Dietary intake and FODMAP score in newly diagnosed patients with inflammatory bowel disease

Results from the IBSEN III cohort

Master thesis by Marte Jerven

Supervisors: Christine Sommer and Monica H. Carlsen

Department of Nutrition, Faculty of Medicine

UNIVERSITY OF OSLO

May 2018

Dietary intake and FODMAP score in newly diagnosed patients with inflammatory bowel disease

Results from the IBSEN III cohort

Master thesis by Marte Jerven

Supervisors: Christine Sommer and Monica H. Carlsen

Department of Nutrition, Faculty of Medicine

UNIVERSITY OF OSLO

May 2018

Dietary intake and FODMAP score in newly diagnosed patients with inflammatory bowel disease

Marte Jerven

http://www.duo.uio.no/

Print: Reprosentralen, University of Oslo

Abstract

Background and aim: Patients with inflammatory bowel disease (IBD), including Crohn`s disease (CD) and Ulcerative Colitis (UC), are vulnerable to malnutrition and deficiency of several micronutrients. Decreased dietary intake and avoidance of several foods are important risk factors. Several patients struggles with symptoms, even when in remission. The majority of the patients believe diet is important for the disease, and they are supported by increasing literature. A diet low in FODMAPs seems to improve gastrointestinal symptoms, but we know little of its impact on disease activity. We aimed to assess the dietary intake in Norwegian IBD patients, and explore potential differences in dietary intakes between UC and CD.

Method: In this project we included adult (≥18 years old), newly diagnosed IBD patients enrolled in the IBSEN III cohort between 1st of January and 8th of December 2017. Data collection on dietary intake was performed using a validated and comprehensive food frequency questionnaire (FFQ). We developed a FODMAP score based on reported intakes of FODMAP containing food items. We used self-reported disease activity scores to explore associations with the FODMAP score.

Results: A total of 187 participants with CD and UC were included in the dietary analyses. The dietary intakes of carbohydrates and vitamin D in both genders, fiber in men and iron and folate in women of reproductive age were lower, and intake of saturated fats in both genders were higher than recommended. Women with UC had a higher intake of alcohol and vegetables compared to women with CD (p=0.004 and p=0.02). Among men, CD patients had a higher intake of bread and meat (p=0.03 and p=0.02). The majority of foods known to contain FODMAPs increased with higher FODMAP score. There were no differences in FODMAP score with higher self-reported disease activity in CD or UC (p=0.51 and p=0.81).

Conclusion: The dietary intake in both UC and CD patients were largely in line with the recommendations. Intakes of vitamin D in both genders and folate and iron in women of reproductive age were lower than recommended, and status of these micronutrients should be monitored. There were some differences in dietary intake between UC and CD, and these differences are likely explained by dietary restrictions. The efficacy of the FODMAP score was satisfying. To explore if dietary intake of FODMAPs is associated with disease activity, future studies should use other outcome measures of disease activity.

Acknowledgement

First, I would like to thank my supervisors, Christine Sommer Dep. of Endocrinology, Morbid Obesity and Preventive Medicine, Oslo University Hospital and Monica H. Carlsen Dep. of nutrition, University of Oslo, for their professional feedback and guidance in this master project. Christine, thank you for being available both on mail and telephone, supporting me throughout the project, and for good advice on how to perform the statistical analyses. I am grateful to Monica, who let me use her office and patiently helped me prepare the dataset before analyses, and for making time for me whenever I had a question.

Further, I would like to thank the project leader in the IBSEN III cohort, Marte L. Hoivik, in addition to several of her coworkers in the project, who has been very kind and including towards me. Marte, I am sincerely thankful for you including me in your research team, letting me attend the ECCO congress in Vienna, and for all of your help on the thesis. Thank you, Elisabeth at Oslo University Hospital and Julie at Akershus University Hospital including several gastroenterologists in these hospitals, for letting me observe consultations and endoscopies providing me with important insights into the patient group.

Thank you, Trine M. Reine Dept. of nutrition, University of Oslo and stable-buddy, for listening and giving me constructive feedback, and for being a friend in demanding periods.

Finally, I am grateful to all of my friends and my family, particularly my partner and my 3 year old son, for being social supports helping me stay positive.

Bærum, May 2018

Marte Jerven

Abbreviations

CD	Crohn’s disease
EEN	Exclusive enteral nutrition
FFQ	Food frequency questionnaire
FODMAP	Fermentable Oligo-, Di- and Monosaccharides And Polyols
FOS	Fructo-oligosaccharides
GOS	Galacto-oligosaccharides
HBI	Harvey Bradshaw index
IBD	Inflammatory bowel disease
IBS	Irritable bowel syndrome
NNR12	Nordic Nutrition Recommendations 2012
PMS	Partial Mayo score
SFA	Saturated fatty acids
UC	Ulcerative colitis

List of tables and figures

Tables

Figures

Table of contents

1 Introduction

1.1 Inflammatory bowel disease

Inflammatory bowel disease (IBD) is a common term for two distinct conditions causing chronic inflammation in the gastrointestinal tract; Crohn's disease (CD) and Ulcerative Colitis (UC). The distribution is approximately 1:3 and female domination in CD and 2:3 and male domination in UC (1-4). While UC is confined to the colon, CD may affect the entire gastrointestinal tract. Establishment of diagnosis is based on clinical evaluation including symptoms and family history combined with endoscopy, imaging, histological and biochemical parameters (5, 6). Furthermore, calprotectin measurements in feces, detected by Norwegian scientists (7), may be useful to screen potential IBD patients and separating them from more unspecific conditions like irritable bowel syndrome (IBS) (8).

The characteristic appearance of CD is focal or patchy discontinuous inflammation which may extend beyond the mucosa in a transmural manner (5). On the other hand, inflammation in UC is generally continuous and confined to the mucosa (6). CD seems to debut earlier than UC, although both conditions most frequently develop in adolescence and early adulthood (3, 4). Usually, disease location stays reasonably unchanged for both CD and UC patients (5, 6). About 50% of IBD patients report a disease course with an initial high activity at diagnosis, followed by a more quiescent disease and less symptoms (9, 10). However, the inflammation in UC may progress in extent, while penetrating and stricturing disease in CD patients may evolve with time (9, 10). Mutual symptoms of both UC and CD, but perhaps signs of more severe disease in UC, are abdominal pain, anorexia and fever (5, 6). Furthermore, patients with UC often experience rectal bleeding or bloody diarrhea, tenesmus, urgency, nocturnal defeceating, faecal incontinence and fatigue, while patients with CD often report chronic diarrhea, weight loss and general discomfort. Surgery may be necessary, and more usual in CD than UC (9, 10).

The etiology of IBD is not yet fully understood. Family history is an established risk factor, at least in Caucasians and Hispanics (5, 11). Since the revolutionary finding in 2001 of the NOD2 gene involved in CD susceptibility (12), >160 loci for IBD has been identified due to modern gene technology (13). Furthermore, smoking is associated with increased risk for CD, while cessation of smoking is associated with increased risk for UC (14). The leading theory

is that IBD develop in genetic susceptible individuals because of an inappropriate immune response to microbiota dysbiosis through interactions with environmental factors (15). Epidemiologic studies of geographic differences in incidence and migration are useful in providing clues on the role of environmental factors in IBD development (16-20). Importantly, genetics seems to be emphasized in early debut of IBD, and environmental factors in late debut, respectively (21). Together with many other suggested determinants (e.g. hygiene, appendectomy, antibiotics), diet has been implicated in both IBD development and disease course (15, 22).

The incidence of IBD has increased in the past decade (16, 23), although a recent systematic review suggested a stabilization of incidence in the west, while the incidence continues to rise in countries adapting to the western lifestyle (24, 25). A high incidence of IBD was reported in Norway (1990-93). The mean annual incidence was 5.8 per 100 000 and 13.6 per 100 000 individuals, for CD and UC respectively (3, 4). Moreover, according to preliminary results from the IBSEN III cohort, the incidence in Norway seems to have increased further (26).

IBD is associated with extensive health-care costs related to the use of medications, hospitalization and work disability, representing a considerable burden to health systems and social economy (27). Dietary interventions may therefore be a cost-effective treatment option, and further research on diet used as treatment on IBD is warranted.

1.2 Diet and IBD

1.2.1 Dietary prevention and risk factors of IBD

Retrospective dietary collection is usual in epidemiologic studies, which makes it challenging to elucidate dietary components or nutrients having protective or harmful impact on development of IBD (28). The western diet high in fat including an unfavorable omega 6:omega 3 ratio, protein (animal-derived in particular), refined sugar and low in fibers from fruit and vegetables has frequently been emphasized as risk factor for IBD (29, 30). There seems to be convincing evidence of increased risk of IBD with high intake of total fat and a high omega 6:omega 3 ratio, in addition to high intake of meat and sugar (15, 28, 30). Other suggested dietary factors that might have a negative impact on IBD development, are salt and different food additives (31-33), which needs further exploration. A diet rich in fruit and vegetables and a favorable omega 6:omega 3 ratio, and possibly high intake of zink and vitamin D, seems to be protective (15, 34), and is recommended in the newly published ESPEN guidelines (35).

IBD patients have a host microbiome that differs from healthy controls (36). Dysbiosis is important in IBD development, and scientist are trying to elucidate which factors contribute to this imbalance in host microbiome (37). Diet influences the composition of the microbiome, and a diet consisting of entirely animal compared to plant-based foods rapidly changed the microbiome in light of different species colonizing the gut (38).

1.2.2 Dietary management of IBD

Currently, there is no recommended diet to treat active disease in IBD patients (35). Exclusive enteral nutrition (EEN) is equally sufficient to corticosteroids in inducing remission in pediatric CD (39), and is preferred as first-line therapy in children with CD (40). In adults, EEN induced remission in 80% (41), but remain controversial mainly due to difficulties with compliance (42). At present, EEN is not recommended to adults neither by ESPEN nor the European Crohn's and Colitis Organization (ECCO) (5, 35). Nevertheless, enteral nutrition is an important accessory therapy to improve nutritional status or treat active disease in selected cases with CD (5, 35). Two probiotics, VSL#3 and Escherichia coli Nissle 1917, are recommended to induce remission and prevent relapse in UC (35, 43), but not in CD (5, 35).

Extensive research on different diets that may improve the management of IBD are in progress (e.g. the specific carbohydrate diet (SCD), omega-3 supplemented diet and paleolithic diet), but with insufficient proof of efficacy at the time (35, 44). However, a diet low in FODMAPs show promise as part of the management strategy due to its apparent ability to ease functional gastrointestinal symptoms in IBD patients (45-51).

FODMAP

FODMAP (Fermentable Oligo-, Di- and Monosaccharides And Polyols) is a designation for undigested and hence unabsorbed carbohydrates, which in the colon are fermented by host-bacteria. In **Table** 1, we present the different constituents of FODMAP, and their most common dietary sources. The concept of prebiotics was introduced in 1995 by Gibson et al (52), and the definition recently updated: «a substrate that is selectively utilized by host microorganisms conferring a health benefit» (53). Among prebiotics, fructo-oligosaccharides (FOS) and inulin, and galacto-oligosaccharides (GOS) were the first recognized (52), and are the most extensive studied (53). Both are important constituents of FODMAP (54).

Fructans: the terminology fructose and FOS may be confusing. Fructans include both FOS and inulin, defined depending on degree of polymerization (DP). They are composed of fructose and glucose (54). While FOS (DP <10) are the most commonly occurring fructan in foods like wheat and onion, the addition of inulin (DP >10) to improve texture and increase fiber content in dietary products is expanding (54, 55).
GOS: composed of glucose, fructose and galactose and present in oligosaccharides with a DP of 3-4 units (54). Fermentation of GOS by intestinal bacteria generally lead to gas-production (54).
Lactose: A disaccharide broken down and absorbed in varying extent depending on the lactase production in the small intestines (54).
Fructose: Ingested together with glucose in approximately equal amounts, or as a component of sucrose, fructose is normally highly absorbed. Due to the facilitated fructose-transporter in the small intestines, humans have the ability to absorb some free fructose, but in about 30%, this capacity is limited (54). Thus, fructose in excess of glucose is available for fermentation in the colon (54).
Polyols: Sugar alcohols unabsorbed by humans (54).
In 2005, Gibson and Shepherd proposed a hypothesis that excessive consumption of these short-chain carbohydrates and polyols may lead to susceptibility to Crohn's disease by

impairing the epithelial barrier function (54). Later, researchers at the Monash University developed the low FODMAP diet (56).

Table 1: Constituents of FODMAP and common food sources

FOOD COMPONENT	DIETARY SOURCES
Fructose	Fruits, honey, high fructose corn syrup
Lactose	Milk and lactose-containing dairy products
Fructans	Wheat, onions, food additive
GOS	Legumes, certain beans, cabbage, onions
Polyols	Apples, pears, plums, sweetener

GOS: Galacto-oligosaccharides

Functional gastrointestinal symptoms typically include bloating, wind, abdominal pain or discomfort and diarrhea caused by water and or gas-production subsequently followed by distension (56). The low FODMAP diet was developed by researchers at the Monash University for individuals with IBS due to its symptom-lowering effect (57). The existence of symptoms compatible with IBS in IBD is prevalent, particularly in CD patients, and included nearly 40% in a previous meta-analysis (58). In a study conducted on Norwegian CD patients in remission, they found that a strict elimination diet including common FODMAPs significantly ameliorated IBS symptoms after only two weeks of intervention (59). Furthermore, the elimination diet seemed to have a greater efficacy in patients with disease located in the small intestines (59). Supportive for a diet low in FODMAP, are provocative studies exploring the effects of FODMAP supplementation, and the subsequent increase of symptoms in study-subjects (46, 49, 60). If the low FODMAP diet can demonstrate to be safe and effective as a long-term management therapy, the self-coping, and thus quality of life in IBD patients will likely improve.

1.3 Dietary beliefs and self-imposed dietary restrictions

Recently, a series of studies investigating IBD patients' view of diet in IBD development and management have been published (**Appendix** I). Between 16-48% of IBD patients believe diet is an important risk factor for IBD development (61-63). Moreover, a range of 57-71% thought diet trigger the disease, leading to exacerbated inflammation (61-64). According to the majority of IBD patients, patients with CD in particular, diet is very important in management of the disease, mostly to control and alleviate symptoms (62, 65-67). Consequently, several patients reported modifying their diet post diagnosis (61, 62, 68). In addition, 39% introduced changes before diagnosis due to annoying symptoms (69).

IBD patients have a reduced quality of life, and gastrointestinal symptoms exert an important effect through increased psychological distress (70, 71). Due to symptoms, many IBD patients avoid favorite foods, refuse to eat away from home and eat different than their family affecting their social life (62, 63, 72). IBD patients desire advice from their caregivers, but in many cases and in UC particular, half or less have been counselled by a dietitian (61-64, 68, 72).

Spicy foods, fatty foods, meat, dairy products, alcoholic beverages, soda, fiber-rich food (including wholemeal products, fruit and vegetables), gas-producing foods (beans and legumes), sugar, nuts, corn and coffee/tea are commonly restricted or avoided by IBD patients (59, 61-65, 67-69, 72-75). Nearly every patient avoid at least one food in active disease (61, 73). CD patients in general, and those with stricturing disease particularly, impose more restrictions in their diet compared to UC patients (61, 62, 73). In exacerbated periods, 52% of the participants in a study preferred to follow a low residue diet (63).

1.4 Nutritional status

In the following sections we will describe common micronutrient deficiencies and malnutrition in IBD patients. With malnutrition we refer to undernutrition, while deficiency means an inadequate status of micronutrients.

1.4.1 Micronutrient deficiency

Micronutrient deficiency is quite prevalent in IBD (**Table** 2). Dietary status of micronutrients depend on various factors including inadequate dietary intake, intestinal losses, malabsorption, increased energy expenditure, drug interactions or failure to administer the correct composited total parenteral nutrition (76). Development of deficiency with time depends on disease progression, and is probably more common among the malnourished patients (61). CD patients with small bowel involvement or previous resections in this area in particular, are vulnerable to malabsorption of B_{12} and fat-soluble vitamins (76).

Table 2: Overview of micronutrients important in IBD

Micronutrient	Prevalence	Consequences of deficiency
Iron	Iron deficiency anemia: 37% (77)	Anemia Decreased quality of life and fatigue (77) Associated with restless leg syndrome
Vitamin D and Calcium	Vitamin D deficiency: 53% in CD and 44% in UC (78)	Reduced bone health Vitamin D deficiency may lead to increased susceptibility of IBD and increased disease activity (79) Vitamin D deficiency may increase risk of colorectal cancer
Zink	-	Poor wound healing
Magnesium	-	Reduced bone health (calcium absorption) Fatigue (Mg-cofactor in ATP-reactions) (80)
Vitamin A	Vary greatly between studies	Reduced vision Poor wound healing
Cobalamin (B_{12})	Deficiency in 11-22% with CD (76)	Megaloblastic anemia Hypercoagulability (due to hyper homocysteinemia)
Folic acid (B_9)	Abnormal levels in up to 30% of IBD patients (76)	Macrocytic megaloblastic anemia Hypercoagulability (due to hyper homocysteinemia) Increased risk of colorectal cancer

Inspired by Hwang et al. (76)

IBD: inflammatory bowel disease, CD: Crohn`s disease, UC: Ulcerative Colitis, Mg: Magnesium, ATP: Adenosine triphosphate

Anemia is common in IBD patients, and CD patients are at higher risk compared to UC patients (81). In Norway, the prevalence of anemia at disease onset was 49 and 20% in CD and UC respectively, and the relative risk significantly higher in IBD patients compared to the background population (82). The main causes are iron deficiency and anemia of chronic disease (83). Reduced dietary intake of iron, intestinal blood loss, reduced absorption due to increased hepcidin levels, malabsorption, use of certain medications and active disease are emphasized as underlying mechanisms (76, 81, 84, 85). Iron deficiency is associated with fatigue and have a negative impact on quality of life (77). Deficiency of folate and B_{12} may lead to megaloblastic anemia, and is more prevalent in CD patients (76). An important risk factor for B_{12} deficiency is previous ileal bowel resection (86). Thus, CD patients are at particular high risk because B_{12} absorption is confined to the ileum (76). Folate deficiency may develop in both UC and CD, and insufficient dietary intake, malabsorption and certain medications are probable causes (76).

Metabolic bone disease is frequent in IBD patients, and low bone mass and osteoporosis affect 20-50% (87). Adequate dietary intake of calcium and vitamin D are warranted to prevent osteoporosis from developing (87). Vitamin D deficiency is more common in IBD patients compared to the general population (88). In a Norwegian study of IBD patients, 53 and 44% of CD and UC patients respectively, were defined as deficient of vitamin D (78). Inadequate dietary intake, malabsorption due to steatorrhea and longer disease duration may lead to vitamin D deficiency (76). Vitamin D is not only important for bone health, but serve a role in our immune system as well (79). Researchers are currently trying to elucidate vitamin Ds impact on IBD, as studies indicate that deficiency may increase the risk of IBD development and prompt a more severe disease course (79). Another important function of vitamin D is to regulate calcium absorption (76). Due to dietary restriction or avoidance of milk and dairy products, the calcium intake is often lower than recommended (89, 90). Furthermore, concomitant magnesium deficiency due to diarrhea, aggravate calcium malabsorption (76). Lastly, admission of systemic steroids is an important risk factor of metabolic bone disease, and consensus guidelines recommend vitamin D and calcium supplementation in these patients (87).

Venous thromboembolism is another important extra-intestinal manifestation of IBD, with more than doubled risk compared to the general population (87). Deficiency of folate in particular, but also B_{12} and B_6 are implicated due to its impact on homocysteine levels, and because IBD patients are at higher risk for hyper homocysteinemia (76).

It is important to be aware that biochemical measures of specific micronutrients change with increased inflammation (35). While ferritin and copper increase, folate, selenium and zinc decrease during periods of exacerbated disease activity. Hence, micronutrient status should be assessed when the disease is quiescent, and recommendations of supplements given accordingly. Researchers may define deficiency differently (e.g. using different cut-off values for biochemical samples), use suboptimal and deviating markers or include participants with and without active disease making the interpretation of results from studies of nutritional status in IBD patients challenging. Furthermore, deficiency of several micronutrients may be usual in the general population, and not a characteristic phenomenon of the disease.

1.4.2 Malnutrition

Studies reporting risk and prevalence of malnutrition in IBD patients vary greatly depending on the definition and method of assessment including factors concerning the study population (e.g. duration of disease, recruitment method), and range from 6-70% (61, 91-95). CD is considered to be at higher risk of malnutrition compared to UC, as it can affect the entire gastrointestinal tract (35). Dietary restriction behavior, previous bowel resections, fistulizing CD and active disease are associated with increased risk of malnutrition in IBD patients (61, 90, 93, 95). Decreased dietary intake was associated with risk of malnutrition in a study of hospitalized subjects with different gastrointestinal diagnoses including IBD (91). Reduced appetite may be a contributive factor leading to a decreased dietary intake. During increased inflammatory activity, 69-71% of IBD patients reported reduced appetite (61, 62).

Although many studies explore avoidance and restriction in IBD patients` diets, there are relative few studies quantifying dietary intake of different foods, and with some conflicting results (74, 75, 96). To our knowledge, dietary intake in Norwegian IBD patients has not been assessed before. It is crucial to increase the knowledge of dietary intakes in this group of patients, as they tend to impose multiple restrictions in their diet. Because the availability of different food items and dietary practices most likely differ from other populations, it is important to do this in Norwegian IBD patients. When we have information on dietary intake, we can explore associations between diet and disease activity. Thus, in the future we might be able to improve the dietary counseling and individualize the dietary advice. Additionally, we might be able to detect different subgroups that might benefit from future interventions with diet or dietary components because of the large and comprehensive data collection in the overall IBSEN III cohort.

2 Aim

The overall aims of this master thesis were to increase the knowledge of dietary intake in patients with IBD and to explore associations between FODMAP score, background data and self-reported disease activity.

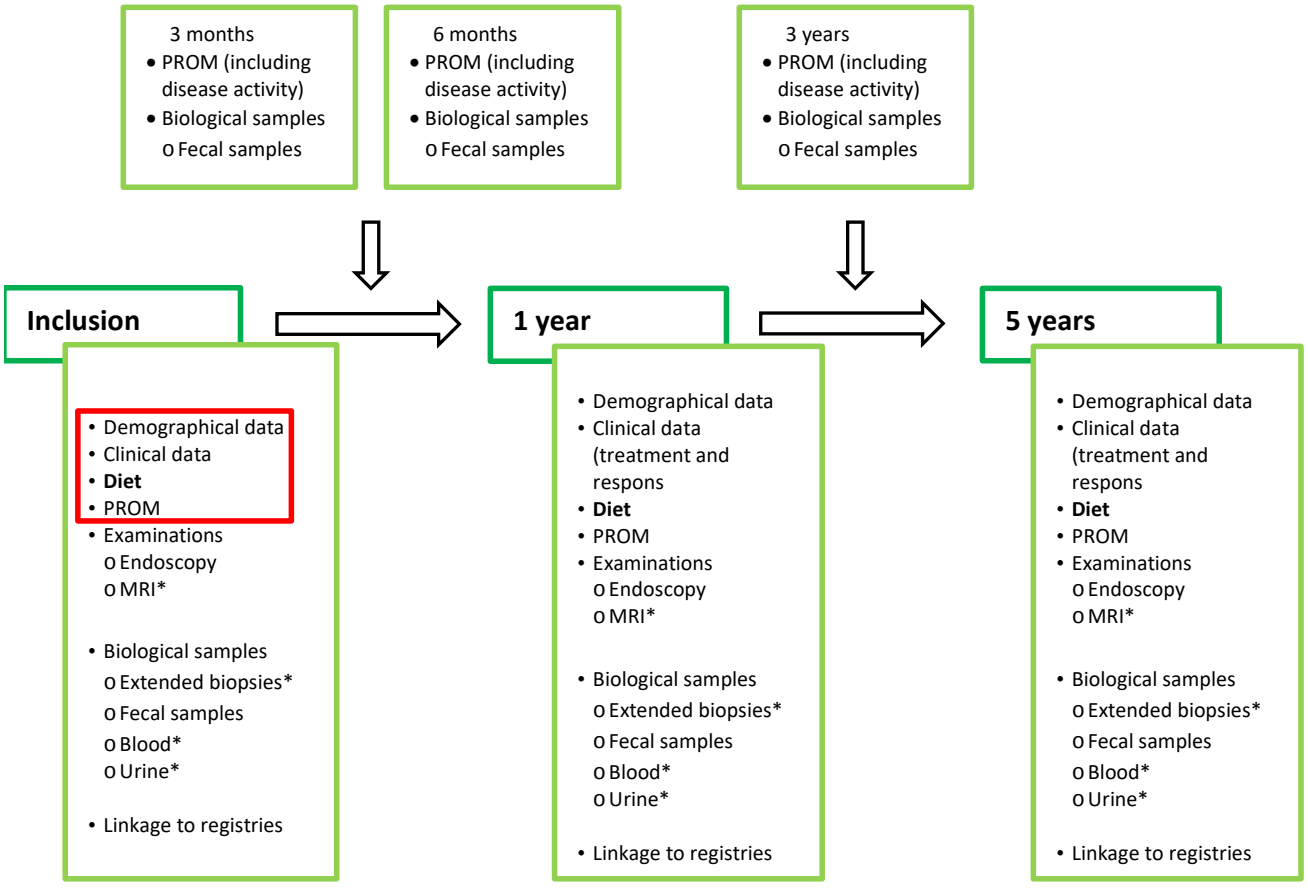
The specific objectives of this master thesis were to:

- describe dietary intake in newly diagnosed IBD patients in relation to dietary recommendations
- compare differences in dietary intake of macro- and micronutrients and different food groups in UC and CD patients, on group level
- develop a FODMAP score, including
    1. Designate a FODMAP factor for each FFQ food item based on the Monash University`s traffic light system for FODMAP content in food items
    2. Multiply the daily intake of each food item with its designated FODMAP factor
    3. Summarize each participant`s FODMAP score into a total FODMAP score
- describe the main dietary sources of FODMAP in the IBD population
- explore associations between FODMAP score and background data
- explore associations between FODMAP score and self-reported disease activity

3 Methods

3.1 Study design

IBSEN III is a prospective population-based inception cohort implying that the participants are included at diagnosis. The study was initiated January 2016, and will continue recruiting until December 2019. Twenty hospitals from the South-Eastern Norway Regional Health Authority are participating in the cohort. This regional health thrust is the largest out of four in Norway, and covers 10 counties and 2.6 million people (97). An outline of the data collection in the study can be viewed in **Figure** 1. Follow-up with physical examinations are performed 1 and 5 years into the cohort. Collection of dietary data is performed at inclusion, and after 1 and 5 years.



*Only biobank centers (Oslo University Hospital, Akershus University Hospital and Vestfold Hospital Trust)

PROM: Patient Reported Outcome Measures, MRI: Magnetic Resonance Imaging

Red square denotes data used in this master project

Figure 3: Overview of data collection in the IBSEN III cohort

This master project is a cross-sectional study of data material collected at inclusion (the red square in Figure 1). Our sample consists of participants included in the study between January 1st and December 8th 2017.

3.2 Study population

The IBSEN III cohort includes treatment naïve cases at all ages. Patients are recruited to the cohort by two separate procedures depending on which hospital they are referred to. At the majority of the participating hospitals (n=17), patients are invited after the endoscopy when the gastroenterologist is reasonably certain that the patient suffer from IBD. Shortly following endoscopy, patients are summoned to a conversation with a doctor or IBD-nurse where they sign the written consent and are included in the cohort. If participants are diagnosed at a private health institution within the South-Eastern region, they are informed about the study by the gastroenterologist performing the endoscopy. After referral to one of the closest located participating hospital, patients are included in the cohort accordingly. They do not have to perform a second endoscopy. There are three biobank centers, Oslo University Hospital, Akershus University Hospital and Vestfold Hospital Trust, taking extended biological samples and MRIs (Figure 1). In these three hospitals, information about the study are sent with the summon to patients when IBD are considered likely and before a definite diagnosis. Thus, a subgroup of the population in the cohort comprise symptomatic non-IBD controls. A doctor or IBD-nurse goes through details about the study and answers questions at the first consultation before endoscopy take place. In every participating hospital, and after written consent are signed, participants receive a folder containing practical information about the study, data-collection and biological sampling.

The following inclusion and exclusion criteria are given in the IBSEN III protocol. The study is registered at clinicaltrials.gov with identification number NCT02727959 (98). Diagnostic criteria are according to Lennard Jones (99).

Inclusion criteria

Ulcerative colitis:

Diagnostic criteria (at least three out of four criteria present):

1. A history of diarrhea and/or pus in stools for more than 4 weeks or repeated episodes.
2. Macroscopic appearance at endoscopy of continuous mucosal inflammation affecting the rectum in continuity with some or the entire colon.
3. Microscopic features on biopsy compatible with UC.
4. No suspicion of CD on small bowel X-ray, ileocolonoscopy or biopsy.

Crohn's disease:

Diagnostic criteria (at least two of four criteria present):

1. History of abdominal pain, weight loss and/or diarrhea for more than three months.
2. Characteristic endoscopic findings of ulceration (aphtous lesions, snail track ulceration) or cobble stoning or radiological features of stricture or cobble stoning.
3. Histopathology consistent with Crohn's disease (epitheloid granuloma of Langerhans type or transmural discontinuous focal or patchy inflammation).
4. Fistula and/or abscess in relation to affected bowel segments.

Exclusion criteria

- Other causes of acute or chronic bowel inflammation must be excluded, i.e. infectious colitis, radiation colitis, diversion colitis, solitary rectal ulcer syndrome, graft versus host disease, diverticular colitis, medication associated colitis, ischemic colitis, microscopic colitis, enema associated colitis.
- Refusal or not able to give informed consent.

In this master project inclusion criteria were completion of the dietary FFQ, CD or UC diagnosis and age ≥ 18 years at inclusion. Participants were excluded from data analysis if they were diagnosed with IBD-unclassified or if important background data collected at inclusion (i.e diagnose, date of birth, sex) were missing. We excluded participants without date of birth, because this information was necessary to match the dietary data with data from the IBSEN III cohort. Participants were excluded if they had an unrealistic high (> 20 000 kJ) or low (< 3500 kJ) energy intake.

3.2.1 Ethics

The IBSEN III cohort has ethical approval from the Regional Committee for Medical and Health Research Ethics, REC South East, Norway (REC no: 2015/946). Written consent are obtained from all participants. Inclusion in the cohort do not imply any changes in treatment, and patients are followed according to local hospital guidelines.

3.3 Data Collection

After inclusion in the cohort, each participant receives a personal account in the web-driven data capture software, Viedoc™. Through this software, participants are given access to different questionnaires opening and closing at pre-set time-intervals. There is a time limit of 28 days to respond after the date of inclusion. After 14 days, if the participant agrees to be contacted after inclusion, a reminder is sent to their mail-address and/or cellphone. Moreover, if the hospital have a routine doing so, they make a personal phone call to participants with missing data, approximately 7 days before deadline. To increase the response rate in this study, the master student called and encouraged participants to respond within the time-limit at Akershus University Hospital in the autumn, 2017.

3.3.1 Dietary data (FFQ)

Dietary data on the participants intake the previous year was assessed using a digital comprehensive semi-quantitative food frequency questionnaire (FFQ), validated at the University of Oslo (100). It was originally developed to collect dietary information in the national population survey Norkost 1997 (101), while the present FFQ is an extended and revised version of the former. The FFQ are available from University of Oslo`s web pages, from a link in Viedoc™ or if the webpage address from the participant-folder is typed into the

web-browser. Participants log in with their personal Bank-ID, and their social security number is stored together with the dietary data at the TSD (Tjenester for sensitive data) databank at the University Center for Information Technology (USIT at University of Oslo). The FFQ includes questions on 269 different food items or composite dishes to capture dietary intakes. Questions are subdivided into 25 different groups comprising related foods (**Appendix** II). To help the participants choose the proper quantity and improve accuracy, the FFQ contained pictures of different portion sizes, household measures, pull-down menus and measures in form of units or slices. Alternatives for estimation of frequency of intake could be ranged from how many times per day/week to times per month the participant consumed a food item or composite dish (examples from the dietary FFQ is given in **Appendix** III).

Total energy intake, macro- and micronutrients with and without dietary supplements, and intake (g/day) of different food groups were computed using the food database KBS AE-14 and KBS software system (KBS, version 7.3, 2017). KBS was developed at the Department of Nutrition, University of Oslo, Norway, and is available to students and researchers at the department.

3.3.2 FODMAP score

Assignment of a FODMAP factor to each food item in the FFQ

The University of Monash, Melbourne, Australia, has developed an application called "Monash University FODMAP diet" which consists of categorization of FODMAP contents in food items. The Monash app was developed for IBS patients particularly, but considered suitable for people with other gastrointestinal diseases (including IBD) adhering to a low FODMAP diet. Depending on the amount of FODMAPs in given portion size(s), the different foods are designated a traffic light: green=low dose; orange=moderate dose; red=high dose. The Monash research team formerly tests all of the included foods to assure quality of the Monash app. They have self-established analytical techniques to identify and quantify FODMAPs (55, 102-104), but the contents in grams per 100g of fresh sample are not published in the app.

We translated the traffic lights from the Monash app into corresponding numerical factors for all the food items in the FFQ. An overview of the different food items and composite dishes and their associated factor is presented in **Appendix** IV. In detail, each food item and

composite dish from the IBSEN III FFQ received factor 0 if the FODMAP content was low (green traffic light), 5 with moderate content (orange traffic light) and 10 if it contained high amounts of FODMAP (red traffic light). In cases where a food item or composite dish was missing in the Monash app, a FODMAP factor was estimated based on the FODMAP containing ingredients in the recipe obtained from KBS, from the declaration on a matching Norwegian product or information from the Norwegian Food Database (www.matvaretabellen.no) (Appendix IV). If the total fraction of medium to high scores of FODMAP ingredients (orange or red traffic light) amounted to or exceeded 40%, the food item or dish received factor 10; were between 5.1-39% it received factor 5; less or equalized 5.0% it received factor 0. For dairy products, we searched the NUTTAB 2010 data base (www.foodstandards.gov.au), to find lactose content in Australian dairy products. Subsequently, we calculated the amount of lactose (which is the major source of FODMAP in dairy products) in the different portion sizes in dairy products available from the Monash app and made cut-off values for lactose content per portion (**Table** 3). Subsequently, we calculated the lactose content in each of the dairy products in the FFQ based on Norwegian serving sizes and gram lactose per 100 grams food obtained from large manufacturers of dairy products in Norway (105, 106).

Table 3: Cut-off values for lactose content (g/portion)

FODMAP factor	**0**	**5**	**10**
Cut of values (g/portion)	≤ 0.9 g/portion	1.0-3.4 g/portion	≥ 3.5 g/portion

FODMAP: Fermentable Oligo-, di- and monosaccharrides and Polyols

Numerical factors for difficult food items with no obvious comparable match in the Monash app (e.g. cloudberries) were determined based on extrapolation of the most similar food items found in the app (Appendix IV), after discussion with the supervisors of this project. Dietary supplements (e.g multivitamins, fish oil supplements etc) were not included in the FODMAP score.

Overall score of FODMAPs based on intake

Each food item intake (g/day) was multiplied with its assigned FODMAP factor, to obtain food item specific FODMAP scores (score/day). Subsequently, the overall FODMAP score for each participant was computed by summarizing the 241 food item specific FODMAP scores. Herbs and spices (10 food items from the FFQ) could not be quantified, and were not included in the overall score. Moreover, we also estimated FODMAP intake-scores based on participants reporting adherence to gluten- and/or lactose-free diets from the IBSEN III FFQ. For participants adhering to gluten- and/or –lactose free diets, FODMAP factors for food items or composite dishes containing gluten or lactose were down-regulated accordingly (Appendix IV).

3.3.3 Background and clinical variables (IBSEN III)

Weight was measured at the hospital, and height self-reported. BMI was calculated by dividing the weight in kilograms by the squared height in meter. Weight and height together with date of birth, age and sex were collected in Viedoc™ by the IBD-nurse at inclusion.

Demographic variables including marital status, highest fulfilled education, occupational status, smoking/smoke-free tobacco (snus) habits and present physical activity were filled in by the participants in Viedoc™. Some IBD-nurses filled in some of this information together with the participant as a practical approach to show them how to use Viedoc™. The background questionnaire also gathered information on previously (last year) or currently adherence to specific diets (**Appendix** V).

Information on self-reported disease activity was gathered in one of the IBSEN III questionnaires. This information was used to calculate self-reported disease activity scores. For UC, the score was based on 2 out of 3 items from the partial Mayo score (PMS) (107, 108) (**Table** 4). For CD, we used 4 out of 5 items from the Harvey Bradshaw index (HBI) (109) (Table 4).

Table 4: Components of the HBI and PMS used to calculate self-reported disease activity scores

	Factors in the scores	**Included in our score (Yes/No)**
Harvey Bradshaw Index	General wellbeing	Yes
	Abdominal pain	Yes
	Abdominal mass	No
	Number of liquid stools per day	Yes
	Complications	Yes
Partial Mayo Score	Stool frequency	Yes
	Rectal bleeding	Yes
	Physician`s global assessment	No

HBI: Harvey Bradshaw index, PMS: partial Mayo score

3.4 Statistics

3.4.1 Statistical analyses

All statistical analyses were performed by the master student, using IBM SPSS statistics version 25 (Chicago, IL, USA). To decide if a variable was normally distributed we assessed mean, median and standard deviation, histogram, Q-Q-Plot and normality tests (Kolmogorov-Smirnov). Continuous variables were when normally distributed, tested with the two-sided Student`s T-test and presented as mean and standard deviation (SD). Non-normally distributed data were tested non-parametrically with Mann-Whitney U and presented as median, 25^{th} and 75^{th} percentiles. A p-value < 0.05 was considered statistically significant. Correlations between continuous variables were tested with Pearson`s correlation coefficient for parametric, and Spearman`s coefficient for non-parametric variables. Categorical data were tested with Chi-square and presented as frequencies (n) and percent. If expected count

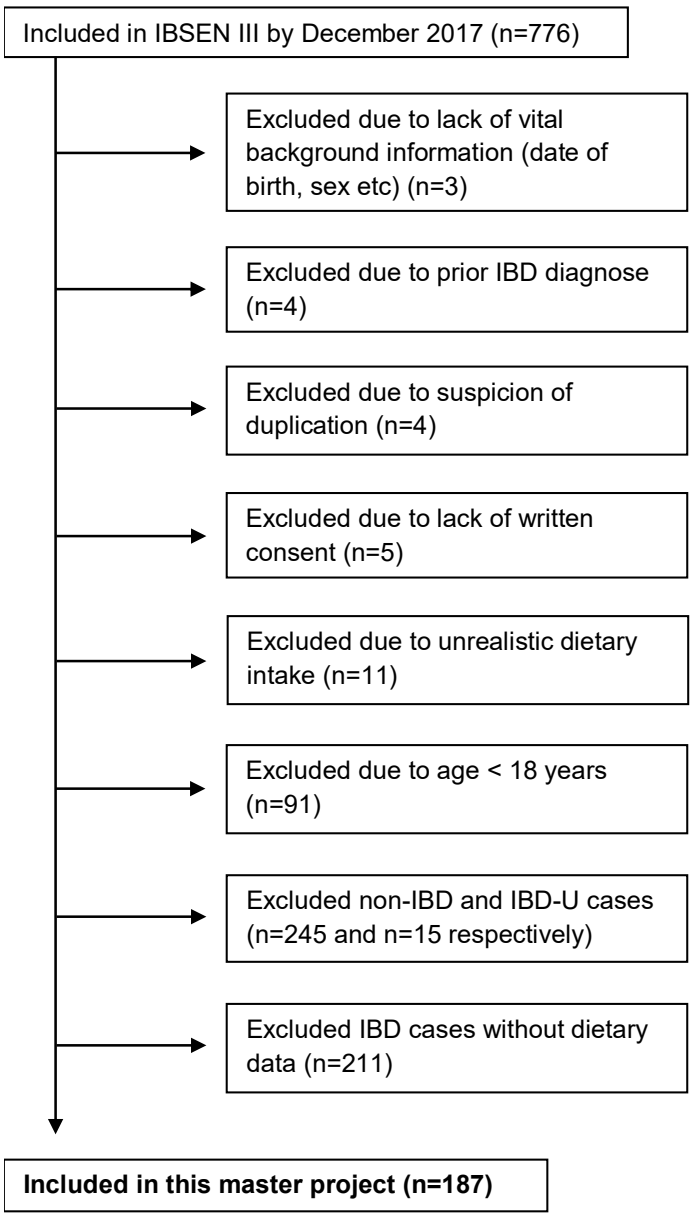
was <5, we used Fisher`s exact test results. In all of the analyses and tables men and women were kept isolated to avoid confounding from gender. To perform variance-analysis, we subdivided the variable of interest into tertiles in ascending order. We used One-way Anova with Bonferroni corrections for parametric and Kruskal Wallis for non-parametric data.

3.4.2 Statistical power

The master student performed a power and sample size estimation using StataSE (version 14), to find what effect size we would be able to detect with our expected sample size. We expect a sample of 50-100 CD and 100-150 UC cases. We calculated power for total energy, calcium and dietary fiber, as we suspect that IBD patients may omit milk, certain fruits, vegetables and whole grain products in their diets (63). Based on means and standard deviations (SD) from Norkost 3 (110), with $p<0.05$ and 80% power, we will with 100 CD and 150 UC cases be able to detect a difference in energy intake of 1198 kJ; calcium of 166 mg; and fiber 3,6g.

4 Results

In total, 187 out of 398 participants aged ≥18 years and diagnosed with CD or UC completed the dietary FFQ (47%). Of the excluded participants with dietary data, 3 participants had an unrealistic low and 8 an unrealistic high energy intake. In **Figure** 2, the selection of included cases are presented in a flowchart.



IBD: Inflammatory bowel disease, IBD-U: Inflammatory bowel disease unclassified

Figure 4: Flowchart of sample used in the master project

4.1 Characteristics of study sample

Of the total IBSEN III sample, 70 (37%) CD patients, and 117 (63%) UC patients were included in this master project. Background characteristics are summarized in **Table** 5.

Table 5: Subject characteristics

	MEN (n=88)		WOMEN (n=99)	
	CD (n=24)	**UC** (n=64)	**CD** (n=46)	**UC** (n=53)
Sex, (%)[a] (n=187)	24 (27%)	64 (73%)	46 (46%)	53 (54%)
Age, years (n=187)	39 (25,51)	42 (29,54)	35 (25,47)	37 (29,45)
Weight, kg (n=182)	86.4 (27.2)	83.8 (13.5)	72.8 (18.1)	72.6 (15.1)
Height, cm (n=182)	182 (7)	182 (5)	167 (8)	169 (7)
BMI (kg/m^2) (n=182)	26.1 (7.4)	25.5 (4.4)	26.0 (5.4)	25.4 (5.1)
Marital status (n=176)				
Married/partner (%)	17 (77%)	41 (67%)	26 (59%)	38 (76%)
Single (%)	5 (23%)	20 (33%)	18 (41%)	12 (24%)
Educational level (n=179)				
≤ 13 years (%)	14 (64%)	30 (48%)	20 (46%)	18 (35%)
> 13 years (%)	8 (36%)	32 (52%)	24 (55%)	33 (65%)
Occupational status (n=178)				
Active worker (%)	17 (77%)	45 (74%)	24 (56%)	34 (67%)
Disabled/rehabilitation (%)	1 (4.5%)	3 (4.8%)	3 (7.0%)	5 (9.8%)
Tobacco (n=179)				
Smoking (%)	3 (14%)	3 (4.8%)	7 (16%)[b]	2 (3.9%)
Smoke-free tobacco (snus) (%)	8 (36%)	22 (36%)	5 (11%)	7 (14%)
Physical activity (n=179)				
Daily (%)	7 (32%)	24 (39%)	6 (14%)	15 (29%)
Weekly (%)	8 (36%)	27 (44%)	20 (46%)	24 (47%)
Less than weekly (%)	7 (32%)	11 (18%)	18 (41%)	12 (24%)
Duration of symptoms, months (n=186)	5 (2,47)	3 (2,9)[c]	7 (4,24)	5 (3,12)[c]

[a] difference in gender dependent of diagnose tested with chi-square, p=0.007

[b] Women with CD tended to smoke more often compared to women with UC tested with chi-square, p=0.076 (Fisher`s exact test)

[c] Trend towards difference in duration of symptoms prior to endoscopy tested with chi-square, p=0.14 and p=0.09 among men and women respectively.

CD: Crohn`s disease, UC: Ulcerative Colitis, BMI: Body mass index

There was a difference in diagnose dependent of gender (p=0.007). Among CD, 66% were women, and among UC 45% were women. The difference in diagnose dependent of gender was still present when we included the IBD-cases without dietary data (n=211) in the former

test (n=398). The youngest participating individual was 18 years old, and the oldest was 80 years old. The majority of the sample was between 30-59 years of age, was married/had a partner and reported to have an occupation. Including IBD-cases without dietary data (n=211) into the analyses, we found that significantly more women with CD smoked pre-diagnosis compared to women with UC (p=0.04), and that participants with CD went through a longer period with symptoms prior to examination compared to UC (men: p<0.001, women: p=0.003). However, these differences disappeared in our sample (n=187), even though a trend was still visible.

Fifty-four percent of the sample was diagnosed at a non-participating hospital, and hence included later into the IBSEN III cohort. Oslo University Hospital, Akershus University Hospital and Vestre Viken Hospital Trust included the majority (47%) of the sample.

Response rate to the dietary FFQ

The response rate was 47%. The average time spent on completing the dietary FFQ was 60 minutes, varying from 20 minutes till 2 hours and 10 minutes. There was no difference in response rate between men and women (p=0.14). Females with CD had a higher rate of response compared to females with UC (61% and 45% respectively, p=0.03).

Men and women who had completed > 13 years of schooling (in Norway: college/university level) had a higher response rate compared to participants with ≤ 13 years of education (in Norway: completed secondary school) (p=0.004 and p=0.04 respectively). In men, 70% with higher compared to 46% with less education completed the dietary FFQ, while in women the distribution was 70% versus 54% respectively. Men and women who smoked prior to diagnosis had a significantly lower response rate (p=0.03), 32% and 41% of smokers compared to 58% and 66% of non-smokers respectively. Among women, being between 30-59 years old was associated with a higher response rate (p=0.01), 59% compared to 44% and 29% for age-groups 18-29 years and 60 years and older respectively. Age had no impact on the response rate for men. Having status as active worker, BMI or using smoke-free tobacco (snus) had no impact on the response rate for men and women.

4.2 Macro- and micronutrients

Except for alcohol intake in women, we found no statistically significant differences comparing macro- and micronutrient intake in CD and UC at inclusion (**Table** 6 and 7).

Table 6: Intake of macronutrients in percent of total energy intake (E%)

	Men (n=88)			**Women (n=99)**		
	CD	**UC**	**p**	**CD**	**UC**	**p**
	n=24	n=64		n=46	n=53	
Percent energy, E%						
Protein, E%	17 (3)	17 (3)	0.84	17 (3)	17 (4)	0.56
Fat, E%	37 (6)	36 (7)	0.42	36 (5)	36 (5)	0.97
SFA, E%	14 (2)	13 (3)	0.24	13 (2)	13 (2)	0.98
MUFA, E%	14 (3)	13 (3)	0.49	13 (2)	13 (3)	0.87
PUFA, E%*	5.9 (4.6,7.3)	5.8 (4.8,6.8)	0.98	5.8 (5.1,6.8)	5.9 (5.0,7.2)	0.79
Omega-3, E%*	1.3 (0.9,1.6)	1.1 (0.8,1.6)	0.41	1.3 (1.0,1.8)	1.2 (0.9,1.8)	0.45
Carbohydrates, E%	42 (6)	43 (8)	0.65	44 (5)	43 (8)	0.57
Added sugar, E%*	6.4 (3.7,11)	6.0 (3.4,9.9)	0.68	6.9 (4.4,9.1)	7.1 (4.3,11)	0.87
Fibre, E%	2.0 (0.5)	2.1 (0.5)	0.74	2.3 (0.6)	2.5 (0.7)	0.054
Alkohol, E%*	1.1 (0.4,2.1)	1.5 (0.6,3.5)	0.18	0.2 (0.1,0.6)	0.7 (0.1,2.2)	**0.004**

* Tested with Mann-Whitney

CD: Crohn`s disease, UC: Ulcerous Colitis, p: p-value, SFA: Saturated fatty acids, MUFA: monounsaturated fatty acids, PUFA: Polyunsaturated fatty acids

Table 7: Intake per person of macro- and micronutrients (quantity/day)

	MEN (n=88)			WOMEN (n=99)		
	CD	**UC**	**p**	**CD**	**UC**	**p**
	n=24	n=64		n=46	n=53	
Quantity per person per day						
Energy, MJ[a]	12.6 (3.7)	11.4 (3.4)	0.16	9.5 (2.8)	9.8 (3.2)	0.61
Protein, g	127 (45)	111 (32)	0.13	97 (35)	95 (31)	0.74
Fat, g*	135 (79,162)	101 (83,139)	0.12	81 (65,111)	91 (70,111)	0.69
SFA, g*	50 (32,62)	38 (30,51)	0.09	32 (26,40)	33 (27,42)	0.62
MUFA, g*	51 (29,61)	38 (30,53)	0.12	29 (24,43)	34 (26,39)	0.74
PUFA, g*	21 (15,24)	18 (13,22)	0.14	15 (11,20)	14 (12,19)	0.93
Omega-3, g*	4.2 (2.9,5.2)	3.4 (2.5,4.4)	0.12	3.0 (2.1,4.4)	3.2 (2.2,4.4)	1.00
Omega-6, g*	17 (13,19)	14 (11,18)	0.18	12 (9,15)	11 (9,15)	0.86
Cholesterol, mg*	420 (263,577)	356 (263,454)	0.33	271 (211,405)	309 (222,399)	0.82
Carbohydrates, g	312 (102)	290 (104)	0.38	244 (74)	255 (107)	0.58
Fibre, g	31 (10)	29 (10)	0.33	26 (8)	30 (11)	0.08
Added sugar, g*	48 (23,81)	37 (21,69)	0.47	36 (22,54)	39 (21,60)	0.86
Alkohol, g*	5.3 (1.8,9.6)	6.1 (2.6,14)	0.33	0.9 (0.3,2.1)	2.2 (0.5,5.9)	**0.004**
Vitamin A, µg*	1493 (889,2081)	1179 (743,1631)	0.08	1130 (812,1593)	1091 (790,1599)	0.93
Vitamin D, µg*	7.2 (5.4,13)	8.1 (5.3,11)	0.59	6.7 (5.4,10)	7.1 (4.8,9.3)	0.56
Vitamin E, mg	18 (7)	17 (6)	0.39	15 (6)	15 (5)	0.67
Thiamine, mg	2.1 (0.7)	1.9 (0,5)	0.12	1.7 (0.5)	1.6 (0.5)	0.84
Riboflavin, mg	2.6 (0.9)	2.4 (0.9)	0.21	2.0 (0.9)	2.0 (0.7)	0.86
Niacin, mg*	31 (26,41)	28 (21,34)	0.10	23 (17,28)	22 (17,27)	0.76
Vitamin B6, mg*	2.4 (1.5,2.9)	2.0 (1.6,2.4)	0.23	1.7 (1.3,2.3)	1.9 (1.4,2.3)	0.48
Folate, µg	369 (132)	338 (99)	0.24	317 (124)	346 (129)	0.27
Vitamin B12, µg*	9.3 (5.4,13)	7.4 (5.7,10)	0.14	6.5 (4.9,9.3)	6.9 (4.7,8.8)	0.67
Vitamin C, mg*	114 (75,171)	112 (82,146)	0.89	122 (62,165)	127 (93,176)	0.10
Calcium, mg*	998 (670,1359)	936 (686,1294)	0.50	881 (660,1141)	859 (705,1099)	1.00
Iron, mg	14 (5)	12 (4)	0.07	11 (3)	11 (4)	0.58
Sodium, g*	3.8 (3.0,4.9)	3.2 (2.6,4.1)	0.08	3.0 (2.2,3.7)	2.6 (2.0,3.4)	0.17
Potassium, g	5.1 (1.7)	4.8 (1.5)	0.34	4.2 (1.6)	4.5 (1.7)	0.28
Magnesium, mg*	477 (318,592)	436 (336,532)	0.34	355 (281,461)	371 (300,492)	0.36
Zinc, mg	17 (6)	15 (4)	0.10	13 (4)	12 (4)	0.61
Selenium, µg*	70 (45,93)	60 (46,76)	0.25	48 (38,65)	54 (36,64)	0.74
Copper, mg	1.5 (0.5)	1.4 (0.5)	0.47	1.3 (0.4)	1.4 (0.6)	0.09
Phosphorus, g	2.2 (0.7)	2.0 (0.6)	0.20	1.8 (0.6)	1.8 (0.6)	0.89

* Tested with Mann-Whitney

[a] Significant difference between men and women ($p<0.001$)

CD: Crohn`s disease, UC: Ulcerous Colitis, p: p-value, SFA: Saturated fatty acids, MUFA: monounsaturated fatty acids, PUFA: Polyunsaturated fatty acids

Women with UC consumed significantly more alcohol than women with CD (p=0.004). The differences were 0.5E% or 1.3g of alcohol per day. There was a trend towards higher absolute intakes of fiber and copper in women with UC, however the intakes were not significantly different. Men with CD had a tendency towards higher intakes of saturated fatty acids (SFA), vitamin A, iron and sodium compared to men with UC.

Several of the participants used dietary supplements. Forty-six percent used liquid or capsulated marine oils, 19% used multivitamins, 7.8% used vitamin C supplements, 7.5% took B-vitamins, 13% used Vitamin D supplements and 4% used an oral iron preparation-liquid or in form of a tablet. When supplements were included in the analysis of vitamin D intake, 53% of the study population had a dietary intake >10 µg.

4.2.1 Dietary intakes in relation to recommendations and Norkost

In **Table** 8 and 9, we present an overview of the intakes of selected macro- and micronutrients, the recommendations from Nordic Nutrition Recommendations 2012 (NNR12) (111), and reported intakes from the Norkost 1997 and Norkost 3 national surveys (101, 110).

Table 8: Dietary intakes in relation to recommendations and national dietary surveys, in women

	Women in our sample (n=99)	NNR12		Norkost 1997 (n=1374) / Norkost 3 (n=925)
	Mean (SD)			**Mean / Mean (SD)**
Protein, E%	17 (3.3)	10-20 E%[a]		16 / 18 (4)
Fat, E%	36 (5.0)	25-40 E%		30 / 34 (7)
SFA, E%	13 (2.1)	< 10 E%		12 / 13 (3)
MUFA, E%	13 (2.6)	10-20 E%		11 / 12 (3)
PUFA, E%	6.1 (1.6)	5-10 E%		5.2 / 6.2 (2.3)
Omega 3, E%	1.3 (0.5)	≥ 1 E%		- / -
Carbohydrates, E%	44 (7.1)	45-60 E%		52 / 44 (8)
Added sugar, E%	8.1 (6.0)	< 10 E%		9.1 / 7.4 (5.2)
Fibre, g	28 (10)	≥ 25 g/d		21 / 22 (8)
Alcohol, g	3.3 (5.2)	< 10 g/d		4 / 6.3 (14.1)
		RI	**LI**	
Vitamin A, µg	1283 (701)	700[b]	400[b]	- / -
Vitamin D, µg	7.8 (4.1)	10[c]	2.5	4.0 / 4.9 (4.3)
Vitamin E, mg	15 (5.3)	8[d]	3[d]	- / 10 (4)
Thiamine, mg	1.6 (0.5)	1.1	0.5[e]	1.2 / 1.4 (0.5)
Vitamin B6, mg	1.9 (0.7)	1.2	0.8	- / 1.5 (0.5)
Folate, µg	332 (127)	300 / 400[f]	100	- / 231 (86)
Vitamin B12, µg	7.3 (3.5)	2	1	- / 6.0 (3.7)
Vitamin C, mg	141 (102)	75	10	118 / 111 (71)
Calcium, mg	950 (451)	800	400	800 / 811 (364)
Iron, mg	11 (3.4)	15 / 9[g]	5[g]	9.5 / 9.9 (3.5)
Magnesium, mg	400 (146)	280	-	- / 346 (110)
Zinc, mg	12 (3.9)	7	4	- / -
Selenium, µg	55 (25)	50	20	- / -

[a] from age ≥65, 15-20 e% from protein is recommended

[b] RE = retinol equivalents

[c] from age ≥75, 20µg is recommended

[d] α-TE = α-tocopherol equivalents

[e] 0.8 mg at energy intakes < 8 MJ/d and 1.0mg/d for elderly

[f] women in reproductive age

[g] post-menopause

SD: standard deviation, SFA: saturated fatty acids, MUFA: monounsaturated fatty acids, PUFA: polyunsaturated fatty acids, RI: recommended intake, LI: Lower intake level

Table 9: Dietary intakes in relation to recommendations and national dietary surveys, in men

	Men in our sample (n=88)	NNR12		Norkost 1997 (n=1298) / Norkost 3 (n=862)
	Mean (SD)			Mean / Mean (SD)
Protein, E%	17 (3.2)	10-20 E%[a]		16 / 18 (4)
Fat, E%	36 (6.4)	25-40 E%		31 / 34 (7)
SFA, E%	13 (2.6)	< 10 E%		12 / 13 (3)
MUFA, E%	14 (2.9)	10-20 E%		11 / 12 (3)
PUFA, E%	6.0 (1.9)	5-10 E%		6 / 6.3 (2.2)
Omega 3, E%	1.3 (0.5)	≥ 1 E%		- / -
Carbohydrates, E%	43 (7.4)	45-60 E%		51 / 43 (8)
Added sugar, E%	8.2 (6.9)	< 10 E%		10 / 7.2 (5.7)
Fibre, g	29 (10)	≥ 35 g/d		25 / 26 (11)
Alcohol, g	8.4 (8.5)	< 20 g/d		8 / 10 (22)
		RI	**LI**	
Vitamin A, µg	1407 (944)	900[b]	500[b]	- / -
Vitamin D, µg	8.4 (3.8)	10[c]	2.5[c]	5.8 / 6.7 (5.7)
Vitamin E, mg	17 (6.5)	10[d]	4[d]	- / 12 (5)
Thiamine, mg	1.9 (0.6)	1.4	0.6[e]	1.6 / 1.9 (0.7)
Vitamin B6, mg	2.1 (0.7)	1.5	1.0	- / 1.9 (0.8)
Folate, µg	346 (109)	300	100	- / 279 (105)
Vitamin B12, µg	8.4 (3.4)	2	1	- / 8.9 (8.0)
Vitamin C, mg	124 (63)	75	10	121 / 105 (77)
Calcium, mg	1021 (469)	800	400	1100 / 1038 (514)
Iron, mg	13 (3.9)	9	7	12 / 13 (4)
Magnesium, mg	449 (135)	350	-	- / 439 (143)
Zinc, mg	15 (4.9)	9	5	- / -
Selenium, µg	65 (24)	60	20	- / -

[a] from age ≥65, 15-20 E% from protein is recommended

[b] RE=Retinol equivalents

[c] from age ≥75, 20 µg is recommended

[d] α-TE=α-Tokoferol equivalents

[e] 0.8 mg at energy intakes < 8 MJ/d and 1.0mg/d for elderly

SD: standard deviation, SFA: saturated fatty acids, MUFA: monounsaturated fatty acids, PUFA: polyunsaturated fatty acids, RI: recommended intake, LI: Lower intake level

The intake of macronutrients were quite similar between men and women in our study sample and the population in Norkost 3. Important exceptions were added sugar, fiber and alcohol. Percent energy from added sugar was within the recommendations, but higher among men and women in our sample than reported in Norkost 3 (Table 8 and 9). Women in the present study had a fiber intake exceeding the daily recommendations, and it was higher than reported in Norkost 3 (Table 8). Men in our sample had a fiber intake lower than recommended, but

higher than reported in Norkost 3 (Table 9). The intake of alcohol in men was not so different between our sample and the Norkost population, while women in our sample had a much lower intake of alcohol than women in Norkost 3.

Intake of micronutrients were all within recommended daily intake, except for Vitamin D in both genders. Seventy-one percent of the study population had a daily dietary intake of vitamin D <10µg. The intake of folate and iron was below recommended in women of reproductive age (aged 15-49 according to WHO) (112). In our sample 80 (81%) women were of reproductive age, but intakes of folate and iron were not different from women older than 49 years (p=0.29). The intake of vitamin D and folate in both genders, and calcium intake in women were higher in our sample than reported in Norkost 3 (Table 8 and 9).

4.3 Consume of different food groups

There were some differences in dietary intake of specific food groups comparing median intakes in UC and CD (**Table** 10).

Table 10: Dietary intake per person of different food groups (g/day)

	Men (n=88)			Women (n=99)		
	CD	**UC**	**p***	**CD**	**UC**	**p***
	n=24	n=64		n=46	n=53	
Gram per person per day						
Bread	223 (173,261)	164 (101,222)	**0.03**	154 (69,190)	103 (59,165)	0.25
Cereals	55 (34,87)	64 (36,135)	0.33	62 (43,163)	91 (47,143)	0.48
Cakes	17 (8,42)	14 (6,37)	0.32	13 (7,32)	19 (9,33)	0.16
Potato	76 (38,106)	59 (32,94)	0.24	56 (34,77)	42 (21,75)	0.19
Vegetables	175 (78,319)	186 (106,257)	0.93	207 (94,315)	272 (194,384)	**0.02**
Fruit and berries	144 (40,197)	95 (61,151)	0.54	99 (40,174)	142 (71,197)	0.07
Juice	71 (15,274)	88 (21,203)	0.82	57 (8,150)	30 (16,85)	0.61
Meat	173 (117,261)	127 (87,187)	**0.02**	113 (70,155)	88 (56,121)	0.07
Lean fish	7 (2,22)	10 (2,24)	0.67	4 (1,23)	12 (3,24)	0.10
Fatty fish	14 (6,29)	15 (8,30)	0.80	15 (6,23)	14 (7,29)	0.95
Eggs	29 (9,44)	24 (13,36)	0.88	15 (9,33)	20 (10,37)	0.64
Milk and yoghurt	193 (77,368)	153 (44,323)	0.44	172 (43,353)	136 (38,310)	0.48
Wholefat (3.5%)	1 (0,2)	0 (0,2)	0.29	0 (0,0)	0 (0,2)	0.56
Semi-skimmed (0.1%)	59 (2,302)	28 (1,156)	0.38	43 (0,168)	4 (0,64)	0.19
Semi-skimmed (0.05-0.07%)	2 (0,11)	0 (0,46)	0.86	1 (0,143)	0 (0,8)	0.33
Skimmed milk (0.01%)	0 (0,2)	0 (0,0)	0.26	0 (0,1)	0 (0,2)	0.32
Cream products (ice cream, sour cream)	21 (8,33)	14 (7,28)	0.53	16 (9,22)	23 (7,48)	0.21
Cheese	18 (13,42)	18 (10,36)	0.37	23 (9,33)	19 (10,38)	0.93
Margarine, butter, oils	27 (8,45)	21 (6,39)	0.29	20 (10,33)	17 (3,32)	0.10
Mayonnaise (spreads, dressing)	5 (2,21)	4 (1,16)	0,29	5 (1,15)	4 (1,10)	0.46
Sugar and sweets (spreads, desserts)	22 (12,37)	25 (13,45)	0,86	23 (11,44)	26 (16,71)	0.14
Coffee	406 (233,886)	431 (116,910)	0,80	87 (0,784)	264 (0,797)	0.57
Tea	22 (5,185)	34 (1,148)	0,49	47 (8,233)	59 (8,310)	0.67
Soda and cordial	252 (94,436)	190 (49,539)	0,97	163 (42,434)	163 (39,450)	1.00
Soda and cordial (sugar)	95 (5,316)	52 (6,228)	0,67	50 (1,186)	8 (4,119)	0.31
Soda and cordial (light)	21 (0,143)	21 (0,304)	0,80	5 (0,143)	36 (5,357)	0.17
Water with/without carbonic acid	843 (443,1216)	843 (421,1136)	0,80	947 (705,1563)	1136 (574,1505)	0.84
Alcoholic drinks (beer, wine and liquor)	95 (42,180)	132 (47,221)	0,45	14 (3,42)	43 (7,94)	**0.008**
Snacks	12 (4,20)	11 (4,21)	0,90	6 (2,13)	8 (2,16)	0.40

*Tested with Mann-Whitney

CD: Crohn`s disease, UC: Ulcerous Colitis, p: p-value,

Men with CD consumed significantly more bread and meat compared to men with UC (59g and 46g, respectively). Women with UC consumed 65g vegetables and 29g alcoholic drinks more per day compared to women with CD (p=0.02 and p=0.008, respectively). Furthermore, there was a trend towards higher intake of fruit and berries, and lower intake of meat in women with UC compared to women with CD (p=0.07 and p=0.07, respectively). Sixty-nine participants did not meet the daily recommended intake of calcium. Of these, 23 participants (33%) had a daily intake of milk equal to 0 grams. The daily iron intake increased significantly with higher intake of meat (p<0.001). It ranged from 9.8-14.4 mg in the lowest to the highest tertile, and a corresponding difference of 4.6 mg. When we separated gender, iron intake still increased with higher intake of meat, but the differences were not significant between all tertiles.

4.4 FODMAP

4.4.1 Differences in total FODMAP score

There were no difference in total FODMAP score between CD and UC (p=0.38), or across any of the following background variables: sex, marital status, educational level, occupational status or use of tobacco (p>0.05). Among participants who reported to follow/had followed the low FODMAP diet the previous year (n=10), the total FODMAP score was significantly lower than the rest of the sample (n=177) (mean difference (95% CI): 3980 score/day (814-7146), p=0.01). Participants who reported to refrain from gluten and lactose (n=10), had a significantly lower total FODMAP score compared to those who did not (n=177) (mean difference (95% CI): 5349 score/day (2226-8472), p=0.001).

The total FODMAP score correlated positively with increasing energy intake (Pearson, r=0.64, p<0.001). There was a weak negative correlation in FODMAP score with increasing age among men (Spearman, r=-0.29, p=0.007). There was no significant association between FODMAP score and BMI (Pearson, r=0.003, p=0.97).

4.4.2 FODMAP score in tertiles for different food groups

For almost every food group containing FODMAPs, the median daily intake increased with higher FODMAP score (**Table** 11). We found no significant difference with higher FODMAP score for vegetable intake.

Table 11: Change in intake of different foods with higher FODMAP score

FODMAP score	Low (Range: 1565-7674)	Medium (Range: 7698-11386)	High (Range: 11550-32910)	p*
	(n=62)	(n=63)	(n=62)	
Food group, g/day				
Bread	119 (56,171)	158 (70,218)	175 (106,253)	**0.03**
Cereals	44 (25,75)	81 (47,137)	119 (58,187)	**<0.001**
Cakes	10 (5,21)	16 (7,29)	32 (10,47)	**<0.001**
Potato	36 (19,65)	57 (29,94)	71 (51,93)	**<0.001**
Vegetables	197 (83,299)	208 (134,371)	250 (133,361)	0.12
Fruit and berries	78 (39,124)	95 (63,193)	150 (91,210)	**<0.001**
Juice	19 (6,104)	61 (18,143)	138 (30,301)	**<0.001**
Meat	94 (66,134)	118 (71,175)	139 (98,208)	**0.001**
Milk and yoghurt	44 (15,104)	193 (70,305)	389 (215,714)	**<0.001**
Wholefat milk (3.5%)	0 (0,0)	0 (0,2)	0 (0,2)	**0.001**
Semi-skimmed milk (0.1%)	2 (0,21)	28 (2,143)	223 (12,418)	**<0.001**
Semi-skimmed milk (0.05-0.07%)	0 (0,2)	0 (0,14)	2 (0,300)	**<0.001**
Skimmed milk (0.01%)	0 (0,0)	0 (0,2)	0 (0,2)	**0.002**
Cream products (ice cream, sour cream)	11 (6,20)	19 (8,33)	22 (11,48)	**0.001**
Margarine, butter, oils	13 (3,25)	20 (6,39)	23 (8,40)	**0.004**
Sugar and sweets (spreads, desserts)	21 (7,37)	28 (16,48)	26 (17,72)	**0.02**
Coffee	378 (3,878)	436 (24,898)	378 (0,782)	0.18
Tea	12 (0,90)	87 (8,218)	80 (6,374)	**0.004**
Soda and cordial	153 (18,479)	187 (72,539)	205 (84,448)	0.33
Soda and cordial (with sugar)	10 (1,146)	36 (5,179)	120 (8,296)	**0.008**
Soda and cordial (light)	5 (0,197)	36 (0,357)	5 (0,143)	0.74
Alcoholic beverages (beer, wine and liquor)	44 (9,91)	50 (13,166)	55 (18,166)	0.20
Snacks	7 (2,14)	8 (4,18)	11 (4,18)	0.34

* Kruskal-wallis test

FODMAP: Fermetable Oligo-, di- and monosaccharides and polyols, p: p-value

Food groups which contributed mostly to the total FODMAP score were fruit/berries and vegetables, bread and cereals and dairy products. They contributed with 23%, 26% and 31% respectively.

4.4.3 Self-reported disease activity at diagnosis

We found no significant differences in FODMAP score with increasing self-reported disease activity in neither UC nor CD (p=0.51 and p=0.81, respectively) (**Table** 12 and 13). The result did not change when we filtered out the participants who had or still followed the FODMAP diet.

Table 12: FODMAP score in relation to self-reported disease activity in UC patients (n=115)

Disease activity (PMS)	Low (Range: 0-1)	Medium (Range: 2-4)	High (Range: 5-6)
	n=47	n=45	n=23
Mean (95% CI)			
FODMAP score (score/day)	9471 (8273-10669)	10198 (8730-11666)	10764 (8607-12920)

Tested with Oneway ANOVA with Bonferroni correction.
UC: Ulcerous Colitis, PMS: partial Mayo score, CI: Confidence Interval

Table 13: FODMAP score in relation to self-reported disease activity in CD patients (n=68)

Disease activity (HBI)	Low (Range: 0-2)	Medium (Range: 3-5)	High (Range: 6-24)
	n=22	n=23	n=23
Mean (95% CI)			
FODMAP score (score/day)	10465 (8220-12709)	11080 (7893-14266)	9999 (8311-11686)

Tested with Oneway ANOVA with Bonferroni correction.
CD: Crohn`s disease, HBI: Harvey-Bradshaw index, CI: Confidence Interval

5 Discussion

5.1 Methodological considerations

5.1.1 Observational studies

Prevalence and risk factors are common outcomes of observational studies (113). Observational studies are useful to generate hypothesis about relations we would like to elucidate more closely. Causality can however not be proven due to the presence of random errors, bias and confounding variables affecting internal validity (113). A low internal validity confines the generalizability-the external validity (113).

Measurement errors are impossible to eradicate, and may explain why observational studies often have deviating and sometimes conflicting results (113). Errors can be random or systematic (113). Random errors are always present to a more or less extent. They lead to increased variability and hence lower precision (113). Consequently, effect estimates are generally attenuated (113). Random errors can be minimized through increased sample size to improve statistical power. Observational studies are prone to selection and information bias (113). Selection bias are especially important for the external validity (113). If the study sample deviates vastly from the population we would like to explore, the validity of the results are confined to the current study population. Information bias can be conscious or unconscious, and the extent depend on the collection method (113). Information bias may lead to wrong conclusions. Confounding variables are factors associated with both the exposure and outcome of a relation we would like to elucidate, but not an effect of neither (114). Usually we perform control over possible confounding variables through adjustments in the statistical analysis (114). Still, it is possible that unknown confounding variables influence the results. It is important to try to rule out possible systematic and confounding errors to avoid misinterpreting and false conclusions.

At present, IBSEN III is an ongoing cohort with dietary follow-up one year after inclusion (initiated January, 2018). The follow-up data were not available in the time-frame offered in this master project, and the design is cross-sectional. A cross-sectional study provides a snap-shot of the current situation (113). Thus, it cannot be used to study alterations in dietary intake over time.

5.1.2 Internal validity

Selection bias

The response rate to the dietary FFQ was 47%, which is fairly low considering the great interest of food and diet in IBD patients (61-65). Analysis of who responded to the dietary FFQ showed that women with CD, non-smoking and higher educated participants had a higher response rate, including women aged between 30-59 years. It is known that smoking and a less healthy diet are more frequent in the lower socioeconomic classes in Norway, and interrelated to degree of education (115). Furthermore, the most usual contributor to why people would like to participate in scientific research is self-interest (113). Thus, it is likely that participants with a greater interest and perhaps also a more healthy diet chose to respond to the dietary FFQ. CD patients in particular, report to have more knowledge of nutrition compared to patients with UC (66), and may explain the higher participation rate among women with CD. Selection bias in our sample is likely due to the moderate response rate, and the differences between the responding and non-responding participants.

The vast majority of the sample was included from large health regions, including Oslo University Hospital, Akershus University Hospital and Vestre Viken Hospital Trust. Some hospitals and the dietary data from their respective participants were excluded due to incomplete information, for instance missing diagnose. Furthermore, some hospitals had a routine in reminding their patients to respond the questionnaires. Thus, the generalizability might be affected by a selection bias due to overrepresentation from specific health regions. However, the data may be more representative, and hence generalizable to the general IBD population, in hospitals having an active approach to obtain more complete data (through reminding).

The most important burden associated with participation in the study was the time-consuming completion of the several questionnaires in the overall IBSEN III cohort. We assume that individuals with severe inflammation and symptoms may have refrained to respond or even participate at all. This could have had an impact on resulting dietary intakes, including the activity scores presented in this study. The dietary FFQ was comprehensive, and likely the most time-consuming, with a mean time of 60 minutes completing the questionnaire. However, FFQs are considered easy to administer compared to more demanding dietary collection methods like keeping a dietary journal or weighed records. Thus, reduced

participant burden caused by the simple dietary collection method likely decreased the risk of selection bias in our sample.

Because of the digital data collection, we might have lost some participants due to restricted resources, e.g. limited access to computer or Internet, or lack of skills in usage of digital devises attributed to a lower socioeconomic status. However, the majority of our study population was quite young, so this should not be a large problem.

Information bias

Dietary FFQ

FFQ is a convenient tool assessing long-term habitual intake in a large population (116). Its utilization is usually to rank individuals and compare characteristics in different groups of the sample. Common disadvantages with FFQs include poor estimation of quantity, few possibilities to specify and difficulties remembering dietary habits for a long time past (116). Access to the dietary FFQ, which was located in a different web site than the rest of the questionnaires, may have contributed to the low response rate. From January and until May 2017, the dietary FFQ was only available from a link in the out handed study-folder, and not from Viedoc^{TM}. Thus, participants may have forgotten to answer the dietary FFQ. Although we believe the incorporation of the link in Viedoc^{TM} improved the response rate, we did not have the numbers to calculate if there was an improvement. In addition, the participants had to complete the entire FFQ at once, because answers were not saved during the filling in of the FFQ. Thus, some data might be lost due to incomplete questionnaires.

Because the FFQ was digital, the risk of missing data due to mistakes when punching or scanning paper versions were decreased. However, there was a risk of random errors if participants ticked the wrong answer. The validation study of the FFQ did not capture signs of systematic misunderstanding of certain questions (100). Thus, this should not be a problem in our results. From the written feedback in the comment field at the end of the FFQ, it might seem like some special food items and diets were considered not sufficiently captured by the FFQ. However, this is not extraordinary for the study sample, but rather a limitation of the FFQ as an assessment method caused by the extensive availability of different foods across borders, rapidly changing dietary trends and the cultural diversity of dietary habits.

The dietary FFQ was designed to reflect dietary intake the preceding year. Every participant was at risk of recall bias. Recall bias is a specific information bias affecting patients because they think more closely about what may have caused their disease (113). Recall bias may be more prominent and lead to more skewness in the dietary intakes for participants who believe diet is important in development in particular, but also management of IBD (61-66). CD patients in particular may be extra concerned with diet, introducing more restrictions than patients with UC (61, 62, 73). However, we believe the interest in those who answered the dietary FFQ was quite similar, which means that recall bias is as much a problem in CD like in UC. Thus, we do not think recall bias leads to differential measurement errors in our study population, like in case-control studies where controls are not exposed to recall bias (113).

There was no deadline to complete the dietary FFQ like it was for the other questionnaires in the IBSEN III cohort (28 days after inclusion). Although participants were supposed to report dietary intakes the preceding year, it is likely that recently introduced dietary changes may have biased their response. Furthermore, due to the presence of symptoms in several months before diagnosis (Table 5), dietary intakes may reflect dietary changes introduced to manage these symptoms. Diagnostic delay from the onset of symptom till diagnosis is set, vary in different studies. Previous studies have reported a median diagnostic delay of 5-9.5 months and 2.4-3.1 months in CD and UC respectively (117-119), and that 39% change their diet pre-diagnosis and over 50% post-diagnosis (61, 62, 69). Thus, we expected that many participants would have introduced some changes to their diet before filling in the dietary FFQ. In light of this, we do not consider the dietary data suitable to study risk factors of disease development.

From the validation study we know that certain macronutrients and foods were under- and overestimated by the dietary FFQ (100). Total energy intake was overestimated by 11% compared to measured energy expenditure by ActiReg® (100). Furthermore, percent energy from fat and added sugar were underestimated while percent energy from carbohydrates and protein was overestimated. The latter resulted from comparing the intakes as measured by the FFQ with 7-days weighed records (100). The mean intake of vegetables, berries, coffee and tea was significantly higher in the FFQ compared to the reference method (100). Due to over- and underestimation of specific foods and macronutrients, we have to be careful comparing our results with Norkost 3 which used 24-hours recall to collect data on dietary intake (110). Also, we cannot extrapolate the results of the validation study to the current study population without being cautious. Because of recall bias, the current study population may overestimate intakes of other foods they believe to have an impact on the disease. On the other hand,

patients with IBD may be extra careful filling in the dietary FFQ due to personal interest in the results from this research, leading to more accurate estimates of intake.

In the validation study, 32% and 8% of the participants were defined as under- and over reporters respectively (100). Under reporters had a significantly lower absolute intake of vegetables, grain products, potatoes, meat, egg, dairy products and butter and margarine (100). Thus, the presence of under reporters in our study could have affected the mean and median intakes. Carlsen et al. suggested: "In future studies employing the FFQ, it might be considered to exclude the 5% highest under- and over reporters" (100). Consequently, we could assume that 60 and 15 participants in our sample were under- and over reporters respectively. Thus, if we were to follow the advice of excluding 5%, the bottom 3 with the lowest and the participant with the highest energy intake should be excluded. Due to our exclusion criteria, the 3 bottom participants with the lowest, and 8 participants with the highest energy intake were excluded. Thus, our results should not be affected notably from under- and over reporters. Furthermore, we assume the problem would be equally distributed among CD and UC patients, and not influence the comparisons of intake between them in any particular direction.

FODMAP score

The most accurate procedure to estimate the total FODMAP intake per person would be based on the analyzed content of FODMAPs in grams per 100g of fresh foods. It was not feasible within the scope of this project to perform such a comprehensive task. Analytical measurements of FODMAP content was not available in the literature for each of the food items or composite dishes in the dietary FFQ. Furthermore, the analyzed content of FODMAPs sometimes deviates substantially when comparing different analytical results (102, 104). Specific ingredients, processing techniques, country-specific factors including agricultural differences all affect the FODMAP content of different foods and products as recognized by Varney et al. (55). Thus, to create a more exact score, we would have to analyze the FODMAP content in foods available in Norway.

Our FODMAP score is confined to the fact that it is based on serving sizes and the resulting inaccuracy. Limitations include for instance that important additives containing or consisting of FODMAPs, for instance inulin which is a popular additive used to increase the fiber content in many products (55), were not included in the assessment. Consequently, some of

the food items and composite dishes may have been misclassified, and assigned with the wrong factor (too low). Because this problem applied to the score of every individual, the rank and order of them would probably not change, unless some were consuming substantially larger amounts of one or more products containing this additive. Spices and herbs (including garlic which is a frequently used spice in Norway) are generally difficult to quantify and the FFQ only recorded frequency of intake. Thus, they were not included in the FODMAP score. However, the contribution in grams from spices and herbs would probably be rather low, and not have an impact on the score to any appreciable extent. Sugar and sweets are a large and complex group of foods, which because of popular sweeteners like sugar polyols, fruit concentrates, fructose-glucose syrup etc., could contain fructose in excess of glucose though the assigned FODMAP factor was 0. However, we believed the contribution of such sugar and sweets would have a minimal effect on the total score.

Further, the FODMAP score is based on computed intakes from the dietary FFQ. Thus, any bias in reported intakes will affect the score accordingly. Vegetables were for instance over-reported by the FFQ in the validation study of the dietary FFQ (100). Foods that were recorded differently dependent of the classification of under- or acceptable reporters may have had impact on the score, but like we discussed in the FFQ section this problem was probably the same for UC and CD patients.

Self-reported disease activity scores

The self-reported disease activity scores were used to explore associations with the FODMAP score. We used HBI for CD, and PMS for UC. A problem with these scores was that they included factors reflecting both disease activity and gastrointestinal symptoms. For HBI, there were 4 factors included in the calculated score. Physical wellbeing, abdominal pain and frequency of liquid stools could be attributed to functional gastrointestinal symptoms, while complications are consequences of the disease. For PMS, rectal bleeding is associated with the presence of inflammation in the intestines, and not a functional gastrointestinal symptom. In light of this, we cannot attribute the results from these analysis solely to functional gastrointestinal symptoms or disease activity alone. To do that, we would have to make separate scores of functional gastrointestinal symptoms and perhaps use an objective marker of disease activity, for instance Calprotectin measurements.

Confounding variables

From the statistical analysis, more women had CD than men, and the contrary for UC. Furthermore, total energy intake was significantly different between men and women. Thus, to prevent confounding from gender, we separated all analysis of dietary intake in males and females. Smoking and symptoms were other potential confounding factors which could affect dietary intake, but there was no difference between CD and UC patients who responded to the dietary FFQ. Hence, we did not adjust for smoking or symptoms. We cannot exclude the possibility of other confounding variables affecting our results.

5.1.3 External validity

We found that our study population has been exposed to selection bias due to the fairly low response rate in the dietary FFQ including the differences in the statistical tests comparing responders vs. non-responders. Our sample represents a higher socioeconomic class of IBD patients who may have a more healthy diet, and caution must be exercised using the results to compare dietary intakes in IBD patients from different social classes. Still, the sample size was rather large, and probably represents individuals from all socioeconomic classes. The dietary data from our sample should therefore be generalizable to other IBD populations.

5.2 Discussion of main findings

We recruited a total sample of 70 CD and 117 UC cases to our project, which was within the recruitment expectations of 50-100 CD and 100-150 UC cases. Except for alcohol consume in women, we found no statistically significant differences in macro- or micronutrient intake between UC and CD. Dietary intakes were mainly within recommended levels from the NNR12 and similar to intakes reported in Norkost 3. Men with CD consumed significantly more bread and meat compared to men with UC, while women with UC consumed significantly more vegetables and alcoholic beverages than women with CD. Intake of most FODMAP containing foods increased with higher FODMAP score. The main sources of FODMAPs were fruit/berries and vegetables, bread and cereals and dairy products.

The dietary intake of selected macro- and micronutrients in men and women in our study population was compared (not statistically) with reported intake from the Norkost 1997 and 3 surveys (101, 110). This was done to compare the intakes in an IBD population to the intake

in the general Norwegian population. Results from Norkost 1997 are perhaps more comparable, reconsidering the present FFQ is a revised version of the FFQ applied at that time. However, the former FFQ was an optical paper version which was more vulnerable to missing data. Furthermore, even though the collection method was different in Norkost 3 (using 24-hours recall), we considered this data to be more up to date. Comparing our results with studies performed in other countries makes interpretation challenging due to deviating dietary habits, available foods, food processing techniques and different agricultural conditions.

5.2.1 Macronutrients

Energy intake

Our study population reported a higher mean energy intake compared to men and women in Norkost 3 (mean difference -0.8 and -0.2 MJ, respectively), although we were not able to test this statistically. The slightly higher intake is likely not explained by age, because like in both Norkost 1997 and Norkost 3, the majority of our participants were between 30-59 years old (61%). From the NNR12, the estimated average energy requirements for this age interval are 11.0 and 8.8 MJ for men and women respectively (111). Results from the validation of the dietary FFQ showed that it underestimated intake of total energy (100), but we think our study population may underestimate less given their interest in nutrition (5.1.2 Internal validity, selection bias). Due to increased inflammation, which is likely at diagnosis, the dietary requirement of protein and possibly energy may be higher than normal (35). On the other hand, the estimated energy requirement from the NNR12 might be too high for this population because of reduced physical activity and strength in IBD patients leading to reduced energy expenditure (120-122).

The average BMI in our sample was 25.7 kg/m^2, which is above normal according to WHO standards (123). Five individuals had a BMI <18.5 kg/m^2, classified as underweight by the same standards. IBD patients have an increased risk of becoming malnourished (61, 91, 95), but BMI may not be the best predictor of risk (93). However, the measured average BMI in our sample could be explained by the load of overweight and obesity which is increasing in IBD patients parallel with the general population (124). Moreover, malnutrition may appear after years of disease. It is important to remember that malnutrition and micronutrient

deficiencies may arise regardless of BMI, and one should be cautious using BMI as a measure of nutritional status in these patients.

Carbohydrates

Percent energy from carbohydrates was below recommended range, and deviated from earlier reported intake in the Norwegian population (101). Carbohydrates were overestimated by the FFQ in the validation study (100), and we believe the intake of carbohydrates may be even lower in our study population. It may be explained by self-imposed dietary restrictions of carbohydrates. Living on a gluten-free diet to a more or less extent is quite normal in IBD patients, and many experience improvements from their gastrointestinal symptoms (125). Gluten and fructans often coexist in foods rich in grains and cereals (55). This might explain why patients with IBD experience less symptoms on a gluten-free diet. In patients thought to have non-coeliac gluten sensitivity, gluten and/or wheat provoking led to worsening of symptoms, but could not be attributed to gluten (126). The participants had been adhering to a diet low in FODMAPs for two weeks which reduced their symptoms significantly (126). A Norwegian intervention study found that fructans, and not gluten, induced symptoms in patients with non-coeliac gluten sensitivity (127).

Fiber

Among women, there was a trend of higher consumption of fiber in UC compared to CD. Women with UC had a higher intake of vegetables, and a trend towards higher intake of fruit and berries. It is possible that women with CD eat less fiber due to dietary guidelines which recommend patients with stricturing CD to be careful with foods like vegetables and fruit rich in insoluble fiber (35). This assumption was largely confirmed in a newly published study from Canada (73). They found that CD patients, and patients with stricturing disease particularly, restricted their diet more compared to patients with UC. Fiber-rich foods, including fruit and raw vegetables, were usually avoided and particularly during active disease (73). However, avoidance of fiber may lead to increased risk of exacerbated inflammation in patients with CD, and is suggestive also in UC (43, 128). In men, we found no difference in fiber intake. This may be due to the presumption that women are more engaged in dietary matters than men, as women with IBD participate in studies exploring diet more often than men (63, 74). In a large American cohort, UC patients reported a greater consumption of leafy- and non-leafy vegetables, tomatoes and fruit compared to CD patients

(74). Furthermore, both CD and UC patients restricted intake of fruit and vegetables while in active disease (74). Zallot et al. found that CD patients more often than UC patients perceived raw vegetables to be a risk of disease flares (63). In our study, fiber intake, particularly in women, was higher compared to reported intakes in Norkost 3. However, this could be due to over-reporting of vegetables in the dietary FFQ because lower intakes and avoidance of fiber is frequently reported in IBD patients (63, 129, 130).

Men with CD consumed more bread compared to men with UC. This result was a bit surprising, given that women with CD tend to eat less fiber than women with UC. Since CD patients generally restrict their diet more compared to UC (73), they may eat more meals containing bread. Furthermore, they may eat gluten-free bread which often contain less fiber than whole-meal bread (131).

Fat

In men with CD there was a trend of higher intake of SFA compared to UC. This may be due to higher intake of foods rich in saturated fats, for instance processed meat. Vagianos et al. found that IBD patients had a higher intake of sausages and bacon compared to controls (75). We found a significantly higher intake of meat in CD patients, but whether it could be attributed to a higher consumption of processed meat is unknown. However, Cohen et al. found that patients with UC consumed less processed meats compared to CD patients (74).

Alcohol

Daily alcohol intake was in line with dietary recommendations. Both men and women in the sample consumed less alcohol than reported intakes from Norkost 3, but the difference was greatest in women (110). Furthermore, women with CD consumed a significantly lower amount of alcoholic beverages compared to women with UC. Alcoholic beverages are frequently avoided by IBD patients (62, 73, 89) as they may increase the risk of flares (132, 133), and exacerbate functional gastrointestinal symptoms in inactive IBD (134).

5.2.2 Micronutrients

Iron

In men with CD, there was a trend of higher dietary intake of iron compared to men with UC. Furthermore, we found that meat consumption was higher in men with CD, in addition to a trend towards the same in women with CD. Cohen et al. found similar results, comparing intake of processed meats in a large group of UC and CD patients (74). A Canadian study reported the opposite, namely a lower intake of meat and poorer iron status in CD, but this study was performed several years ago (96). Furthermore, they proposed that blood loss, and not dietary intake, was a more important cause of iron deficiency (96).

In our study, intake of iron increased significantly with higher meat consumption. Women of reproductive age had a mean daily iron intake that was lower than recommended in the NNR12. Meat is an important source of heme-iron, which has greater bioavailability than vegetable non-heme iron (135). Thus, restriction of meat, which is reported in studies of dietary behavior in IBD patients (65, 74, 75), may be an important risk factor of iron deficiency anemia, particularly in women of reproductive age. We cannot conclude if a low meat consumption in CD leads to a poorer iron status because we have no biochemical results to support our data. However, in a study from Iceland, ferritin status was lower in patients who restricted their intake of meat (89).

A high meat consumption, especially of red and processed meats, is associated with an increased risk of relapse in UC patients (133). Tasson and her coworkers reported that a high meat consumption was associated with increased disease activity, but this effect disappeared in the adjusted risk analysis (136). However, they did not separate CD and UC patients, and CD was overrepresented. An increased risk of flares may be the reason of a lower intake of meat, and thus iron in UC patients of our sample. On the other hand, an excessive iron intake can increase inflammation both directly, and indirectly through promoting the growth of harmful bacteria and may enhance oxidative stress (44). Thus, iron status should be routinely measured and supplementation be in agreement with professional counseling, and only if deficiency is confirmed (35). Oral iron supplementation remain controversial due to research in mice showing that an iron-reduced diet prevented the development of chronic inflammation (137).

Vitamin D

The median vitamin D intake in our sample was below the recommended reference from NNR12, and only 29% had a dietary intake exceeding 10µg. A cross-sectional study performed in Iceland found a similar high prevalence of inadequate intake in addition to high prevalence of vitamin D deficiency in IBD patients (89). Vagianos and colleagues reported that 1/3 of patients with IBD had an inadequate intake, in addition to a positive correlation of intake with vitamin D status in CD patients in remission (96). Noteworthy, when we included the intake of vitamin D supplements in the analysis, 53% of our sample had an intake exceeding 10µg.

While our sample had a higher mean intake of vitamin D compared to men and women participating in Norkost 3, Portuguese patients with CD had a significantly lower intake of vitamin D compared to controls (138). Hence, we cannot exclude the possibility of over-estimated intake of vitamin D in our sample due to recall bias. On the other hand, the likely introduction of dietary changes before and shortly after diagnosis, may have led to an increased intake of vitamin D.

Beside vitamin D`s important function in bone health (1.4.1 Micronutrient deficiency), it may seem like vitamin D also serve a role in disease activity. Norwegian CD and UC patients with vitamin D deficiency had a higher disease activity as indicated by HBI and rate of relapses previous year in CD and calprotectin levels in UC (78). In a randomized, placebo-controlled Danish study, the relapse rate was lower in subjects receiving vitamin D supplements, although not significant (139). Furthermore, poor Vitamin D status was associated with more severe disease in a prospective observational study (140). Decreased inflammation was measured in UC patients with active disease after supplementation with vitamin D (141). Thus, it is important to monitor and consider to recommend a vitamin D supplement in IBD patients with a moderate dietary intake. In patients using systemic steroids, which is a risk factor of metabolic bone disease, supplements of both vitamin D and calcium are recommended (87). However, our data are inconclusive because we do not possess biochemical measurements to show whether a low dietary intake of vitamin D are indicative of deficiency or if use of supplements are indicative of an improved status.

Sunlight is an important source of vitamin D. In a Canadian study, they found depending on cut-off values, that participants recruited during fall/winter season had a higher prevalence of

vitamin D deficiency (96). Norwegians who live in northern latitudes may be less exposed to sunlight during winter. Thus, we should consider to recommend a vitamin D supplement in winter season.

Calcium

In our sample we found that the median dietary intake of calcium was sufficient according to recommended levels, and similar to intakes in Norkost 3. Previous studies have frequently reported avoidance of milk and dairy products in IBD patients, and its negative impact on calcium intake (89, 138). The calcium intake was lower than recommended by NNR12 in 33% of participants who had a daily dietary intake of milk equal to 0g. Prior to the study, we hypothesized that several IBD patients in Norway would restrict intake of milk and other lactose containing dairy products. Due to the highly improved availability of lactose restricted/free products in Norway, restriction and avoidance of milk and dairy may not be as widespread. However, in those individuals not consuming dairy products, a calcium supplement may be required.

Folate and vitamin C

In our study, the intake of folate and vitamin C was above recommended level, except for folate intake in women of reproductive age. However, we did not have specific questions regarding folate supplements. Thus, the actual intake may be higher than presented for this age group. Intakes exceeded that of men and women in Norkost 3, especially of folate. The high reported intake in our study may be explained by overestimation of vegetable and berry consumption in the dietary FFQ (5.1.2 Internal validity). Due to avoidance of vegetables (5.2.2 Micronutrients, fiber), we were expecting a dietary intake of folate inferior of the general population. A suboptimal intake of folate, which is stored in small amounts by the body and depend on continuously refill, is probably the main risk of developing deficiency (96). Folate deficiency is common in individuals with IBD, in CD particularly (142), and macrocytic megaloblastic anemia may develop as a consequence (76). In Norway we do not fortify cereals and grain products like some other countries, for instance the United States. Thus, the Norwegian population, and IBD patients in particular, could be at higher risk of folate deficiency.

Sodium

In men with CD, there was a trend of higher sodium intake compared to men with UC. Furthermore, the median intakes in both UC and CD patients of both genders were above recommended level (111). In murine models, a diet rich in salt leads to increased experimental colitis through enhanced pro-inflammatory cytokine production (31, 32). This warrants for further research. Meanwhile, we may safely advice IBD patients to be cautious with dietary salt due to its blood pressure increasing effect leading to an increased risk of cardiovascular disease (143).

Micronutrient intake in relation to Norwegian recommendations and Norkost

Both sexes had an inadequate intake of vitamin D, and intake of iron and folate were lower than recommended for women of reproductive age (n=80). Compared to the sample in Norkost 3 representing the general Norwegian population, the mean intakes were higher for nearly all micronutrients in our sample of IBD patients. This could be a genuine diagnose specific difference because IBD patients are more aware of their diet and may try to eat healthier. However, it could also be explained by the different dietary collection methods or simply by chance. Our subjects were exposed to recall bias, which may have affected our results. Furthermore, the results are presented without the contribution of supplements. Thus, the intake may be even higher, at least for some individuals. Some supplements, for instance substitution of folate during pregnancy, were not taken into consideration by the FFQ. Consequently, the intake of some micronutrients may be incorrectly low.

The reference values of micronutrient intake in NNR12 are suitable to assess dietary intakes on group level. Individuals with intakes below references could be at risk of deficiency. Albeit, we cannot know for certain whether an intake below the average requirement lead to deficiency or if intakes exceeding the average requirement are sufficient to avoid deficiency. Clinical and biochemical data are necessary to rule out if a suspected deficiency exist or not (111). Depending on several factors (1.4.1 Micronutrient deficiency), the requirement of different compounds may be enhanced in IBD patients, and reference values presented from the NNR12 may not cover their dietary needs.

Even though the overall intake of micronutrients in our study sample seems to be more adequate than we might expected, the intake may change with time. As a consequence of the disease and dietary restriction behavior, differences in intake of micronutrients between UC,

CD and the general population may be more prominent with time. In many studies exploring dietary intakes and risk of malnutrition, they find that restriction/avoidance of certain dietary components and loss of appetite are implicated (61, 62, 90, 138). Loss of appetite in active disease was explained by reduced levels of ghrelin in a newly published study (144). Experiencing several flares and gradually breakdown of the body over years living with a chronic disease can affect both motivation and the effort of eating healthy. In addition, people with IBD are pelted with well-intentioned dietary advices from friends, family as well as health professionals. For all of the reasons listed above it is of great importance that IBD patients are regularly screened for malnutrition and micronutrient deficiencies so that patients at risk can be offered proper advice from a dietitian. Further, we do not know to what extent the dietary compounds where actually utilized by each individual. Malabsorption of various nutrients are common depending on disease location, previous resections and current disease activity (76). The dietary requirements of several nutrients might be enhanced due to increased losses, drug interactions or increased energy expenditure (76).

Dose-response studies of micronutrients often have a U-shaped curve, in which a low intake pose a risk of deficiency and a high intake pose a risk of toxicity (145). Hence, supplements should not be routinely recommended, but rather be according to dietary advice provided by health professionals, preferably a dietitian. A consequence of taking numerous dietary supplements are that many contain the same compounds leading to an excessive total intake of some nutrients. Furthermore, some micronutrients, e.g. iron, may have a negative impact, and should be recommended with caution and only in established deficiency.

5.2.3 FODMAP score

The intake of different foods known to contain FODMAPs successfully increased with higher FODMAP score, indicating that the design of the FODMAP score was satisfying. This was true for all of the main categories which contributed mostly to the total FODMAP score, except for vegetables. Indeed, the intake of vegetables increased with higher FODMAP score, but the difference was not significant. Vegetables comprise a large group of different foods, which contains various amounts of FODMAPs. Hence, if we divided vegetables into groups for their FODMAP content, we may have found a statistical significant difference.

5.2.4 FODMAP and self-reported disease activity

In our study we explored if the FODMAP score increased with a higher self-reported disease activity, but we found no such relation. For CD, this may be explained by the calculation of HBI which included the addition of self-reported stool frequency the previous day. From the commentary field, it seemed like many patients answered this question on the day before endoscopy. Accordingly, many would have taken laxatives to empty their intestines preparing for the examination. Thus, the stool frequency may be incorrectly high compared to the normal situation. In the PMS for UC, this problem was avoided because stool frequency was subdivided into sequences with scores from 0-3. Like we discussed earlier, (5.1.2 Internal validity), HBI and PMS include factors on symptoms that may be attributed to functional gastrointestinal symptoms as well as factors related to the inflammatory process.

A growing body of evidence indicate that a low FODMAP diet decreases functional gastrointestinal symptoms in patients with IBS and IBD (1.2.2 Dietary management of IBD). However, its influence on disease activity is largely unknown. In a Danish study IBD-patients reported a more indolent disease course after dietary treatment with a low FODMAP diet (48). On the contrary, in a case-control study comparing active and inactive CD patients and controls, the different factors of the HBI increased with lower intakes of fructans (146). The authors discussed if this result could be explained by the assumption that patients with active disease avoid more foods, and that symptoms may be caused by other food components (146).

There are concerns about the long-term effects of FODMAP lowering diets because it affects the microbial environment of the intestines (147). The initial strict avoidance of all FODMAP rich foods are supposed to be accompanied by subsequent reintroduction to avoid too many restrictions that may increase the risk of malnutrition (148). In a follow-up study only 16% of the sample continued on a strict low FODMAP, while 84% followed advice on reintroduction of foods (48). Wheat, dairy products and onions were most commonly not reintroduced (48). One long-term study of low FODMAP diet in IBS patients found that the dietary intake was satisfying (149). Patients that report to follow a low FODMAP diet should receive proper information to avoid unnecessary dietary restrictions.

6 Conclusion

The resulted dietary intakes were in high agreement with recommendations in NNR12, except for some macro- and micronutrients. Deficiency of vitamin D, folate and iron seems to be common in IBD patients, and should probably be routinely monitored and corrected if deficiencies exist.

We found few differences in dietary intakes of macro- and micronutrients between UC and CD patients, except for alcohol in women. Differences in dietary restriction behavior may explain the differences in dietary intake of certain foods between CD and UC. Due to a more extensive restriction behavior in CD patients, more distinct differences between the two entities may develop with time. To increase the knowledge of foods which can replace the avoided items and thus prevent the development of deficiencies, patients with CD and UC should be counselled by a dietitian.

The efficacy of the FODMAP score was satisfying. It may be used in future studies to explore associations with symptoms and disease activity in IBD. We found no associations between the FODMAP score and self-reported disease activity. Future studies should use other or multiple outcome measures to explore FODMAP intake in relation to disease activity.

7 References

1. Sjoberg D, Holmstrom T, Larsson M, Nielsen AL, Holmquist L, Ekbom A, et al. Incidence and clinical course of Crohn's disease during the first year - results from the IBD Cohort of the Uppsala Region (ICURE) of Sweden 2005-2009. Journal of Crohn's & colitis. 2014;8(3):215-22.
2. Sjoberg D, Holmstrom T, Larsson M, Nielsen AL, Holmquist L, Ekbom A, et al. Incidence and natural history of ulcerative colitis in the Uppsala Region of Sweden 2005-2009 - results from the IBD cohort of the Uppsala Region (ICURE). Journal of Crohn's & colitis. 2013;7(9):e351-7.
3. Moum B, Vatn MH, Ekbom A, Aadland E, Fausa O, Lygren I, et al. Incidence of Ulcerative Colitis and Indeterminate Colitis in Four Counties of Southeastern Norway, 1990–93 A Prospective Population-Based Study. Scandinavian journal of gastroenterology. 1996;31(4):362-6.
4. Moum B, Vatn MH, Ekbom A, Aadland E, Fausa O, Lygren I, et al. Incidence of Crohn's Disease in Four Counties in Southeastern Norway, 1990–93 A Prospective Population-Based Study. Scandinavian journal of gastroenterology. 1996;31(4):355-61.
5. Gomollon F, Dignass A, Annese V, Tilg H, Van Assche G, Lindsay JO, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management. Journal of Crohn's & colitis. 2017;11(1):3-25.
6. Magro F, Gionchetti P, Eliakim R, Ardizzone S, Armuzzi A, Barreiro-de Acosta M, et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 1: Definitions, Diagnosis, Extra-intestinal Manifestations, Pregnancy, Cancer Surveillance, Surgery, and Ileo-anal Pouch Disorders. Journal of Crohn's & colitis. 2017;11(6):649-70.
7. Roseth AG, Fagerhol MK, Aadland E, Schjonsby H. Assessment of the neutrophil dominating protein calprotectin in feces. A methodologic study. Scandinavian journal of gastroenterology. 1992;27(9):793-8.
8. Fagerhol MK. Calprotectin, a faecal marker of organic gastrointestinal abnormality. The Lancet. 2000;356(9244):1783-4.
9. Solberg IC, Lygren I, Jahnsen J, Aadland E, Hoie O, Cvancarova M, et al. Clinical course during the first 10 years of ulcerative colitis: results from a population-based inception cohort (IBSEN Study). Scandinavian journal of gastroenterology. 2009;44(4):431-40.
10. Solberg IC, Vatn MH, Hoie O, Stray N, Sauar J, Jahnsen J, et al. Clinical course in Crohn's disease: results of a Norwegian population-based ten-year follow-up study. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2007;5(12):1430-8.
11. Shi HY, Levy AN, Trivedi HD, Chan FKL, Ng SC, Ananthakrishnan AN. Ethnicity Influences Phenotype and Outcomes in Inflammatory Bowel Disease: A Systematic Review and Meta-analysis of Population-based Studies. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2018;16(2):190-7.e11.
12. Hugot JP, Chamaillard M, Zouali H, Lesage S, Cezard JP, Belaiche J, et al. Association of NOD2 leucine-rich repeat variants with susceptibility to Crohn's disease. Nature. 2001;411(6837):599-603.
13. Jostins L, Ripke S, Weersma RK, Duerr RH, McGovern DP, Hui KY, et al. Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. Nature. 2012;491(7422):119-24.

14. Higuchi LM, Khalili H, Chan AT, Richter JM, Bousvaros A, Fuchs CS. A prospective study of cigarette smoking and the risk of inflammatory bowel disease in women. The American journal of gastroenterology. 2012;107(9):1399-406.
15. Ananthakrishnan AN. Epidemiology and risk factors for IBD. Nature reviews Gastroenterology & hepatology. 2015;12(4):205-17.
16. Burisch J, Pedersen N, Cukovic-Cavka S, Brinar M, Kaimakliotis I, Duricova D, et al. East-West gradient in the incidence of inflammatory bowel disease in Europe: the ECCO-EpiCom inception cohort. Gut. 2014;63(4):588-97.
17. Damas OM, Avalos DJ, Palacio AM, Gomez L, Quintero MA, Deshpande AR, et al. Inflammatory bowel disease is presenting sooner after immigration in more recent US immigrants from Cuba. Alimentary pharmacology & therapeutics. 2017;46(3):303-9.
18. Benchimol EI, Mack DR, Guttmann A, Nguyen GC, To T, Mojaverian N, et al. Inflammatory bowel disease in immigrants to Canada and their children: a population-based cohort study. The American journal of gastroenterology. 2015;110(4):553-63.
19. Li X, Sundquist J, Hemminki K, Sundquist K. Risk of inflammatory bowel disease in first- and second-generation immigrants in Sweden: a nationwide follow-up study. Inflammatory bowel diseases. 2011;17(8):1784-91.
20. Barreiro-de Acosta M, Alvarez Castro A, Souto R, Iglesias M, Lorenzo A, Dominguez-Munoz JE. Emigration to western industrialized countries: A risk factor for developing inflammatory bowel disease. Journal of Crohn's & colitis. 2011;5(6):566-9.
21. Duricova D, Burisch J, Jess T, Gower-Rousseau C, Lakatos PL. Age-related differences in presentation and course of inflammatory bowel disease: an update on the population-based literature☆. Journal of Crohn's and Colitis. 2014;8(11):1351-61.
22. Ng SC, Bernstein CN, Vatn MH, Lakatos PL, Loftus EV, Jr., Tysk C, et al. Geographical variability and environmental risk factors in inflammatory bowel disease. Gut. 2013;62(4):630-49.
23. Molodecky NA, Soon IS, Rabi DM, Ghali WA, Ferris M, Chernoff G, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology. 2012;142(1):46-54.e42; quiz e30.
24. Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. Lancet (London, England). 2017.
25. Ng SC, Tang W, Ching JY, Wong M, Chow CM, Hui AJ, et al. Incidence and phenotype of inflammatory bowel disease based on results from the Asia-pacific Crohn's and colitis epidemiology study. Gastroenterology. 2013;145(1):158-65.e2.
26. Kristensen V, Opheim R, Ricanek P, Huppertz-Hauss G, Perminow G, Detlie T, et al. P816 IBSEN III—a new population-based inception cohort from South-Eastern Norway2018. S526-S7 p.
27. Burisch J, Jess T, Martinato M, Lakatos PL. The burden of inflammatory bowel disease in Europe. Journal of Crohn's & colitis. 2013;7(4):322-37.
28. Hou JK, Abraham B, El-Serag H. Dietary intake and risk of developing inflammatory bowel disease: a systematic review of the literature. The American journal of gastroenterology. 2011;106(4):563-73.

29. Statovci D, Aguilera M, MacSharry J, Melgar S. The Impact of Western Diet and Nutrients on the Microbiota and Immune Response at Mucosal Interfaces. Frontiers in immunology. 2017;8:838.
30. Lewis JD, Abreu MT. Diet as a Trigger or Therapy for Inflammatory Bowel Diseases. Gastroenterology. 2017;152(2):398-414.e6.
31. Monteleone I, Marafini I, Dinallo V, Di Fusco D, Troncone E, Zorzi F, et al. Sodium chloride-enriched Diet Enhanced Inflammatory Cytokine Production and Exacerbated Experimental Colitis in Mice. Journal of Crohn's & colitis. 2017;11(2):237-45.
32. Tubbs AL, Liu B, Rogers TD, Sartor RB, Miao EA. Dietary Salt Exacerbates Experimental Colitis. Journal of immunology (Baltimore, Md : 1950). 2017;199(3):1051-9.
33. Chassaing B, Koren O, Goodrich JK, Poole AC, Srinivasan S, Ley RE, et al. Dietary emulsifiers impact the mouse gut microbiota promoting colitis and metabolic syndrome. Nature. 2015;519(7541):92-6.
34. Ananthakrishnan AN, Khalili H, Konijeti GG, Higuchi LM, de Silva P, Korzenik JR, et al. A prospective study of long-term intake of dietary fiber and risk of Crohn's disease and ulcerative colitis. Gastroenterology. 2013;145(5):970-7.
35. Forbes A, Escher J, Hébuterne X, Kłęk S, Krznaric Z, Schneider S, et al. ESPEN guideline: Clinical nutrition in inflammatory bowel disease. Clinical Nutrition. 2017;36(2):321-47.
36. Machiels K, Joossens M, Sabino J, De Preter V, Arijs I, Eeckhaut V, et al. A decrease of the butyrate-producing species Roseburia hominis and Faecalibacterium prausnitzii defines dysbiosis in patients with ulcerative colitis. Gut. 2014;63(8):1275-83.
37. Tamboli CP, Neut C, Desreumaux P, Colombel JF. Dysbiosis in inflammatory bowel disease. Gut. 2004;53(1):1-4.
38. David LA, Maurice CF, Carmody RN, Gootenberg DB, Button JE, Wolfe BE, et al. Diet rapidly and reproducibly alters the human gut microbiome. Nature. 2014;505(7484):559-63.
39. Swaminath A, Feathers A, Ananthakrishnan AN, Falzon L, Li Ferry S. Systematic review with meta-analysis: enteral nutrition therapy for the induction of remission in paediatric Crohn's disease. Alimentary pharmacology & therapeutics. 2017;46(7):645-56.
40. Ruemmele FM, Veres G, Kolho KL, Griffiths A, Levine A, Escher JC, et al. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. Journal of Crohn's & colitis. 2014;8(10):1179-207.
41. O'Morain C, Segal AW, Levi AJ. Elemental diet as primary treatment of acute Crohn's disease: a controlled trial. British medical journal (Clinical research ed). 1984;288(6434):1859-62.
42. Zachos M, Tondeur M, Griffiths AM. Enteral nutritional therapy for induction of remission in Crohn's disease. The Cochrane database of systematic reviews. 2007(1):Cd000542.
43. Harbord M, Eliakim R, Bettenworth D, Karmiris K, Katsanos K, Kopylov U, et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 2: Current Management. Journal of Crohn's & colitis. 2017;11(7):769-84.
44. Lee D, Albenberg L, Compher C, Baldassano R, Piccoli D, Lewis JD, et al. Diet in the pathogenesis and treatment of inflammatory bowel diseases. Gastroenterology. 2015;148(6):1087-106.

45. Yoon SR, Lee JH, Lee JH, Na GY, Lee KH, Lee YB, et al. Low-FODMAP formula improves diarrhea and nutritional status in hospitalized patients receiving enteral nutrition: a randomized, multicenter, double-blind clinical trial. Nutrition journal. 2015;14:116.
46. Cox SR, Prince AC, Myers CE, Irving PM, Lindsay JO, Lomer MC, et al. Fermentable carbohydrates (FODMAPs) exacerbate functional gastrointestinal symptoms in patients with inflammatory bowel disease: a randomised, double-blind, placebo-controlled, cross-over, re-challenge trial. Journal of Crohn's & colitis. 2017.
47. Gearry RB, Irving PM, Barrett JS, Nathan DM, Shepherd SJ, Gibson PR. Reduction of dietary poorly absorbed short-chain carbohydrates (FODMAPs) improves abdominal symptoms in patients with inflammatory bowel disease-a pilot study. Journal of Crohn's & colitis. 2009;3(1):8-14.
48. Maagaard L, Ankersen DV, Vegh Z, Burisch J, Jensen L, Pedersen N, et al. Follow-up of patients with functional bowel symptoms treated with a low FODMAP diet. World journal of gastroenterology. 2016;22(15):4009-19.
49. Halmos EP, Christophersen CT, Bird AR, Shepherd SJ, Muir JG, Gibson PR. Consistent Prebiotic Effect on Gut Microbiota With Altered FODMAP Intake in Patients with Crohn's Disease: A Randomised, Controlled Cross-Over Trial of Well-Defined Diets. Clinical and translational gastroenterology. 2016;7:e164.
50. Prince AC, Myers CE, Joyce T, Irving P, Lomer M, Whelan K. Fermentable Carbohydrate Restriction (Low FODMAP Diet) in Clinical Practice Improves Functional Gastrointestinal Symptoms in Patients with Inflammatory Bowel Disease. Inflammatory bowel diseases. 2016;22(5):1129-36.
51. Pedersen N, Ankersen DV, Felding M, Wachmann H, Vegh Z, Molzen L, et al. Low-FODMAP diet reduces irritable bowel symptoms in patients with inflammatory bowel disease. World journal of gastroenterology. 2017;23(18):3356-66.
52. Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. The Journal of nutrition. 1995;125(6):1401-12.
53. Gibson GR, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. Nature reviews Gastroenterology & hepatology. 2017;14(8):491-502.
54. Gibson PR, Shepherd SJ. Personal view: food for thought--western lifestyle and susceptibility to Crohn's disease. The FODMAP hypothesis. Alimentary pharmacology & therapeutics. 2005;21(12):1399-409.
55. Varney J, Barrett J, Scarlata K, Catsos P, Gibson PR, Muir JG. FODMAPs: food composition, defining cutoff values and international application. J Gastroenterol Hepatol. 2017;32 Suppl 1:53-61.
56. Gibson PR. History of the low FODMAP diet. Journal of Gastroenterology and Hepatology. 2017;32:5-7.
57. Schumann D, Klose P, Lauche R, Dobos G, Langhorst J, Cramer H. Low fermentable, oligo-, di-, mono-saccharides and polyol diet in the treatment of irritable bowel syndrome: A systematic review and meta-analysis. Nutrition (Burbank, Los Angeles County, Calif). 2018;45:24-31.
58. Halpin SJ, Ford AC. Prevalence of symptoms meeting criteria for irritable bowel syndrome in inflammatory bowel disease: systematic review and meta-analysis. The American journal of gastroenterology. 2012;107(10):1474-82.

59. Komperod MJ, Sommer C, Mellin-Olsen T, Iversen PO, Roseth AG, Valeur J. Persistent symptoms in patients with Crohn's disease in remission: An exploratory study on the role of diet. Scandinavian journal of gastroenterology. 2017:1-6.
60. Benjamin JL, Hedin CR, Koutsoumpas A, Ng SC, McCarthy NE, Hart AL, et al. Randomised, double-blind, placebo-controlled trial of fructo-oligosaccharides in active Crohn's disease. Gut. 2011;60(7):923-9.
61. Casanova MJ, Chaparro M, Molina B, Merino O, Batanero R, Duenas-Sadornil C, et al. Prevalence of Malnutrition and Nutritional Characteristics of Patients With Inflammatory Bowel Disease. Journal of Crohn's & colitis. 2017.
62. Limdi JK, Aggarwal D, McLaughlin JT. Dietary Practices and Beliefs in Patients with Inflammatory Bowel Disease. Inflammatory bowel diseases. 2016;22(1):164-70.
63. Zallot C, Quilliot D, Chevaux JB, Peyrin-Biroulet C, Gueant-Rodriguez RM, Freling E, et al. Dietary beliefs and behavior among inflammatory bowel disease patients. Inflammatory bowel diseases. 2013;19(1):66-72.
64. Holt DQ, Strauss BJ, Moore GT. Patients with inflammatory bowel disease and their treating clinicians have different views regarding diet. Journal of human nutrition and dietetics : the official journal of the British Dietetic Association. 2017;30(1):66-72.
65. Kinsey L, Burden S. A survey of people with inflammatory bowel disease to investigate their views of food and nutritional issues. European journal of clinical nutrition. 2016;70(7):852-4.
66. Tinsley A, Ehrlich OG, Hwang C, Issokson K, Zapala S, Weaver A, et al. Knowledge, Attitudes, and Beliefs Regarding the Role of Nutrition in IBD Among Patients and Providers. Inflammatory bowel diseases. 2016;22(10):2474-81.
67. Triggs CM, Munday K, Hu R, Fraser AG, Gearry RB, Barclay ML, et al. Dietary factors in chronic inflammation: food tolerances and intolerances of a New Zealand Caucasian Crohn's disease population. Mutation research. 2010;690(1-2):123-38.
68. Skrautvol K, Naden D. Nutrition as long-term care as experienced by persons living with inflammatory bowel disease: a qualitative study. Holistic nursing practice. 2015;29(1):22-32.
69. Maconi G, Ardizzone S, Cucino C, Bezzio C, Russo AG, Bianchi Porro G. Pre-illness changes in dietary habits and diet as a risk factor for inflammatory bowel disease: a case-control study. World journal of gastroenterology. 2010;16(34):4297-304.
70. Knowles SR, Graff LA, Wilding H, Hewitt C, Keefer L, Mikocka-Walus A. Quality of Life in Inflammatory Bowel Disease: A Systematic Review and Meta-analyses-Part I. Inflammatory bowel diseases. 2018;24(4):742-51.
71. Naliboff BD, Kim SE, Bolus R, Bernstein CN, Mayer EA, Chang L. Gastrointestinal and psychological mediators of health-related quality of life in IBS and IBD: a structural equation modeling analysis. The American journal of gastroenterology. 2012;107(3):451-9.
72. Prince A, Whelan K, Moosa A, Lomer MC, Reidlinger DP. Nutritional problems in inflammatory bowel disease: the patient perspective. Journal of Crohn's & colitis. 2011;5(5):443-50.
73. Bergeron F, Bouin M, D'Aoust L, Lemoyne M, Presse N. Food avoidance in patients with inflammatory bowel disease: What, when and who? Clinical nutrition (Edinburgh, Scotland). 2017.

74. Cohen AB, Lee D, Long MD, Kappelman MD, Martin CF, Sandler RS, et al. Dietary patterns and self-reported associations of diet with symptoms of inflammatory bowel disease. Digestive diseases and sciences. 2013;58(5):1322-8.
75. Vagianos K, Clara I, Carr R, Graff LA, Walker JR, Targownik LE, et al. What Are Adults With Inflammatory Bowel Disease (IBD) Eating? A Closer Look at the Dietary Habits of a Population-Based Canadian IBD Cohort. JPEN Journal of parenteral and enteral nutrition. 2016;40(3):405-11.
76. Hwang C, Ross V, Mahadevan U. Micronutrient deficiencies in inflammatory bowel disease: from A to zinc. Inflammatory bowel diseases. 2012;18(10):1961-81.
77. Gonzalez Alayon C, Pedrajas Crespo C, Marin Pedrosa S, Benitez JM, Iglesias Flores E, Salgueiro Rodriguez I, et al. Prevalence of iron deficiency without anaemia in inflammatory bowel disease and impact on health-related quality of life. Gastroenterologia y hepatologia. 2017.
78. Frigstad SO, Hoivik M, Jahnsen J, Dahl SR, Cvancarova M, Grimstad T, et al. Vitamin D deficiency in inflammatory bowel disease: prevalence and predictors in a Norwegian outpatient population. Scandinavian journal of gastroenterology. 2017;52(1):100-6.
79. Mouli VP, Ananthakrishnan AN. Review article: vitamin D and inflammatory bowel diseases. Alimentary pharmacology & therapeutics. 2014;39(2):125-36.
80. Galland L. Magnesium and inflammatory bowel disease. Magnesium. 1988;7(2):78-83.
81. Filmann N, Rey J, Schneeweiss S, Ardizzone S, Bager P, Bergamaschi G, et al. Prevalence of anemia in inflammatory bowel diseases in european countries: a systematic review and individual patient data meta-analysis. Inflammatory bowel diseases. 2014;20(5):936-45.
82. Hoivik ML, Reinisch W, Cvancarova M, Moum B. Anaemia in inflammatory bowel disease: a population-based 10-year follow-up. Alimentary pharmacology & therapeutics. 2014;39(1):69-76.
83. Gasche C, Lomer MC, Cavill I, Weiss G. Iron, anaemia, and inflammatory bowel diseases. Gut. 2004;53(8):1190-7.
84. Martinelli M, Strisciuglio C, Alessandrella A, Rossi F, Auricchio R, Campostrini N, et al. Serum Hepcidin and Iron Absorption in Paediatric Inflammatory Bowel Disease. Journal of Crohn's & colitis. 2016;10(5):566-74.
85. Semrin G, Fishman DS, Bousvaros A, Zholudev A, Saunders AC, Correia CE, et al. Impaired intestinal iron absorption in Crohn's disease correlates with disease activity and markers of inflammation. Inflammatory bowel diseases. 2006;12(12):1101-6.
86. Headstrom PD, Rulyak SJ, Lee SD. Prevalence of and risk factors for vitamin B(12) deficiency in patients with Crohn's disease. Inflammatory bowel diseases. 2008;14(2):217-23.
87. Harbord M, Annese V, Vavricka SR, Allez M, Barreiro-de Acosta M, Boberg KM, et al. The First European Evidence-based Consensus on Extra-intestinal Manifestations in Inflammatory Bowel Disease. Journal of Crohn's & colitis. 2016;10(3):239-54.
88. Sadeghian M, Saneei P, Siassi F, Esmaillzadeh A. Vitamin D status in relation to Crohn's disease: Meta-analysis of observational studies. Nutrition (Burbank, Los Angeles County, Calif). 2016;32(5):505-14.
89. Vidarsdottir JB, Johannsdottir SE, Thorsdottir I, Bjornsson E, Ramel A. A cross-sectional study on nutrient intake and -status in inflammatory bowel disease patients. Nutrition journal. 2016;15(1):61.

90. Lim HS, Kim SK, Hong SJ. Food Elimination Diet and Nutritional Deficiency in Patients with Inflammatory Bowel Disease. Clinical nutrition research. 2018;7(1):48-55.
91. Gheorghe C, Pascu O, Iacob R, Vadan R, Iacob S, Goldis A, et al. Nutritional risk screening and prevalence of malnutrition on admission to gastroenterology departments: a multicentric study. Chirurgia (Bucharest, Romania : 1990). 2013;108(4):535-41.
92. Mijac DD, Jankovic GL, Jorga J, Krstic MN. Nutritional status in patients with active inflammatory bowel disease: prevalence of malnutrition and methods for routine nutritional assessment. European journal of internal medicine. 2010;21(4):315-9.
93. Rocha R, Santana GO, Almeida N, Lyra AC. Analysis of fat and muscle mass in patients with inflammatory bowel disease during remission and active phase. The British journal of nutrition. 2009;101(5):676-9.
94. Valentini L, Schaper L, Buning C, Hengstermann S, Koernicke T, Tillinger W, et al. Malnutrition and impaired muscle strength in patients with Crohn's disease and ulcerative colitis in remission. Nutrition (Burbank, Los Angeles County, Calif). 2008;24(7-8):694-702.
95. Nguyen GC, Munsell M, Harris ML. Nationwide prevalence and prognostic significance of clinically diagnosable protein-calorie malnutrition in hospitalized inflammatory bowel disease patients. Inflammatory bowel diseases. 2008;14(8):1105-11.
96. Vagianos K, Bector S, McConnell J, Bernstein CN. Nutrition assessment of patients with inflammatory bowel disease. JPEN Journal of parenteral and enteral nutrition. 2007;31(4):311-9.
97. The Norwegian government. Helse Sør-Øst [cited 2018 19/01]. Available from: https://www.regjeringen.no/no/dep/hod/org/etater-og-virksomheter-under-helse--og-omsorgsdepartementet/tilknyttede-virksomheter/helse-sor-ost/id485242/.
98. Høivik LM. Inflammatory Bowel Disease in South Eastern Norway (IBSENIII) 2016 [updated 2017 19/9; cited 2017 24/10]. Available from: https://clinicaltrials.gov/ct2/show/NCT02727959?term=IBSEN+III&rank=1.
99. Lennard-Jones JE. Classification of inflammatory bowel disease. Scandinavian journal of gastroenterology Supplement. 1989;170:2-6; discussion 16-9.
100. Carlsen MH, Lillegaard IT, Karlsen A, Blomhoff R, Drevon CA, Andersen LF. Evaluation of energy and dietary intake estimates from a food frequency questionnaire using independent energy expenditure measurement and weighed food records. Nutrition journal. 2010;9:37.
101. Statens råd for ernæring og fysisk aktivitet. Norkost 1997: Landsomfattende kostholdsundersøkelse blant menn og kvinner i alderen 16-79 år.; 1999.
102. Muir JG, Rose R, Rosella O, Liels K, Barrett JS, Shepherd SJ, et al. Measurement of short-chain carbohydrates in common Australian vegetables and fruits by high-performance liquid chromatography (HPLC). Journal of agricultural and food chemistry. 2009;57(2):554-65.
103. Muir JG, Shepherd SJ, Rosella O, Rose R, Barrett JS, Gibson PR. Fructan and free fructose content of common Australian vegetables and fruit. Journal of agricultural and food chemistry. 2007;55(16):6619-27.
104. Biesiekierski JR, Rosella O, Rose R, Liels K, Barrett JS, Shepherd SJ, et al. Quantification of fructans, galacto-oligosacharides and other short-chain carbohydrates in processed grains and cereals. Journal of human nutrition and dietetics : the official journal of the British Dietetic Association. 2011;24(2):154-76.

105. Tine. Laktoseinnhold i noen utvalgte TINE produkter 2017 [updated 2017 01/10; cited 2018 22/03]. Available from: https://www.tine.no/helse/sunt-kosthold/artikler/_attachment/398569?_ts=15a7009989f.
106. Q-meieriene. Laktoseinnholdet i Q-produkter 2016 [updated 2016 01/10; cited 2018 22/03]. Available from: https://www.q-meieriene.no/Nyheter/Laktoseinnholdet-i-Qprodukter.
107. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. The New England journal of medicine. 1987;317(26):1625-9.
108. Lewis JD, Chuai S, Nessel L, Lichtenstein GR, Aberra FN, Ellenberg JH. Use of the noninvasive components of the Mayo score to assess clinical response in ulcerative colitis. Inflammatory bowel diseases. 2008;14(12):1660-6.
109. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet (London, England). 1980;1(8167):514.
110. Helsedirektoratet. Norkost 3 en landsomfattende kostholdsundersokelse blant menn og kvinner i norge i alderen 18-70-år 2010-11. 2012.
111. Nordic Council of Ministers. Nordic Nutrition Recommendations 2012 2014 [cited 2018 03/04].
112. WHO. Infertility definitions and terminology [cited 2018 11/04]. Available from: http://www.who.int/reproductivehealth/topics/infertility/definitions/en/.
113. Laake P, Hjartaaker A, Thelle DS, Veieroed MB. Epidemiologiske og kliniske forskningsmetoder: Gyldendal Norsk Forlag AS; 2007.
114. Kirkwood RB, Sterne JAC. Medical Statistics. 2. ed: Blackwell Science Ltd; 2003.
115. Dahl E, Bergsli H, Van der Wel AK. Sosial ulikhet i helse: En norsk kunnskapsoversikt. 2014.
116. Biro G, Hulshof KF, Ovesen L, Amorim Cruz JA. Selection of methodology to assess food intake. European journal of clinical nutrition. 2002;56 Suppl 2:S25-32.
117. Lee DW, Koo JS, Choe JW, Suh SJ, Kim SY, Hyun JJ, et al. Diagnostic delay in inflammatory bowel disease increases the risk of intestinal surgery. World journal of gastroenterology. 2017;23(35):6474-81.
118. Nguyen VQ, Jiang D, Hoffman SN, Guntaka S, Mays JL, Wang A, et al. Impact of Diagnostic Delay and Associated Factors on Clinical Outcomes in a U.S. Inflammatory Bowel Disease Cohort. Inflammatory bowel diseases. 2017;23(10):1825-31.
119. Romberg-Camps MJ, Hesselink-van de Kruijs MA, Schouten LJ, Dagnelie PC, Limonard CB, Kester AD, et al. Inflammatory Bowel Disease in South Limburg (the Netherlands) 1991-2002: Incidence, diagnostic delay, and seasonal variations in onset of symptoms. Journal of Crohn's & colitis. 2009;3(2):115-24.
120. Werkstetter KJ, Ullrich J, Schatz SB, Prell C, Koletzko B, Koletzko S. Lean body mass, physical activity and quality of life in paediatric patients with inflammatory bowel disease and in healthy controls. Journal of Crohn's & colitis. 2012;6(6):665-73.
121. Zaltman C, Braulio VB, Outeiral R, Nunes T, de Castro CL. Lower extremity mobility limitation and impaired muscle function in women with ulcerative colitis. Journal of Crohn's & colitis. 2014;8(6):529-35.
122. Tew GA, Jones K, Mikocka-Walus A. Physical Activity Habits, Limitations, and Predictors in People with Inflammatory Bowel Disease: A Large Cross-sectional Online Survey. Inflammatory bowel diseases. 2016;22(12):2933-42.

123. WHO. Body mass index - BMI [cited 2018 09/04]. Available from: http://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi.
124. Singh S, Dulai PS, Zarrinpar A, Ramamoorthy S, Sandborn WJ. Obesity in IBD: epidemiology, pathogenesis, disease course and treatment outcomes. Nature reviews Gastroenterology & hepatology. 2017;14(2):110-21.
125. Herfarth HH, Martin CF, Sandler RS, Kappelman MD, Long MD. Prevalence of a gluten-free diet and improvement of clinical symptoms in patients with inflammatory bowel diseases. Inflammatory bowel diseases. 2014;20(7):1194-7.
126. Biesiekierski JR, Peters SL, Newnham ED, Rosella O, Muir JG, Gibson PR. No effects of gluten in patients with self-reported non-celiac gluten sensitivity after dietary reduction of fermentable, poorly absorbed, short-chain carbohydrates. Gastroenterology. 2013;145(2):320-8.e1-3.
127. Skodje GI, Sarna VK, Minelle IH, Rolfsen KL, Muir JG, Gibson PR, et al. Fructan, Rather Than Gluten, Induces Symptoms in Patients With Self-Reported Non-Celiac Gluten Sensitivity. Gastroenterology. 2018;154(3):529-39.e2.
128. Brotherton CS, Martin CA, Long MD, Kappelman MD, Sandler RS. Avoidance of Fiber Is Associated With Greater Risk of Crohn's Disease Flare in a 6-Month Period. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2016;14(8):1130-6.
129. James SL, Christophersen CT, Bird AR, Conlon MA, Rosella O, Gibson PR, et al. Abnormal fibre usage in UC in remission. Gut. 2015;64(4):562-70.
130. Walton M, Alaunyte I. Do patients living with ulcerative colitis adhere to healthy eating guidelines? A cross-sectional study. The British journal of nutrition. 2014;112(10):1628-35.
131. Thompson T. Folate, iron, and dietary fiber contents of the gluten-free diet. Journal of the American Dietetic Association. 2000;100(11):1389-96.
132. Swanson GR, Tieu V, Shaikh M, Forsyth C, Keshavarzian A. Is moderate red wine consumption safe in inactive inflammatory bowel disease? Digestion. 2011;84(3):238-44.
133. Jowett SL, Seal CJ, Pearce MS, Phillips E, Gregory W, Barton JR, et al. Influence of dietary factors on the clinical course of ulcerative colitis: a prospective cohort study. Gut. 2004;53(10):1479-84.
134. Swanson GR, Sedghi S, Farhadi A, Keshavarzian A. Pattern of alcohol consumption and its effect on gastrointestinal symptoms in inflammatory bowel disease. Alcohol (Fayetteville, NY). 2010;44(3):223-8.
135. Gulec S, Anderson GJ, Collins JF. Mechanistic and regulatory aspects of intestinal iron absorption. American journal of physiology Gastrointestinal and liver physiology. 2014;307(4):G397-409.
136. Tasson L, Canova C, Vettorato MG, Savarino E, Zanotti R. Influence of Diet on the Course of Inflammatory Bowel Disease. Digestive diseases and sciences. 2017;62(8):2087-94.
137. Werner T, Wagner SJ, Martinez I, Walter J, Chang JS, Clavel T, et al. Depletion of luminal iron alters the gut microbiota and prevents Crohn's disease-like ileitis. Gut. 2011;60(3):325-33.
138. Sousa Guerreiro C, Cravo M, Costa AR, Miranda A, Tavares L, Moura-Santos P, et al. A comprehensive approach to evaluate nutritional status in Crohn's patients in the era of biologic therapy: a case-control study. The American journal of gastroenterology. 2007;102(11):2551-6.

139. Jorgensen SP, Agnholt J, Glerup H, Lyhne S, Villadsen GE, Hvas CL, et al. Clinical trial: vitamin D3 treatment in Crohn's disease - a randomized double-blind placebo-controlled study. Alimentary pharmacology & therapeutics. 2010;32(3):377-83.
140. Kabbani TA, Koutroubakis IE, Schoen RE, Ramos-Rivers C, Shah N, Swoger J, et al. Association of Vitamin D Level With Clinical Status in Inflammatory Bowel Disease: A 5-Year Longitudinal Study. The American journal of gastroenterology. 2016;111(5):712-9.
141. Garg M, Hendy P, Ding JN, Shaw S, Hold G, Hart A. The effect of vitamin D on intestinal inflammation and faecal microbiota in patients with ulcerative colitis. Journal of Crohn's and Colitis. 2018:jjy052-jjy.
142. Yakut M, Ustun Y, Kabacam G, Soykan I. Serum vitamin B12 and folate status in patients with inflammatory bowel diseases. European journal of internal medicine. 2010;21(4):320-3.
143. Frisoli TM, Schmieder RE, Grodzicki T, Messerli FH. Salt and hypertension: is salt dietary reduction worth the effort? The American journal of medicine. 2012;125(5):433-9.
144. Ghomraoui FA, Alotaibi ST, Alharthi MA, Asiri SS, Almadi MA, Alharbi OR, et al. Plasma ghrelin and leptin in patients with inflammatory bowel disease and its association with nutritional status. Saudi journal of gastroenterology : official journal of the Saudi Gastroenterology Association. 2017;23(3):199-205.
145. Renwick AG. Toxicology of micronutrients: adverse effects and uncertainty. The Journal of nutrition. 2006;136(2):493s-501s.
146. Anderson JL, Hedin CR, Benjamin JL, Koutsoumpas A, Ng SC, Hart AL, et al. Dietary intake of inulin-type fructans in active and inactive Crohn's disease and healthy controls: a case-control study. Journal of Crohn's & colitis. 2015;9(11):1024-31.
147. Halmos EP, Christophersen CT, Bird AR, Shepherd SJ, Gibson PR, Muir JG. Diets that differ in their FODMAP content alter the colonic luminal microenvironment. Gut. 2015;64(1):93-100.
148. O'Keeffe M, Lomer MC. Who should deliver the low FODMAP diet and what educational methods are optimal: a review. J Gastroenterol Hepatol. 2017;32 Suppl 1:23-6.
149. O'Keeffe M, Jansen C, Martin L, Williams M, Seamark L, Staudacher HM, et al. Long-term impact of the low-FODMAP diet on gastrointestinal symptoms, dietary intake, patient acceptability, and healthcare utilization in irritable bowel syndrome. Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society. 2018;30(1).

8 Appendix

Appendix I: Overview of studies exploring dietary beliefs in IBD patients

Study	Dietary beliefs in IBD patients
Casanova et al. (2017) Spain (61) *Prevalence of Malnutrition and Nutritional Characteristics of Patients With Inflammatory Bowel Disease.*	48% thought diet is important in development of IBD 68% believed diet trigger disease activity, and 86% avoided certain foods in active disease 66% made changes to their diet post diagnosis, with CD implementing more restrictions than UC did 87% desired nutritional guidance from professionals 69% had reduced appetite in active disease
Bergeron et al. (2017) Canada (73) *Food avoidance in patients with inflammatory bowel disease: What, when and who?*	CD patients (especially those with structuring disease) restricted their diet more than UC patients did (38% higher exclusion rate) In active disease, nearly every patient avoided at least one food
Holt, Strauss, Moore (2017) Australia (64) *Patients with inflammatory bowel disease and their treating clinicians have different views regarding diet.*	71% thought diet have an impact on disease activity 61% felt caregivers neglected their belief in diet 46% had seen dietitian (CD more often than UC had)
Limdi, Aggarwal, McLaughlin (2016) England (62) *Dietary Practices and Beliefs in Patients with Inflammatory Bowel Disease.*	48% believed diet is an important risk factor of IBD 57% believed diet trigger disease activity (CD more than UC) 56% changed their diet post diagnosis, and 68% restricted their diet (CD more than UC) 73% reported reduced appetite during relapse (CD more than UC) Less than ¼ avoided eating away from home, but 2/3 stayed away from their favorite food to prevent relapse 50% had received dietary advice (31% from dietitian), and 67% desired nutritional guidance, primarily from dietitian (45%)
Kinsey and Burden (2016) England (65) *A survey of people with inflammatory bowel disease to investigate their views of food and nutritional issues.*	51% thought diet is important to control symptoms
Tinsley et al. (2016) USA (66) *Knowledge, Attitudes, and Beliefs Regarding the Role of Nutrition in IBD Among Patients and Providers.*	59% believed diet was important in managing IBD (CD more than UC) CD patients reported more frequently than UC patients did to have good/very good knowledge of nutrition
Skrautvol, Naden (2015) Norway (68) *Nutrition as long-term care as experienced by persons living with inflammatory bowel disease: a qualitative study.*	Several of the participants had modified their diet post diagnosis, and had attempted different diets Patients were very interested in food, and desired advice from health professionals
Zallot et al. (2013) France (63)	16% believed diet initiated the disease 58% thought diet is a risk factor of relapse

Dietary beliefs and behavior among inflammatory bowel disease patients.	67% avoided certain foods to prevent relapse 1/5 refused to eat away from home to prevent relapse Half of the participants (52%) preferred to follow a low residue diet in exacerbated periods 47% had received nutritional advice from dietitian (CD more frequently compared to UC). Additionally 53% desired dietary advice
Prince et al. (2011) England (72) *Nutritional problems in inflammatory bowel disease: the patient perspective.*	82% reported having problems with food and nutrition-the majority related to symptoms More CD than UC patients (94% vs. 64% respectively) reported problems with weight-mainly unintentional weight-loss The majority reported that food affected different social activities 47% had visited dietitian (CD more frequently compared to UC)
Maconi et al. (2010) Italy (69) *Pre-illness changes in dietary habits and diet as a risk factor for inflammatory bowel disease: a case-control study.*	39% made changes pre diagnosis due to symptoms
Triggs et al. (2010) New Zealand (67) *Dietary factors in chronic inflammation: food tolerances and intolerances of a New Zealand Caucasian Crohn's disease population.*	>66 % reported that dietary modifications alleviated disease activity

IBD: inflammatory bowel disease, CD: Crohn`s disease, UC: Ulcerative colitis

Appendix II: Overview of the 25 food groups applied in the dietary FFQ

Group 1: Bread

Group 2: Butter/Margarine/Other types of fat on bread

Group 3: Spreads

Group 4: Cereals

Group 5: Yoghurt

Group 6: Cold drinks (glass)

Group 7: Cold drinks (bottled)

Group 8: Alcoholic beverages

Group 9: Warm drinks

Group 10: Composite dishes (with meat)

Group 11: Composite dishes (with seafood)

Group 12: Composite dishes (other)

Group 13: Potatoes/Rice/Pasta

Group 14: Vegetables

Group 15: Sauce/Dressing/Accessories to cold and warm dishes

Group 16: Fats used in cooking

Group 17: Fruit

Group 18: Berries

Group 19: Spices/Herbs

Group 20: Nuts/Seeds

Group 21: Dessert/Wheat buns/Cakes

Group 22: Chocolate/Candy/Snacks

Group 23: Marine oils/omega-3 supplements

Group 24: Other supplements

Group 25: Distribution of meals

Appendix III: Examples of questions from the dietary FFQ

3. Hvilke typer pålegg spiser du?

Tenk på hvor mange skiver brød, rundstykker, knekkebrød og lignende du vanligvis spiser i løpet av en uke. Hvor mange skiver i uken spiser du med de følgende påleggstypene?

	Til antall skiver per uke											
	Aldri	Sjelden	0.5	1-2	3-4	5-6	7-8	9-10	11-15	16-20	21-25	26 eller flere
Brunost/prim *	◉	○	○	○	○	○	○	○	○	○	○	○
Lett/mager brunost/prim *	◉	○	○	○	○	○	○	○	○	○	○	○

8. Alkoholholdige drikker

Hvor ofte drikker du vanligvis de ulike typene drikker i listen under?

"g/mnd" betyr antall ganger i måneden, "g/uke" betyr antall ganger i uken, "g/dag" betyr antall ganger per dag.

	Aldri	Sjelden	1-3 g/mnd	1-3 g/uke	4-6 g/uke	1-2 g/dag	3-4 g/dag	5-6 g/dag	7-8 g/dag	9-10 g/dag	≥11/dag
Øl, sterk øl, pils (0.5L) *	◉	○	○	○	○	○	○	○	○	○	○
Lettøl (0.5L) *	○	◉	○	○	○	○	○	○	○	○	○

15. Saus, dressing og lignende tilbehør til varme og kalde retter

Hvor ofte spiser du brun og hvit saus? *

○ Aldri ○ Sjelden ○ 1-3/mnd ◉ 1/uke ○ 2-3/uke ○ 4-5/uke ○ 6-7/uke ○ ≥ 8/uke

Hvor stor porsjon spiser du? *

○ A:  ○ B:  ○ C:  ○ D: 

Hvor mange porsjoner spiser du til et måltid? *

Velg ...

Appendix IV: Overview of the assignment of FODMAP factors to each item in the dietary FFQ

Food item / composed dish (specifications)	Match in FODMAP-app	Source	FODMAPs in ingredients	Factor
White Bread	Bread, wheat, white			10*
Wholemeal bread (25-50 %)		Recipe	60 %	10*
Wholemeal bread (50-75 %)		Recipe	59 %	10*
Wholemeal bread (75-100 %)		Recipe	59 %	10*
Crispbread, light		Wasa frokost knekkebrød	89 %	10*
Crispbread, dark		Wasa Husman knekkebrød	100 %	10*
Norwegian brown cheese		Tine Gubrandsdalsost	5.6 g lactose/portion	10**
Norwegian brown cheese, fat reduced		Tine Lettere Gubrandsdalsost	5.6 g lactose/portion	10**
Cheese, white	Cheese, Swiss			0
Cheese, white, fat reduced	Cheese, Swiss			0
Cheese, soft, dessert	Cheese, soft, white mould coated			0
Cheese spread	Cheese, cream			5**
Cheese spread, fat reduced	Cheese, cream			5**
Liverpâtè		Recipe	4,7 %	0
Liverpâtè, fat reduced		Recipe	25 %	5
Saveloy		Recipe	30 %	5**
Ham	Pork			0
Sandwichfilling, chicken	Chicken			0
Salami		Recipe	2,0 %	0
Caviar		Mills Kaviar Original	≈0 %	0
Mackerell in tomato sauce, canned		Stabburet makrell 170g	≈0 %	0
Salmon, graved/smoked	Fish			0
Salmon, canned in oil	Salmon, plain, canned in brine			0
Anchovy/Sardines, canned	Sardines, plain, canned in oil			0
Tuna, canned	Tuna, plain, canned in oil/brine			0
Eggs	Eggs			0
Jam, unspecified	Jam, Mixed berries			10
Jam, unspecified, light	Jam, Mixed berries			10
Honey	Honey			10
Peanut butter	Peanut butter			0
Chocolate spread		Recipe	≈0 %	0
Sweet spread		Recipe	20 %	5
Cottage cheese	Cheese, cottage, creamed			0
Mayonnaise based spread		Recipe	17 %	5
Mayonnaise based spread, fat reduced		Recipe	17 %	5
Oatmeal porridge		Recipe	44 %	10**
Muesli	Muesli, plain			10*
Muesli with dried fruit	Flakes of wheat, corn, rice, oats, dried fruit, nuts			10*

Cornflakes	Flakes of corn			5
Honnicorn		Kelloggs Smacks Honni Korn	56 %	10*
Cereal		Kelloggs All-bran Plus	87 %	10*
Jam, unspecified	Jam, Mixed berries			10
Sugar, white	Sugar, white			0
Yoghurt, natural	Yoghurt, natural, regular			10**
Yoghurt, fruit		Tine fruktyoghurt	6.4 g lactose/portion	10**
Yoghurt, muesli		Tine Gomorgen yoghurt	7.3 g lactose/portion	**10****
Yoghurt, fruit, light		Fjorland Yoplait 00%	7.3 g lactose/portion	10**
Yoghurt, muesli, light		Tine Gomorgen yoghurt	7.3 g lactose/portion	**10****
Yoghurt, fruit, light (Skyr)		Q-meieriene Skyr	≈0.2 g lactose/portion	0
Yoghurt, fruit, light (Skyr)		Q-meieriene Skyr	≈0.2 g lactose/portion	0
Yoghurt, dessert		Tine Gomorgen yoghurt	7.3 g lactose/portion	**10****
Rice pudding		Tine rislunsj	4.5 g lactose/portion	10**
Milk, full cream, cow (3,5-3,9%)	Milk, full cream, cow			10**
Milk, reduced fat, cow (1-1,2%)	Milk, reduced fat, cow			10**
Milk, reduced fat, cow (0,5-0,7%)	Milk, reduced fat, cow			10**
Milk, skim, cow (0,1%)	Milk, skim, cow			10**
Milk, cultured		Tine Cultura	8.8 g lactose/portion	10**
Milk, cultured		Tine Biola	8.0 g lactose/portion	10**
Chocolate milk	Milk, full cream/reduced fat/skim, cow			10**
Milk, cultured		Tine Drikkeyoghurt	11 g lactose/portion	10**
Orange juice	Orange, 99% blend (reconstituted and fresh)			5
Apple juice	Apple, 99% blend (reconstituted and fresh)			10
Grape juice	Grapes, red/thompson			0
Berry juice		Recipe	22 %	5
Smoothie	Berry fruit blend (from juice bar)			10
Cordial (prepared)		Lerum husholdningssaft	5,2 %	5
Cordial, light		Fun light	≈0 %	0
Carbonated water (Farris)		Norwegian Food database	≈0 %	0
Soda		Norwegian Food database	≈0 %	0
Soda, light		Norwegian Food database	≈0 %	0
Ice tea		Recipe	7,0 %	5
Ice tea, light		Recipe	8,7 %	5
Beer, alcoholfree	Beer			0
Energy drink (Battery, Red Bull)		Norwegian Food database	≈0 %	0
Pale beer	Beer			0
Beer, light	Beer			0
Alcopop (Smirnoff Ice, Breezer)		Recipe	11 %	5
Red wine	Wine, red			0
White wine	Wine, white			0

Wine, sweet	Wine, sticky			10
Rum	Rum			10
Drink		Recipe	25 %	5
Coffee, filtered	Instant, regular, black			0
Coffee, boiled	Instant, regular, black			0
Instant coffee	Instant, regular, black			0
Espresso	Espresso, regular, black			0
Caffè Latte	Espresso, regular with cow's milk			10**
Cappuccino with milk	Espresso, regular with cow's milk			10**
Hot chocolate		Recipe	78 %	10**
Tea, black	Tea, black, strong, made up with water			5
Tea, green	Tea, green, strong, made up with water			0
Tea, herbal	Tea, herbal, strong, made up with water			10
Sugar	Sugar, white/brown			0
Sugar	Sugar, white/brown			0
Sweetener (Natreen tablet)		Recipe	0 %	0
Milk, full cream, cow (3,5-3,9%)	Milk, full cream, cow			10**
Sausage		Recipe	34 %	5**
Sausage, fat reduced		Recipe	3,8 %	0
Sausage, chicken/turkey		Prior kjøttpølse kylling+kalkun	0,9 %	0
Hot dog		Recipe	35 %	5**
Hot dog, chicken/turkey		Prior grillpølse kylling+kalkun	≈0 %	0
Hamburger with bread		Recipe	30 %	5*
Meat patty		Recipe	4,7 %	0
Meatballs		Recipe	6,9 %	5**
Casserole with mince		Recipe	24 %	5
Casserole, chicken/turkey mince		Recipe	29 %	5
Taco, shells		Recipe	5,9 %	5**
Taco, burrito		Recipe	38 %	5
Kebab		Recipe	13 %	5*
Lasagna		Recipe	60 %	**10***/**
Pizza		Recipe	41 %	10*
Pie		Recipe	45 %	**10***/**
Spring roll		Springroll from meny.no	48 %	10*
Beef	Beef			0
Pork	Pork			0
Roast	Pork/beef/chicken/lamb			0
Roast (Roe deer, Red deer, elk etc)	Pork/beef/chicken/lamb			0
Norwegian lamb stew		Recipe	1.0 %	0
Stew		Recipe	≈0 %	0
Bacon	Pork			0
Chicken with skin	Chicken			0
Chicken without skin	Chicken			0

Chicken leg	Chicken			0
Turkey	Chicken			0
Wok		Recipe	10 %	5
Casserole, spanish		Recipe	16 %	5
Fish pudding		Recipe	56 %	10**
Fish balls, canned		(Values like fish pudding)		10**
Cod	Fish			0
Cod, filet	Fish			0
Cod, breaded		Recipe	16 %	5*
Sardines/Herring	Fish			0
Mackerel	Fish			0
Salmon/Trout	Fish			0
Sushi		Main ingredients: fish and rice	< 5.0 %	0
Fish casserole		Recipe	10 %	5
Fish au gratin		Recipe	36 %	5**
Shellfish	Prawns, peeled			0
Wok with seafood		Recipe	12 %	5
Porrigde made with sour cream		Recipe	≈100 %	**10****
Rice porrigde		Recipe	63 %	10**
Pancakes		Recipe	87 %	**10****
Tomato soup		Toro tomatsuppe	<2.5 %	0
Gratin of cauliflower		Recipe	72 %	10
Noodles	Noodles, egg			5*
Omelet	Eggs			0
Potatoes, boiled	Potato, unpeeled			0
Mashed potatoes		Recipe	33 %	5**
Potato salad		Recipe	25 %	5**
Potatoes au gratin		Recipe	22 %	5**
Fried potatoes	Potato, unpeeled			0
Pommes frites	Potato, unpeeled			0
Pommes frites	Potato, unpeeled			0
Rice	Rice, white/brown			0
Pasta	Pasta, wheat			10*
Hot dog bun		Recipe	54 %	10*
Carrot	Carrot			0
Cabbage	Cabbage, common			0
Rutabagas/Swede	Rutabagas/Swede			0
Cauliflower	Cauliflower			10
Broccoli	Broccoli (whole)			0
Brussels sprout	Brussels sprout			0
Onion	Onion (shallots,spanish red, spring, white)			10
Lettuce	Lettuce (alle typer)			0
Bell pepper	Bell pepper (rød/grønn)			0
Avocado	Avocado			10

Tomato	Tomato, common			0
Cucumber	Cucumber, common			0
Corn	Corn Kernels, canned/Baby corn, canned			5
Vegetable mix		Recipe	59 %	10
Lettuce mix		Recipe	0 %	0
Legumes, unspecified				5
Brown sauce		Recipe	0,2 %	0
Bèaernaise sauce		Recipe	14 %	5**
Margarin/butter	Butter/margarin			0
Spiced butter		Recipe	≈0 %	0
Mayonnaise	Mayonnaise, regular fat			0
Mayonnaise, fat reduced	Mayonnaise, low fat			0
Cream, sour, high fat (35%)	Cream, sour			5**
Cream, sour, fat reduced (18%)	Cream, sour			5**
Cream, sour, low fat (5-10%)	Cream, sour			5**
Dressing		Recipe	≈0 %	0
Dressing, fat reduced		Recipe	≈0 %	0
Dressing, oil		Recipe	≈0 %	0
Soya sauce	Soy sauce			0
Pesto	Pesto sauce			5
Pasta sauce	Pasta sauce, tomato-based			10
Salsa		Recipe	15 %	5
Ketchup	Ketchup, sweetened with sucrose			5
Mustard	Mustard			0
Apple	Apple, pink lady			10
Pear	Pear, packham, firm, peeled			10
Banana	Banana, common (ripe/unripe)			5
Orange	Orange, navel			0
Clementine	Clementine			0
Nectarine	Nectarine			10
Kiwi	Kiwi (gold/grønn)			0
Grapes	Grapes			0
Melon, honeydew	Melon, honeydew			0
Raisins	Raisins			5
Dried fruit		Recipe	100 %	10
Strawberry	Strawberry			0
Raspberry	Raspberry			0
Blueberry	Blueberry			0
Cloudberry	Extrapolated Strawberry/Raspberry/Blueberry			0
Redcurrant	Extrapolated Strawberry/Raspberry/Blueberry			0
Lingonberry	Extrapolated Strawberry/Raspberry/Blueberry			0
Cherries	Cherries			10
Almonds	Almonds			0
Peanuts	Peanuts			0

Cashews	Cashews			10
Hazelnuts	Hazelnuts			0
Walnuts	Walnuts			0
Pine nuts	Pine nuts			0
Flax-/Linseeds	Flax seeds/Linseeds			0
Seeds, sunflower	Seeds, sunflower			0
Ice-cream	Ice-cream, vanilla			5**
Ice lolly		Recipe/Lerum husholdningssaft	9.1 %	5
Fruit, canned		Eldorado fruktcocktail	51 %	10
Fruit salad		Recipe	47 %	10
Caramel pudding		Tine Piano Karamellpudding	5.9 g lactose/portion	10**
Vanilla sauce		Recipe	88 %	10**
Whipped cream	Cream, whipped			0
Wheat bun		Recipe	78 %	**10***
Cinnamon bun		(Values like wheat bun)	78 %	**10***
Danish pastry		Recipe	49 %	**10***/**
Muffin		Recipe	52 %	**10***/**
Cake		Recipe	43 %	**10***/**
Waffles		Recipe	66 %	**10****
Brownie		Recipe	47 %	**10***/**
Cream cake		Recipe	60 %	**10***/**
Biscuit, unspecified	Biscuit, chocolate chip/ Biscuit, oatcakes			5*
Chocolate, milk	Chocolate, milk			5
Chocolate, dark	Chocolate, dark			0
Chocolate dark (70%)	Chocolate, dark			0
Confectionery	Chocolate, dark			0
Lozenge		Brynild Dent Oi	31 %	5
Candy		Brynild bringebærdrops	0 %	0
Sweets, not chocolate		Main ingredient: Fructose-glucose sirup	< 5.0 %	0
Chips	Chips, potato crisps, plain			0
Chips	Chips, potato straws, salted			0

* Food item removed from overall score for participants on gluten-free diet. Highlighted factors were changed from 10 till 5.

** Food item removed from overall score for participants on lactose-free diet. Highlighted factors were changed from 10 till 5.

When a participant reported to live on a gluten- and lactose-free diet, the highlighted food items were removed from the overall score, unless for pie and lasagna which remained factor 5 due to vegetable content.

Appendix V: Dietary information from IBSEN III questionnaires

Kosthold

Har du det siste året (hele året eller deler av året) fulgt et spesielt kosthold (for eksempel vegetar, glutenfri, lavkarbo, lavFODMAP etc.) #86

( ) Ja ( ) Nei

Hvis ja, hvilket kosthold (flere svar mulig)?

#87

- [ ] Veganer
- [ ] Glutenfri
- [ ] Laktoseredusert/laktosefri
- [ ] Lavkarbo/høyfett
- [ ] LavFODMAP
- [ ] Annet

Antall måneder veganer

Antall måneder glutenfri

Antall måneder laktoseredusert/laktosefri

Antall måneder lavkarbo/høyfett

Antall måneder LavFODMAP

Spesifiser kort annet kosthold

Antall måneder annet kosthold

Prøver du ut et spesielt kosthold nå? #88

( ) Ja ( ) Nei

Hvis ja, hvilket kosthold (flere svar mulig)? #89

- [ ] Vegetar
- [ ] Glutenfri
- [ ] Laktoseredusert/laktosefri
- [ ] Lavkarbo/høyfett
- [ ] LavFODMAP
- [ ] Annet

Spesifiser kort