avføringsvaner? (marker på linja)

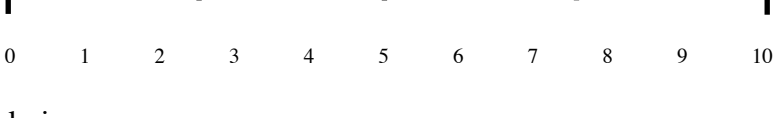
0% 100 %



Veldig fornøyd Veldig misfornøyd

5. Angi med en strek på linja nedenfor hvor mye dine IBS- plager påvirker livet ditt generelt.

0% 100 %



Liten påvirkning Stor påvirkning

TILLEGGSSPØRSMÅL

Lider du av følgende:

a) Kvalme og/eller oppkast?

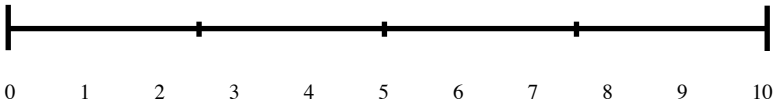
0% 100 %

Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

b) Vanskelig for å spise opp alt ved måltidet?

0 % 100 %

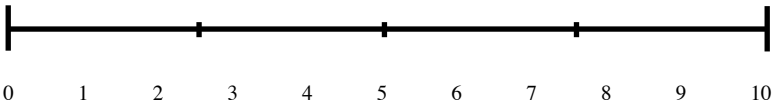


Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

c) Hodepine?

0 % 100 %

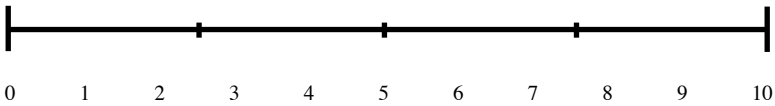


Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

d) Ryggsmerter?

0 % 100 %

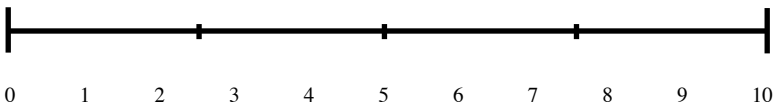


Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

e) Uopplagt eller trøtt?

0 % 100 %

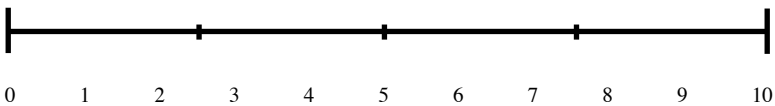


Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

f) Raping og/eller gassavgang?

0 % 100 %

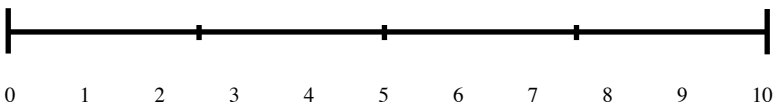


Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

g) Halsbrann?

0 % 100 %

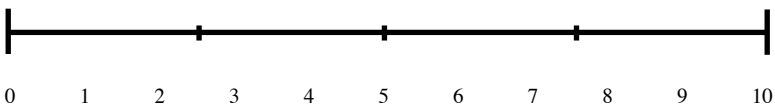


Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

h) Hyppig eller plutselig trang til vannlating?

0 % 100 %

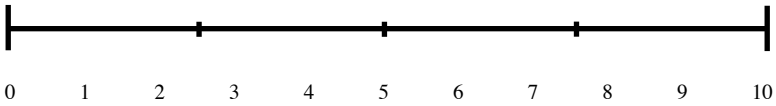


Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

i) Smerter i låret?

0 % 100 %

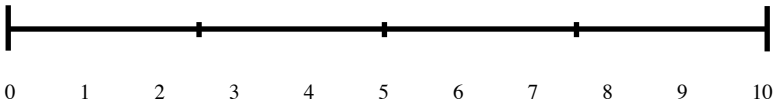


Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

j) Smerter i muskler og ledd?

0 % 100 %



Aldri Hele tiden

0 1 2 3 4 5 6 7 8 9 10

Appendix 13: IBS-SQ

Diagnostikk av IBS-symptomer etter Roma III

DATO: ……..

NAVN: ……..…… ALDER: ……..

1. IBS-KRITERIER (Sett ring rundt svaret)

Spørsmål	**Svar**	
1.1 Har du vært plaget av smerter eller ubehag i magen i minst 3 dager per måned i løpet av de siste 3 månedene?	Ja	Nei
1.2 Har du hatt disse plagene i 6 måneder eller mer?	Ja	Nei
1.3 Er plagene forbundet med endret hyppighet av avføring?	Ja	Nei
1.4 Er plagene forbundet med endret form eller utseende av avføringen?	Ja	Nei
1.5 Reduseres plagene dersom du får tømt deg skikkelig for avføring?	Ja	Nei

2. TILLEGGSSPØRSMÅL FOR Å KARAKTERISERE PLAGENE (Sett ring rundt svaret)

Spørsmål	**Svar**	
2.1 Hvis du har diaré, hender det at avføringen er fast inn i mellom?	Ja	Nei
2.2 Hvis du har forstoppelse, hender det at avføringen er løs inn i mellom?	Ja	Nei
2.3 Er ufullstendig tømming av avføring et problem for deg?	Ja	Nei
2.4 Har du avføring om natta?	Ja	Nei
2.5 Hva har du mest av?	Diaré	
	Forstoppelse	
	Om lag likt	

3. KVANTITERING AV IBS SYMPTOMER
Angis på en skala frå 0 til 10 der 0 = ingen symptomer og 10 = alvorlige symptomer
(Kane, Am J Gastroenterol 2003)

(Angi med tall frå 0 til 10)

Spørsmål	**Svar**
3.1 Kvalme	
3.2 Oppblåsthet	
3.3 Magesmerter	
3.4 Forstoppelse	
3.5 Diaré	
3.6 Anoreksi (ulyst på mat)	

Appendix 14: SF-NDI

SF-NDI (Spørreskjema om livskvalitet)

Sett kryss ved ett tall

Spenning

1. Har ditt følelsesmessige velvære forstyrret av dine mageproblemer i løpet av de siste to ukene?

   1 p – Ikke i det hele tatt
   2 p – Litt
   3 p – En del
   4 p – Ganske mye
   5 p – Svært mye

2. Har du vært irritabel, anspent eller frustrert på grunn av dine mageproblemer i løpet av de siste to ukene?

   1 p – Ikke i det hele tatt
   2 p – Litt
   3 p – En del
   4 p – Ganske mye
   5 p – Svært mye

Innflytelse på daglige aktiviteter

3. Har din evne til å holde på med fritidsaktiviteter (rekreasjon, hobbyer, idrett, sosialt samvær osv.) vært forstyrret av dine mageproblemer i løpet av de siste to ukene?

   1 p – Ikke i det hele tatt
   2 p – Litt
   3 p – En del
   4 p – Ganske mye
   5 p – Svært mye

4. Har gleden ved dine fritidsaktiviteter (rekreasjon, hobbyer, idrett, sosialt samvær osv.) vært forstyrret på grunn av dine mageproblemer i løpet av de siste to ukene?

   1 p – Ikke i det hele tatt
   2 p – Litt
   3 p – En del
   4 p – Ganske mye
   5 p – Svært mye
   1 p – Ikke relevant (jeg har ikke kunnet gjøre noen av disse tingene de siste to ukene)

Spising/drikking

5. Har mageproblemene dine forstyrret deg i hva du har kunnet spise og drikke (inkludert når, hva og hvor mye) i løpet av de siste to ukene?

   1 p – Ikke i det hele tatt
   2 p – Litt
   3 p – En del
   4 p – Ganske mye
   5 p – Svært mye

6. Har din mulighet til å nyte mat og drikke vært forstyrret på grunn av dine mageproblemer i løpet av de siste to ukene? (Vennligst ta med i betraktningen din matlyst og hvordan du føler deg etter at du har spist eller drukket).

   1 p – Ikke i det hele tatt
   2 p – Litt
   3 p – En del
   4 p – Ganske mye
   5 p – Svært mye

Kunnskap/kontroll

7. Har du, i løpet av de siste to ukene, lurt på om du alltid kommer til å ha disse mageproblemene?

   1 p – Nesten aldri
   2 p – Noen ganger
   3 p – Ganske ofte
   4 p – Veldig ofte
   5 p – Hele tiden

8. Har du, i løpet av de siste to ukene, lurt på om mageproblemene dine kan skyldes en svært alvorlig sykdom (for eksempel kreft eller hjerteproblemer)?

   1 p – Nesten aldri
   2 p – Noen ganger
   3 p – Ganske ofte
   4 p – Veldig ofte
   5 p – Hele tiden

Arbeid/studier

9. Har din evne til å arbeide eller studere vært forstyrret av dine mageproblemer i løpet av de siste to ukene?

   1 p – Ikke i det hele tatt
   2 p – Litt
   3 p – En del
   4 p – Ganske mye
   5 p – Svært mye
   1 p – Ikke relevant (jeg verken arbeider eller studerer)

10. Har mageproblemene dine forstyrret trivselen i ditt arbeide eller dine studier i løpet av de siste to ukene?

    1 p – Ikke i det hele tatt
    2 p – Litt
    3 p – En del
    4 p – Ganske mye
    5 p – Svært mye
    1 p – Ikke relevant (jeg har verken arbeidet eller studert i løpet av de siste ukene)

Din helse og trivsel

Dette spørreskjemaet handler om hvordan du ser på din egen helse. Disse opplysningene vil hjelpe oss til å få vite hvordan du har det og hvordan du er i stand til å utføre dine daglige gjøremål. ***Takk for at du fyller ut dette spørreskjemaet!***

For hvert av de følgende spørsmålene vennligst sett et ☒ i den ene luken som best beskriver ditt svar.

1. Stort sett, vil du si at din helse er:

Utmerket	Meget god	God	Nokså god	Dårlig
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. De neste spørsmålene handler om aktiviteter som du kanskje utfører i løpet av en vanlig dag. Er din helse slik at den begrenser deg i utførelsen av disse aktivitetene nå? Hvis ja, hvor mye?

	Ja, begrenser meg mye	Ja, begrenser meg litt	Nei, begrenser meg ikke i det hele tatt
a Moderate aktiviteter som å flytte et bord, støvsuge, gå en tur eller drive med hagearbeid	☐ 1	☐ 2	☐ 3
b Gå opp trappen flere etasjer	☐ 1	☐ 2	☐ 3

3. I løpet av den siste uken, hvor ofte har du hatt noen av de følgende problemer i ditt arbeid eller i andre av dine daglige gjøremål på grunn av din fysiske helse?

	Hele tiden	Mye av tiden	En del av tiden	Litt av tiden	Ikke i det hele tatt
a Du har utrettet mindre enn du hadde ønsket	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Du har vært hindret i å utføre visse typer arbeid eller gjøremål	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

4. I løpet av den siste uken, hvor ofte har du hatt noen av de følgende problemer i ditt arbeid eller i andre av dine daglige gjøremål på grunn av følelsesmessige problemer (som f.eks. å være deprimert eller engstelig)?

	Hele tiden	Mye av tiden	En del av tiden	Litt av tiden	Ikke i det hele tatt
a Du har utrettet mindre enn du hadde ønsket	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b Du har utført arbeidet eller andre gjøremål mindre grundig enn vanlig	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. I løpet av den siste uken, hvor mye har smerter påvirket ditt vanlige arbeid (gjelder både arbeid utenfor hjemmet og husarbeid)?

Ikke i det hele tatt	Litt	En del	Mye	Svært mye
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

(SF-12v2® Health Survey Acute, Norway (Norwegian))

6. Disse spørsmålene handler om hvordan du har følt deg og hvordan du har hatt det <u>den siste uken</u>. For hvert spørsmål, vennligst velg det svaralternativet som best beskriver hvordan du har hatt det. Hvor ofte i løpet av <u>den siste uken</u> har du…

		Hele tiden	Mye av tiden	En del av tiden	Litt av tiden	Ikke i det hele tatt
a	Følt deg rolig og harmonisk?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b	Hatt mye overskudd?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c	Følt deg nedfor og deprimert?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. I løpet av <u>den siste uken</u>, hvor ofte har din <u>fysiske helse eller følelsesmessige problemer</u> påvirket din sosiale omgang (som det å besøke venner, slektninger osv.)?

Hele tiden	Mye av tiden	En del av tiden	Litt av tiden	Ikke i det hele tatt
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Takk for at du fylte ut dette spørreskjemaet!

Appendix 16: Study protocol

The effect of low FODMAP-diet in patients with radiation-induced small bowel disease

Pilot study: is a low FODMAP-diet an effective approach for reducing symptoms in patients with radiation-induced small bowel disease?

Researcher: Trine Larsen
Group leader: Trygve Hausken
Collaborators: Synne Otteraaen Ystad, Gülen Arslan Lied, Nils Hovdenak, Guro Vaagbø and Bernd Müller

Background

Radiation-induced small bowel disease is a common side effect following ionizing radiation therapy used to treat cancer in, or in organs surrounding the gastrointestinal (GI) tract (1). Because of localization close to specific organs the cancer types related to this symptom disease are GI, urological and gynecological cancers. The damage to the small bowel gives symptoms that are similar to those seen in irritable bowel disease (IBS), and includes abdominal pain/discomfort, bloating, diarrhea, constipation, nausea and faecal urgency. In addition anorexia, malabsorptions and rectal bleeding can also be seen as a result of radiation damage. The severity and type of symptoms vary with the applied dose of radiations used, which areas in GI that are affected, the degree of tissue damage and factors other than radiation which might decrease blood flow in bowel tissue (hypertension, diabetes, smoking etc.). The most frequent cause of these symptoms is small bowel bacterial overgrowth. Other contributors to the development of chronic symptoms are the degree of immunosuppression during radiation treatment, specific drugs and the degree of damage to mucosa, submucosa and GI stem cells (2). The terms used to describe these symptoms vary. Traditionally the term "radiation enteritis" was used, but this indicates that there is an inflammation in the bowel, which is not always the case. "Radiation enteropathy" or "Radiation-induced small bowel disease/damage (RISBD)" are probably more appropriate (1). RISBD is categorized in acute or chronic damage. The acute symptoms are more self-limiting and only present during the radiation therapy period. In this study we will focus on patients who suffer from chronic radiation injury, which develops between 18 months and 6 years after radiation therapy is completed. Cancer treatment is steadily improving and the number of cancer survivors is increasing (3). Consequently the numbers of patients suffering from RISBD also increase, and some reports suggest that 90% of patients receiving this type of cancer therapy develop bowel symptoms in some degree (4). The condition is known to be underreported, but should be taken seriously as it often affects the quality of life (3). One of the reasons that the disease is under diagnosed, is both that a clear definition of the symptoms, and a routine management are missing (3).

The available management of chronic RISBD includes antibiotics against bacterial overgrowth in small bowel, bile salt sequestering agents, exclusion diets, supportive enteral diets, supplements of micronutrients, parenteral nutrition, hyperbaric oxygen therapy (HBO), antioxidants, anti-inflammatory agents, endoscopic therapies and surgery (1).

In Norway, there are available brochures that are given to the patients after finishing radiation therapy where RISBD is noted as a possible side effect. The brochures include counseling information about food groups that can be excluded to reduce GI symptoms. The principles the patients are encouraged to follow are to eat a diet low in lactose and fat and to avoid food that induces bowel gas, contains a lot of spices or has a hard baking crust. The brochures also advise patients to eat small and more frequent meals, and to distribute the fat intake over several meals (5). To what extent this approach is followed is not known. There has also been used a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) for this group of patients. The reported results seem to be positive regarding improvements in symptoms, but trials on FODMAP exclusion diet have not been published (1).

Hyperbaric oxygen therapy (HBOT)

As changes in the microvascular function are thought to be the principal factor of the malfunction of radiation-injured organs, interventions counteracting the resulting hypoxia might be beneficial.

Hyperbaric oxygen treatment (HBOT) is a treatment modality where patients breathe 100 % oxygen in an ambient pressure exceeding 2 ATA. Hyperoxygenation of hypoxic tissues has been shown to stimulate neoangiogenesis in irradiated tissue and thereby improve cellular function. In Norway, radiation injury to the GI system is an approved indication for HBOT and all elective HBOT is centralized to the Norwegian National Unit for Planned Hyperbaric Oxygen Treatment at Haukeland University hospital in Bergen. The patients are treated as outpatients in a monoplace chamber where they breathe 100% oxygen for 90 minutes daily at an ambient pressure of 2,4 ATA. They are treated five days a week until a total of 30 treatments (6, 7).

FODMAP is an acronym referring to fermentable oligosaccharides, disaccharides, monosaccharides and polyols. These are complex names for a collection of carbohydrates commonly found in the modern western diet, highlighted as putative triggers of gastrointestinal symptoms (8). FODMAPs are small osmotic active molecules that are poorly absorbed in the small intestine and rapidly fermented by intestinal bacteria with production of gases (hydrogen, methane, carbon dioxide) and short chain fatty acids (SCFAs, e.g., acetic, propionic and butyric acid) (9). The resultant increased luminal volume (both water and gas), leads to bloating, flatulence and abdominal pain/discomfort. In addition, the increased intestinal gas and water delivery together with the generation of SCFAs can alter bowel motility, which may contribute to diarrhoea and/or constipation (10).

Poor absorption of most FODMAPs is common, but this physiological malabsorption is usually tolerated in healthy people. Although everyone will experience uncomfortable symptoms when ingesting large enough quantities of FODMAPs, the threshold and the severity of symptoms will be individual. It has been shown that FODMAPs are especially problematic for people with IBS (10).

Dr. Sue Shepherd developed the "low FODMAP diet" in 1999, and since then positive results from several high-quality studies have made the diet become increasingly accepted and recommended as one of the most effective therapies in patients with IBS (11).

Since the symptoms and pathophysiology of IBS and RISBD show similarities, it is of significant interest to study the effect of a low FODMAP diet in patients with RISBD in the setting of a controlled clinical trial.

Purpose

Questions to be answered:

1. Are GI symptoms alleviated in patients with RISBD when adapting to a low FODMAP diet?
   If so, which symptoms are alleviated and to what degree?
2. Will a low FODMAP diet have any influence on quality of life in subjects with RISBD?

Null hypothesis: There will be no differences in symptoms before and after an intervention with low FODMAP diet

Alternative hypothesis: The study objects will experience a relief in symptoms when eating a diet low in FODMAP's

Design and methods

The study will be conducted as an open, prospective, pilot intervention study with an intervention group consisting of approximately 18 subjects. The participants will be recruited between August and January 2017 from Norwegian National Unit for Planned Hyperbaric Oxygen Treatment, Section for Gynecological cancer at the "Women´s Clinic" and Medical Department at Haukeland University Hospital. In addition we will make an attempt to recruit patients through advertisement within The Association of Gynecological Cancer Patients in Norway, a patient association affiliated the Norwegian Cancer Society.

The participants will be contacted by a letter and receive an offer to participate in the study. At baseline the subjects will be asked to do sign a written consent, do a 3-day prospective food record and answer questionnaires regarding grade of tissue damage,

symptoms and quality of life. These will be sent to the study holder by mail or e-mail in prior to the introduction of the intervention. The subjects will receive diet counseling on how to follow a low FODMAP diet by telephone communication, and detailed written information about the diet will be sent by mail/e-mail. The participants that live in the area close to Bergen, will be asked to meet up in person to fill out the forms, and get diet counseling. The intervention period will be four weeks.

At the end of the intervention the participants will again answer the questionnaires for symptoms and quality of life, make a 3-day food record and fill out a low FODMAP compliance form. During the following six weeks after ending the study, the participant will be asked to again fill out the compliance form to see if they to any degree are adapting the diet to their regular eating habits.

After the end of the study, participants will be offered to receive counseling on how to reintroduce FODMAP's. This is an approach to find out which of the FODMAP's are giving IBS symptoms in the individual subject.

Study subjects

Inclusion criteria

- Subjects between 18-70 years of age
- Filled informed written consent
- Patients who suffer from radiation induced small bowel disease
- Patients referred and accepted for HBOT with IBS-symptoms
- IBS-symptoms confirmed by the Rome III-criterion
- IBS-symptoms with/without bleeding

Exclusion criteria

- Patients already eating a diet low in FODMAP's (If so they have to stop the diet for 3 weeks before entering the study)
- Patients already receiving HBOT

Data collection

1. IBS-SSS: IBS-Severity Scoring System
2. Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders
3. RTOG: Radiation therapy oncology group – toxicity grading scale
4. SF-NDI: Short Form Nepean Dyspepsia Index
5. 3-day prospective food record – analysis with "Kostholdsplanleggeren"
6. Low FODMAP compliance form
7. Continuing of diet after hyperbaric therapy 4-8 weeks (compliance form)

Ethics

There is no risk of harm in this study. The intervention and the data collection may be perceived as demanding for some, but it will not cause any harm to the participants.

The study is voluntarily and the participants can withdraw from the study at any point without providing any justification.
The study will not delay the start of HBOT, or affect any other treatment the participants are receiving.
The study will be presented to the Regional Committee for Medical Research Ethics (REK).

Data analyzing and statistics
The data will be summarized in figures and/or tables. SPSS will be used to perform statistical analysis.

Timetable

February – April 2016	Writing of protocol and applying to REK
June – January 2017	Recruiting of patients and performance of study
February – March 2017	Data analysis
April – May 2017	Writing of master thesis and data presentation

Publication plan
There will be made an effort to get the paper published in an international journal read by professions like clinical dietitians, oncologist and gastroenterologists etc.

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