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Prevalence of Avoidant/Restrictive Food Intake Disorder and Association with Nutrition Status in Patients with Inflammatory Bowel Diseases

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PREVALENCE OF AVOIDANT/RESTRICTIVE
FOOD INTAKE DISORDER AND ASSOCIATION WITH NUTRITION STATUS IN
PATIENTS WITH INFLAMMATORY BOWEL DISEASES

A Thesis

Presented to

The Faculty of the Department of Nutrition, Food Science and Packaging

San José State University

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

by

Emily Ruth Yelencich

December 2020

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The Designated Thesis Committee Approves the Thesis Titled

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December 2020

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ABSTRACT

PREVALENCE OF AVOIDANT/RESTRICTIVE FOOD INTAKE DISORDER AND ASSOCIATION WITH NUTRITION STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

by Emily R. Yelencich

There is a large body of research on the relationship between inflammatory bowel disease (IBD) and diet; however, few conclusive, generalizable recommendations have been determined. Regardless, IBD patients often alter their normal dietary intake, which is concerning considering the prevalence of malnutrition in the IBD population.

Avoidant/restrictive food intake disorder (ARFID) is a feeding disorder that was recently added to the Diagnostic and Statistical Manual of Mental Disorders and its prevalence and impact on the nutritional status of IBD patients has not previously been described. In this study ARFID risk was measured using the Nine-Item ARFID Screen and in the 161 outpatient, adult IBD participants 17% were at ARFID risk. Participants who avoid food, regardless of disease status, had significantly higher ARFID risk scores than those who do not avoid food. Participants who reported symptoms of diarrhea, pain, no appetite, and fullness were significantly more likely to be at ARFID risk than those who did not.

Nutritional risk was measured using the Patient Generated-Subjective Global Assessment (PG-SGA). ARFID risk score and nutritional risk score were positively correlated ($r_s = 0.196$, $P = 0.024$), indicating that participants with a higher ARFID risk score were also at risk for malnutrition. These results demonstrate that IBD patients should be regularly screened for malnutrition and food avoidance, endorsing the critical role of a registered dietitian as part of the IBD patient care team.

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LIST OF ABBREVIATIONS

ARFID—avoidant/restrictive food intake disorder
AUC—area under the curve
BMI—body mass index
CD—Crohn’s disease
CI—confidence interval
DHA—docosahexaenoic acid
DSM-5—Diagnostic and Statistical Manual of Mental Disorders
EPA—eicosapentaenoic acid
ESPEN—European Society for Clinical Nutrition and Metabolism
FODMAP—fermentable oligo-, di-, mono-saccharides and polyols
FFQ—food frequency questionnaire
HBI—Harvey Bradshaw Index
IBD—inflammatory bowel disease
IBD-AID—anti-inflammatory diet
IQR—interquartile range
LFD—low FODMAP diet
MTLWSI—Modified Truelove and Witts Severity Index
MUFA—mono-unsaturated fatty acids
NCM—Nutrition Care Manual
NIAS—Nine Item Avoidant/Restrictive Food Intake Disorder Screen
OR—odds ratio
PG-SGA—Scored Patient-Generated Subjective Global Assessment
PUFA—poly-unsaturated fatty acids
SCD—Specific Carbohydrate Diet
SD—standard deviation
UC—ulcerative colitis
UCLA—University of California, Los Angeles

CHAPTER 1

Literature Review

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory illness that encompasses two diagnoses: Crohn's disease (CD) and ulcerative colitis (UC). There is no cure for CD or UC and the best outcome for people with IBD is to remain in remission, while managing uncomfortable and disruptive functional gastrointestinal symptoms. Disease etiology and status in IBD is multifactorial and influenced by a combination of genetic and environmental factors (Nahikian-Nelms, 2006). One of the primary environmental factors that people with IBD can manipulate is diet. While many diets have been suggested for the management of functional gastrointestinal symptoms and disease management, there is a lack of easily accessible, conclusive, dietary recommendations on which patients can make dietary choices. Even so, it is well documented that people with IBD believe that their dietary choices influence their disease status (Jowett et al., 2004; Limdi, Aggarwal, and McLaughlin, 2016; Zallot et al., 2013). This leads patients with IBD to alter their dietary intake based on advice from the internet (Marsh et al., 2019; Tinsley et al., 2016; Zallot et al., 2013) and under the direction of clinical providers who do not always feel they have sufficient nutrition care resources or adequate nutrition training (Raman, & Coderre, 2009; Scolapio, Buchman, & Floch, 2008; Tinsley et al., 2016). When this independent, unsupervised approach at dietary intake is combined with confusion about what defines the most appropriate diet for IBD, patients run the risk of developing restrictive eating behaviors that can result in deficient

nutritional intake, increasing their risk for malnutrition (Vidarsdottir, Johannsdottir, Thorsdottir, Bjornsson, & Ramel, 2016). This review will present research about diet and IBD onset and disease course, specific diets for IBD treatment and management, and the dietary beliefs, disordered eating behaviors and eating disorders, and nutritional risks of people with IBD.

Inflammatory Bowel Disease Etiology

In both CD and UC, the delicate homeostasis of the gastrointestinal immune system is compromised, leading to varying degrees of intestinal inflammation (Kim, & Cheon, 2017). Due to the multifactorial nature of IBD, the exact etiology has not been identified; however, according to the Crohn's and Colitis Foundation of America (2014), the predominant theory is that a disturbance in the normal immune system response leads to a dysfunctional immune system attack on the healthy microbiota in the intestine, leading to chronic intestinal inflammation. While it is difficult to determine the exact combination of factors that lead to this abnormal immune response, it is clear that people with a genetic predisposition are more susceptible to developing IBD in response to a combination of environmental factors. Environmental factors include diet, smoking, antibiotic treatment, geography, and stress (Ananthakrishnan, 2015). Research has shown that dietary factors can contribute to the development of IBD by altering the composition of the gut microbiota and by directly regulating gastrointestinal immune cells (Sugihara, Morhardt, & Kamada, 2019). These disruptions can lead to an abnormal inflammatory response, resulting in the development of CD or UC. Once the homeostasis of the gastrointestinal immune cells and microbiota is compromised, dietary factors can further

exacerbate or ameliorate the disease (Sugihara, Morhardt, & Kamada, 2019). The complexity of the relationship between dietary intake, microbiota, and inflammatory response makes studying the effects of diet on IBD complicated and important.

Impact of Diet on IBD

Diet and IBD onset. Most research on the relationship between diet and IBD has focused on disease onset. In a literature review by Spooren et al. (2013), researchers found 36 studies investigating diet and IBD onset, compared to six studies investigating diet and disease relapse. Conclusions from these studies vary; however, they highlight dietary factors that are associated with higher risk of developing IBD such as total fat, protein, and sugar, and they suggest that a high intake of fruits and vegetables may be protective against disease onset.

One area of research about dietary intake prior to disease onset is lipid intake. In Reif et al. (1997), researchers calculated the relative risk of developing UC between the highest and lowest tertiles of poly-unsaturated fatty acids (PUFA), mono-unsaturated fatty acids (MUFA), and cholesterol intake. They found that people in the highest tertile of PUFA, MUFA, and cholesterol intake were 6.54, 3.66, and 5.57 times more likely to develop UC, respectively, than those in the lowest tertile. In Geerling et al. (2000), researchers confirmed Reif et al. (1997), finding that people in the highest tertile of PUFA and MUFA intake were 5.1 and 33.9 times more likely to develop UC, respectively, compared to those in the lowest tertile intake.

There are many types of PUFA and John et al. (2010) focused on the association of two omega-3 PUFAs with disease onset: eicosapentaenoic acid (EPA) and

docosahexaenoic acid (DHA). Researchers found that people in the highest tertile of DHA intake were 79% less likely to develop UC compared to people in the lowest tertile. The odds ratio (OR) trend across tertiles was 0.47 (95% confidence interval (CI): 0.25–0.89). Researchers did not find a significantly protective effect of intakes in the highest tertiles of EPA or total omega-3 PUFA compared to intakes in the lowest tertiles. In a large scale, prospective cohort study that investigated fatty acid intake and IBD onset, Chan et al. (2014) also found a protective effect of DHA on the onset of CD, with a 94% reduction in the odds of developing incident CD for participants with the highest quintile of DHA intake and a significant OR trend across quintiles.

Inversely, research has shown high omega-6 PUFA intake increases risk of developing both UC and CD (Amre et al., 2007; Tjonneland et al., 2009). Amre et al. (2007) found that children with a high omega-6 intake were nearly twice as likely to develop CD compared to healthy controls and Tjonneland et al. (2009) found that adults with the highest intake of the omega-6 fatty acid, linoleic acid, were nearly two and a half times more likely to develop UC. Multiple studies investigating the association between high total omega-6 intake and the onset of UC have demonstrated a trend toward higher risk; however, they have not reached statistical significance (Geerling et al., 2000; Sakamoto et al., 2005).

Other studies that looked at dietary intake and the risk of developing IBD did not find significant associations between IBD onset and lipid intake (Jantchou, Morois, Clavel-Chapelon, Boutron-Ruault, & Caronnel, 2010; Tragnone et al., 1995). These studies did find significant results for different nutrients. Jantchou et al. (2010) found that individuals

in the highest tertile for protein intake were 3.31 times more likely to develop IBD than those in the lowest. Tragnone et al. (1995) also saw a significant difference in total protein intake between people with IBD (91.3 standard deviation (SD) $\pm$ 18.6g) and healthy controls (80.9 SD $\pm$ 15.5g) and Opstelten et al. (2018) concluded that IBD patients consume an additional 3.5g of protein per day compared to healthy controls. Conversely, a number of other studies did not find significant differences or increased risk ratios between protein intake and disease onset (Geerling et al., 2000; Hart et al., 2008; Sakamoto et al, 2005; Reif et al., 1997).

Tragnone et al. (1995) and Opstelten et al. (2018) also found a positive association between IBD onset and the consumption of carbohydrates. Tragnone et al. (1995) found that people with IBD consumed significantly more total carbohydrates (331.3 SD $\pm$ 89.3g), starches (202.6 SD $\pm$ 70.3g), and refined sugar (101.43 SD $\pm$ 37.08g) compared to healthy controls (232.5 SD $\pm$ 67.9g, 126.8 SD $\pm$ 42.4g, 83.5 SD $\pm$ 30.6g, respectively). Again, Opstelten et al. (2018) confirmed these findings, demonstrating that IBD patients consumed an average of 10.1g of additional carbohydrates per day compared to healthy controls. Other studies did not find significant differences or increased risk between carbohydrate intake and disease onset (Geerling et al., 2000; Hart et al., 2008; Jantchou et al., 2010; Sakamoto et al, 2005).

Spooren et al. (2013) reviewed 32 studies investigating the effects of fruit and vegetable intake on IBD onset and found that over half did not find any significant associations; however, 13 studies did show a protective effect. Compared to people with a low intake of fruits and vegetables, Porro and Panza (1985) found that people with a

high intake of fruits and vegetables had a relative risk of developing UC between 0.30 and 0.38. Similarly, Hansen et al. (2011) found that people who ate fruits daily were 61% less likely to develop CD and 44% less likely to develop UC. People who ate vegetables daily were 59% less likely to develop CD and 49% (95% CI: 0.31–0.84) less likely to develop UC. Unlike the dietary constituents previously reviewed, none of the articles reviewed by Spooren et al. (2013) showed an increased risk of developing IBD for people with a high intake of fruits and vegetables.

These studies demonstrate the inconsistent evidence regarding the role of dietary factors in the onset of IBD. The inconsistent results could be related to methodological differences and the inaccuracy inherent in collecting dietary data. Methodologically, studies used a variety of instruments for collecting dietary intake, from food frequency questionnaires (FFQ), to 7-day food diaries. Each instrument has strengths and limitations, and each will lead to different conclusions (Thompson et al., 2015). Another methodological problem is that most studies use FFQs to measure the dietary intake of participants; however, absolute intake cannot be reliably measured through this instrumentation. Instead, dietary intake is ranked; however, there are no set standards, across studies, for what constitutes a high, medium, or low intake. This complicates the interpretation of how dietary factors impact risk of IBD onset and relapse. These studies highlight the inconsistent results that contribute to confusion in the field for both medical practitioners as well as IBD patients.

Diet and IBD relapse. Similarly, there are varying results in the limited research on how diet impacts IBD disease course. In a cross-sectional study, Tasson et al. (2017)

examined the association between the current diet and disease status of participants. They found that participants with the highest intake of legumes and potatoes had a 79% lower risk of active disease. This study did not account for disease course over time, or any changes in dietary intake in response to disease course.

In a prospective study, Opstelten et al. (2018) followed IBD participants for two years, monitoring them for disease relapse. Thirty percent of participants relapsed, and researchers associated 'high' or 'low' intake of macronutrients with relapse. They found that participants who consumed a diet high in total fat, saturated fat, and mono-unsaturated fat were 37%, 77%, and 63% less likely to relapse, respectively. Conversely, participants with a high intake of dietary fiber were 3.65 times more likely to relapse.

Jowett et al. (2004) followed UC patients for one year to observe dietary intake and relapse. They found that individuals in the highest tertile of all meat (excluding fish) intake were 3.74 times more likely to relapse compared to those in the lowest tertile. Individuals with a high consumption of red and processed meats were 6.88 times more likely to relapse compared to those in the lowest tertile. Jowett et al. (2004) did not find any significant differences between fat or carbohydrate intake and risk of relapse.

These studies each identify a different macronutrient that may be associated with a higher risk of relapse. The inconsistent results may be due to similar methodological differences in the research about diet and IBD onset. These findings confirm that the complicated relationship between diet and IBD extends from disease onset throughout disease course.

Dietary Effects of Specific Diets on IBD

Even with varying results about the impact of diet on disease onset and relapse, there is a collection of research investigating the impact of IBD specific diets on disease course and symptom management. In their guidelines for clinical nutrition in IBD, the European Society for Clinical Nutrition and Metabolism (ESPEN) delivered a strong consensus that “there is no ‘IBD diet’ that can be recommended to promote remission in patients with active disease” (Forbes et al., 2017). They also agreed that research does not support a generalizable, optimal diet for maintaining disease remission (Forbes et al., 2017). Additionally, in a review for the Academy of Nutrition and Dietetics Evidence Analysis Library, weak/limited evidence was found to support the efficacy of medical nutrition therapy for gastrointestinal disorders (excluding celiac disease); however, only one, poor quality review article met the inclusion criteria for the review. In the absence of evidenced based medical nutrition therapy guidelines, the Academy of Nutrition and Dietetics’ Nutrition Care Manual offers some guidance to practicing dietitians. It advises that the primary goals of nutrition intervention should be to identify impediments to adequate oral intake, correct or compensate for malabsorption, and meet increased nutritional requirements while correcting for nutritional deficiencies and losses. When a patient is in an acutely active disease phase, their nutrient absorption, transit time, and/or ability to consume food orally may be impaired. If a patient cannot meet their needs orally, enteral or parenteral nutrition may be necessary; however, this treatment is not intended to induce remission in adult IBD patients (Eiden et al., 2003; Forbes et al., 2017). A patient in active disease who can consume food orally, should eat small,

frequent meals that are low in fat and fiber and high in protein and calories, ultimately aiming for a normal diet (Eiden et al., 2003). In disease remission, the Nutrition Care Manual recommends adjusting the diet of a patient based on their changing gastrointestinal function, prioritizing energy and protein intake to support weight management and nutrient intake. While the Nutrition Care Manual does not provide specific dietary recommendations on how to manage functional gastrointestinal symptoms or on how to reduce the risk of relapse, researchers continue to explore how adherence to particular diets such as the Specific Carbohydrate Diet, the low fermentable oligo-, di-, mono-saccharides and polyols diet, and the anti-inflammatory diet impact disease course and symptom presentation.

IBD and the Specific Carbohydrate Diet. The Specific Carbohydrate Diet (SCD) aims to induce and maintain drug-free remission in IBD patients by eliminating the consumption of disaccharides and most polysaccharides. The proposed mechanism for the SCD is that people with IBD produce too much intestinal mucus, inhibiting disaccharidases in the luminal brush border. This prevents the proper digestion and absorption of disaccharides, leading to intestinal injury and functional gastrointestinal symptoms (Gottschall, 1994). While the diet and pathway are not endorsed by any professional dietetic organizations, there is evidence that the SCD impacts the microbiome and can exacerbate or diminish inflammation (Kakodkar, Mikolaitis, Engen, & Mutlu, 2013).

In studies on the SCD in the adult IBD population, results have shown a positive effect. In a self-reported survey of 50 adults who self-treated their IBD with the SCD,

66% experienced clinical remission after a mean diet duration of 9.9 months. Several subjects also stopped corticosteroid therapy while on the SCD (Kakodar, Farooqui, Mikolaitis, & Mutlu, 2015). In another study, 417 IBD patients in a SCD support group participated in a self-reported survey. After two months of following the SCD 33% of participants reported remission, and after both six and twelve months, 42% reported remission. Of the participants who reported reaching remission, 13% reported that they experienced remission in less than two weeks, 17% reported that it took from two weeks to a month, 36% reported that it took from one to three months, and 34% reported that it took more than three months. For individuals who reported reaching remission, 47% reported an improvement in abnormal laboratory values (Suskind et al., 2016). While these studies highlight and confirm the positive perception of the SCD, there have not been rigorous, placebo-controlled studies to verify the efficacy of the diet.

IBD and the anti-inflammatory diet. The anti-inflammatory diet (IBD-AID) is another IBD specific diet that is based on the tenets of the SCD and is not endorsed by any professional dietetic organizations. The IBD-AID upholds the theory that consuming lactose and refined or processed complex carbohydrates can lead to gastrointestinal injury and inflammation. It also places an additional emphasis on the importance of pre- and probiotics in gut health, balancing the composition of fatty acid intake, and ensuring sufficient micronutrient intake based on individual assessment. It also suggests altering food texture to reduce intact fiber and improve absorption.

The proper implementation of and adherence to this diet is difficult due to its multi-component, individualized nature. This barrier was emphasized by the high withdrawal

rate in a study from the researchers who developed the IBD-AID (Olendzki et al., 2014). Initially dietitians met with 37 IBD patients about the IBD-AID; however, only 11 participants were included in the analysis due to withdrawal (13 participants) or incomplete data (13 participants). The 11 participants (8 CD, 3 UC) who met the inclusion criteria followed the IBD-AID for at least four weeks, recording their dietary intake and symptoms. Participants with CD had a mean reduction of their Harvey Bradshaw Index (HBI) score from 11 (range: 0–20) to 1.5 (range: 0–3), indicating that all participants reached disease remission ($HBI \leq 4$). Participants with UC had a mean reduction of their Modified Truelove and Witts Severity Index (MTLWSI) score from 7 (range: 6–8) to 0, indicating that all participants reached disease remission ($MTLWSI \leq 2$). While these results suggest a promising effect of the IBD-AID, they should be interpreted with skepticism due to the small sample size and lack of control/placebo groups. Furthermore, the association of the researchers with and investment in the diet may have impacted results by influencing the recruitment process or the level of dietary guidance that participants received. More research, from unaffiliated groups is required before the diet is recommended and implemented.

IBD and the low fermentable oligo-, di-, mono-saccharides and polyols diet.

While the SCD and IBD-AID eliminate complex carbohydrates, the low fermentable oligo-, di-, mono-saccharides and polyols diet (LFD) takes the opposite approach, restricting specific simple carbohydrates. Also, unlike the SCD and IBD-AID, the LFD is not intended to be followed, comprehensively, in the long-term. Instead, it is intended to be an elimination diet with a reintroduction period aimed at identifying dietary triggers

unique to each individual. This diet significantly reduces or eliminates the intake of short-chain carbohydrates, fructose, lactose, fructans, polyols, and galacto-oligosaccharides. These carbohydrates are poorly absorbed and highly fermentable, leading to functional gastrointestinal symptoms like diarrhea, gas, and bloating (Gibson, & Shepherd, 2005). Many studies have shown that the LFD successfully manages functional gastrointestinal symptoms in people with irritable bowel syndrome (Böhn et al., 2015; de Roest et al., 2013; Staudacher, Whelan, Irving, & Lomer, 2017). In an observational study by de Roest et al. (2013), participants with irritable bowel syndrome responded to a symptom severity survey that used a 7-point Likert scale to assess the impact of the LFD on multiple functional gastrointestinal symptoms. Researchers found that adherence to the LFD was associated with the significant improvement of bloating, abdominal pain, gas, and diarrhea.

Because many people with IBD have functional gastrointestinal symptoms, the LFD has also been tested on and prescribed to people with IBD. In an observational study performed on an IBD cohort, 56% of participants on the LFD reported improvement in their overall functional gastrointestinal symptoms, indicating that the LFD can be a useful symptom management tool for people with IBD (Gearry et al. 2009). In another prospective, intervention study, Pedersen et al. (2017) randomly assigned people with IBD to the LFD or to a normal diet for six weeks, collecting irritable bowel syndrome symptom severity surveys at baseline and after the intervention. Researchers found that after six weeks, the LFD group showed a significantly lower median irritable bowel syndrome symptom severity score (median: 115) than the normal group (median: 170).

When analyzed by disease type, researchers saw a significant irritable bowel syndrome symptom severity score improvement in participants with CD on the LFD (median: 58) compared to participants with CD on the normal diet (median: 220). The irritable bowel syndrome symptom severity score did not significantly improve for participants with UC on the LFD (median: 120) compared to participants with UC on the normal diet (median: 141).

While symptom management is important for patients with IBD it does not necessarily reflect the disease status of a patient or the ability of a diet to control disease maintenance or relapse. While Pedersen et al. (2017) did not see a significant improvement of irritable bowel syndrome symptoms in UC participants; the Simple Clinical Colitis Index, used to measure UC disease activity, significantly decreased in the LFD group (baseline: 3, week 6: 1). In the normal diet group, the UC disease activity did not change (baseline: 2, week 6: 2). Crohn's disease participants on the LFD did not experience a significant reduction in their HBI disease activity score. This indicates that the LFD may be more effective in disease management for IBD patients with UC than CD. One factor that may have influenced these results was that there were fewer participants with CD than UC and it is possible that there were not enough CD participants to achieve sufficient power and observe a significant improvement in disease activity. While research on the LFD demonstrates conditionally positive results for symptom management and disease activity management, it is a very restrictive diet that merits further research into the long-term effects on nutrition status in people with IBD.

Dietary Beliefs and Eating Behaviors of People with IBD

Based on the complicated nature of the previously reviewed diets and the inconsistent methodologies and conclusions, it is not surprising that the IBD patient population is uncertain about the best diet to follow for their disease. Even with this confusion, it has been shown that IBD patients do believe that diet plays a role in their disease course and that they hold strong dietary beliefs.

In a study performed by Limdi et al. (2016) on 400 IBD patients, researchers found that 48% of participants believed that diet could be an initiating factor for IBD and 57% of participants identified diet as a potential cause of relapse. In a similar study, Zallot et al. (2013) found that 57.8% of IBD participants believed that food could lead to IBD relapse; however, only 15.6% of participants thought that food could initiate IBD. Similarly, Jowett et al. (2004) found that 68% of UC participants believed that their dietary choices impacted their disease and 39% believed that specific foods lead to relapse. While a higher percentage of IBD patients hold beliefs about how food negatively impacts their disease status, Limdi et al. (2016) also found that 16% of IBD patients thought that specific foods could improve their IBD symptoms.

Jowett et al. (2004) found that the food groups dairy, fruits, and vegetables were most commonly avoided due to the perception that they had a negative impact on disease status. The food groups that were most commonly reported to be the most beneficial to the disease status of participants were fruits, vegetables, breads, cereals, and potatoes. Participants in Cohen et al. (2013) reported that yogurt and rice improved IBD symptoms and identified 18 foods or food groups that exacerbate symptoms. Some of the most

commonly reported, detrimental foods were non-leafy and leafy vegetables, spicy foods, nuts, fried foods, milk, and red meat.

While IBD patients hold many beliefs about how food impacts their disease course, this does not necessarily mean that they alter their diets based on those beliefs; however, many studies have investigated eating behavior in the IBD population and have shown that between 49-90% of IBD patients do avoid specific foods (Bergeron, Bouin, D'Aoust, Lemoyne, & Presse, 2018; Holt, Strauss, & Moore, 2017; Jowett et al., 2004; Marsh et al., 2019; Walton, & Alaunyte, 2014; Vidarsdottir et al., 2016). Similarly, Jowett et al. (2004) found that 22% of participants ate more of the foods they perceived to help their disease.

Cohen et al. (2013) also investigated the connection between food beliefs and eating behaviors by comparing food frequency questionnaires of IBD participants to their food beliefs. Results showed that participants do alter their intake based on the perceived benefit or harm of a food or food group. Patients who reported that red meat, dairy, or sugar exacerbated their symptoms had a significantly lower intake of those items, while patients who reported that cereal, milk, fruit, or whole grains improved symptoms had a significantly higher intake of those items. These studies provide foundational evidence that dietary restriction is a relevant eating behavior in the IBD population.

Disordered Eating in the IBD Population

The fact that many IBD patients engage in restrictive eating behaviors indicates that the population may be at a high risk for disordered eating and eating disorders (Quick, Byrd-Bredbenner, & Neumark-Sztainer, 2013). Research on the prevalence of disordered

eating in the IBD population is limited; however, using the Eating Attitudes Test eating disorder screener, Wabich, Bellaguarda, Joyce, Keefer, and Kinsinger, (2020) found that 13% of IBD patients are at a high risk for an eating disorder. When IBD patient responses to the Eating Attitudes Test screener were analyzed by gender, high eating disorder risk increased to between 18–20% for female IBD patients (Satherley, Howard, & Higgs, 2016; Wabich et al., 2020).

In a retrospective study, Wotton, James, and Goldacre (2016) examined the comorbidity of autoimmune disease and eating disorder by calculating the likelihood that people who were admitted to the hospital for an eating disorder were prospectively admitted again for an autoimmune disorder and vice-versa. Wotton et al. (2016) calculated a risk ratio, comparing the likelihood that the control group, people who were admitted to the hospital for “minor conditions,” were prospectively hospitalized for an autoimmune disease or an eating disorder. Compared to the control group, females who were initially admitted for anorexia nervosa were about two times more likely to be hospitalized for UC and CD in the future (2.25 and 1.97, respectively). Females who were initially admitted for CD were 2.82 times more likely than the control group to be hospitalized for anorexia nervosa in the future and females who were initially admitted for UC were 1.91 times more likely than the control group to be hospitalized for anorexia nervosa in the future. These results show that severe eating disorders are present in female IBD patients and that there may be a correlation between the two diagnoses.

When specified, the primary eating disorders that these studies investigated were anorexia nervosa and bulimia nervosa; however, based on the knowledge that IBD

patients engage in food avoidance and restrictive eating, they may also be at a high risk for the eating disorder diagnosis, avoidant/restrictive food intake disorder (ARFID). ARFID was introduced into the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) in 2013 to broaden the scope of what was previously known as feeding disorder of infancy and early childhood. The new ARFID diagnosis is applicable to individuals of any age whose avoidant/restrictive eating behaviors but lead to insufficient caloric and/or nutrient intake, causing at least one of the following symptoms: weight loss, nutritional deficiency, dependence on nutritional supplements, or psychosocial impairment. The DSM-5 describes three categories that can lead to the symptoms of ARFID: avoidance of many foods based on their sensory properties (“picky eating”), low appetite or limited interest in eating, and fear of negative consequences, such as choking or vomiting from eating (American Psychiatric Association, 2013). Clinical diagnostic criteria for ARFID requires a disturbed eating or feeding experience that is not motivated by weight or body image concerns and that results in one or more of the following outcomes: nutritional deficiency as a result of insufficient food intake, significant weight loss, dependence on enteral or oral supplements, or impaired psychological function. If a patient also has a mental or physical illness, the feeding disturbance must exceed any feeding disturbances that are typically associated with the condition or disorder. Finally, patients who do not have sufficient food access or who have cultural practices that change eating patterns should not be diagnosed with ARFID (Katzman, Norris, & Zucker, 2018).

Because of the limited amount of research on eating disorders in the IBD population and the relatively new diagnostic criteria of ARFID, there are no studies that have looked

at the prevalence of ARFID in IBD patients specifically; however, a case study from Ilzarbe et al. (2017) highlights that this may be a relevant diagnosis that is overlooked in the IBD population. The 20-year-old subject of the case study had a CD diagnosis and an eating disorder not otherwise specified. Ilzarbe et al. (2017) found the patient to have significant weight loss in the previous year and described her eating habits as restrictive, explaining that the patient is more comfortable using enteral nutrition. They also specified that the patient did not have body image disturbance or fear of gaining weight. While the patient was diagnosed with eating disorder not otherwise specified, her symptoms meet the criteria for ARFID, and this would have been an appropriate diagnosis that may have led to a more targeted and effective treatment regimen. This case study highlights the concurrent incidence of IBD and ARFID while also showing that without awareness and screenings, ARFID goes undiagnosed.

In two studies that investigated the prevalence of ARFID in patients with GI disorders, researchers found that between 12–21% of participants met the ARFID diagnostic criteria (Harer, Jagielski, Riehl, & Chey, 2019; Zia, Riddle, DeCou, McCann, & Heitkemper, 2017). Harer et al. (2019) retrospectively evaluated the medical charts of adult gastroenterology patients who had been referred to gastroenterology behavioral health providers and found that 12.6% met the criteria for ARFID. Of those that met the ARFID criteria, 14.3% had an IBD diagnosis. Zia et al. (2017) measured the prevalence of many eating disorders, including ARFID, in adults with functional gastrointestinal disorders. Results showed that 21% of participants met the criteria for ARFID. These studies confirm the theoretical framework that ARFID is a relevant diagnosis for patients

with IBD and they affirm the need to investigate the prevalence of ARFID in the IBD population specifically, especially considering that they are a population that is at a high risk for impaired nutritional status.

To evaluate ARFID diagnosis Harer et al. (2019) retrospectively evaluated the medical charts of participants, screening for DSM-5 ARFID diagnostic criteria. The authors did not go into detail on the screening process; however, this retrospective process could have missed critical elements that may have led to, or invalidated, an ARFID diagnosis. For example, determining food access or cultural practices may not have been possible the medical records of participants. In their adult cohort, Zia et al. (2017) implemented the ARFID Canadian Pediatric Surveillance Program Questionnaire, an instrument validated for use in a child population that may not have been appropriate for the adult population of the study.

Another recent instrument that has been validated to screen for ARFID risk in an adult population is the Nine Item Avoidant/Restrictive Food Intake Disorder Screener (NIAS) (Zickgraf, & Ellis, 2018). The NIAS is structured based on the three domains of eating disturbances in the DSM-5: avoidance of foods due to sensory properties, poor appetite or limited interest in eating, and fear of negative consequences from eating. The NIAS has been used to identify avoidant and restrictive eating behaviors in children, adolescents, adults who are healthy, and adults who were previously determined to have eating difficulties (Elkins, & Zickgraf, 2018; Zickgraf, & Elkins, 2018; Zickgraf, Ellis, & Essayli, 2019). It has not been used in the IBD population; however, in a study of adult patients with symptoms of gastroparesis and dyspepsia, the NIAS was used to screen for

ARFID (Murray, Jehangir, Silvernale, Kuo, & Parkman 2020).

To establish a clinical cutoff score, Ellis, Zickgraf, Whited, and Galloway (2017) implemented the NIAS in a general sample of college students and in a sample of adults who were known to have eating difficulties. Participants completed the NIAS and an ARFID Symptoms Checklist that explicitly assesses the DSM-5 ARFID diagnostic criteria. Using a receiver operating characteristic curve analysis and the area under the curve (AUC), researchers determined that the NIAS was a good screener for ARFID in both the general and selected samples ($AUC_{\text{general}} = 0.87$, $AUC_{\text{selected}} = 0.80$). In the general sample a cutoff of 24 demonstrated good sensitivity (0.74) and specificity (0.84). In the selected sample, a cutoff score of 28 demonstrated adequate sensitivity (0.71) and specificity (0.68). Researchers hypothesized that the group selected for eating difficulties required a higher cutoff score because the symptoms associated with their eating difficulties may have added complexity to their cases that could not be accounted for by the screener.

Malnutrition in the IBD Population

Malnutrition in IBD patients is a serious condition as it is associated with negative outcomes such as increased risk of non-elective surgery, increased length of hospital stay, and increased mortality (Forbes et al., 2017). Many studies, using a variety of methodologies, have shown that malnutrition is prevalent in the IBD population. In one study that used unintentional weight loss as an indicator for malnutrition, researchers found that 68.4% of IBD patients with active disease met the criteria for malnutrition and that 31.6% met the criteria for severe malnutrition (Mijač, Janković, Jorga, & Krstić

(2010). Similarly, Benjamin, Makharia, Kalaivani, & Joshi (2008) found that 52.6% of patients with active or quiescent CD could be classified as malnourished based on a collection of anthropomorphic measurements. Benjamin et al. (2008) also found that participants with active CD were 7.5 times likelier to be malnourished than participants with quiescent CD.

While it is important to estimate the prevalence of malnutrition, these studies do not identify any nutrients that are specifically associated with malnutrition in IBD. Filippi, Al-Jaouni, Wiroth, Hébuterne, & Schneider (2006) investigated specific deficiencies by collecting data on both dietary intake as well as serum nutritional biochemical markers in participants with quiescent CD and a matched control group. From an analysis of 3-day prospective food records that were completed by participants, researchers found that female CD patients had significantly lower mean daily intakes of β -carotene, vitamins B1, B6, and C, and magnesium and significantly higher daily intakes of zinc compared to controls. Male CD patients had significantly lower mean daily intakes of β -carotene and vitamin C. From the biochemical analysis, researchers found that 84% of participants had low plasma concentration of vitamin C and copper, 77% had low plasma concentrations of niacin and 65% had low plasma concentration of zinc. Using the Nutritional Risk Index and albumin levels (Prasad et al., 2016), researchers found that 29% of participants were at moderate or severe risk for malnutrition.

These studies demonstrate the prevalence of malnutrition in IBD, but they do not specify the association with restriction. Given the evidence that people with IBD do restrict their intake according to their dietary beliefs, it is reasonable to expect that they

may have nutrient deficiencies secondary to their dietary restriction. Jowett et al. (2004) addressed this question by looking at three high-risk nutritional factors for IBD patients who restrict their diets: folate, calcium, and fiber. Researchers did not find a significant difference in folate or fiber intake between participants who believed that foods rich in folate or fiber (ex. legumes, vegetables) were detrimental and those who did not. Folate sufficiency in the IBD population was confirmed when Marcil et al. (2019) measured serum folate and found that only 2.6% of participants had abnormally low results. Jowett et al. (2004) did find that participants who believed that dairy was detrimental had a significantly lower median calcium intake compared to participants who did not hold this belief. This study shows that food beliefs and eating behaviors can impact micronutrient intake and the under-consumed micronutrients identified by Filipi et al. (2006) should also be investigated.

One patient-reported screening instrument that identifies patients at nutritional risk and is designed to reduce the burden of a comprehensive nutritional assessment in the clinical setting is the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF). The PG-SGA SF is a shortened version of the full-length Patient Generated-Subjective Global Assessment which was developed as a continuous score with a low score indicating well-nourished nutritional status and a high score indicating higher risk of malnutrition (Jager-Wittenaar, & Ottery, 2017). The four areas of the PG-SGA SF address: weight history and acute weight change, changes in dietary intake, symptoms that have impacted dietary intake, and changes to activities and function. The full-length PG-SGA has been validated to measure nutritional risk in in ambulatory oncology

settings (Bauer, Capra, & Ferguson, 2002; Isenring, Bauer, & Capra, 2003), an internal medicine ward (Pinho et al., 2017), and in non-oncology surgery patients (Huang et al., 2014). Subsequently, the PG-SGA SF has been validated as an analogous tool to the Patient Generated-Subjective Global Assessment (PG-SGA) for screening for nutritional risk (Abbott, Teleni, McKavanagh, Watson, McCarthy, & Isenring, 2016; Gabrielson et al., 2013). In their validation study on outpatient oncology patients, Gabrielson et al. (2013) found a strong, significant correlation between the full-length PG-SGA and the PG-SGA SF ($r = 0.984$, $P < 0.001$). They also found that, with a sensitivity of 93.8% and a specificity of 77%, the PG-SGA SF is comparable to the full-length PG-SGA (sensitivity: 0.97, specificity: 0.77). Possible PG-SGA SF scores range from 0–36 and Gabrielson et al. (2013) found that the optimal cutoff score for capturing patients with malnutrition was six or greater. While the PG-SGA has been used in IBD studies (Casanova et al., 2017; Lim, Kim, Hong, & Kim, 2014), it has not been validated in an IBD population.

Dietary Assessment Methodology in IBD

Many types of dietary assessment instrumentation have been used in the IBD population. Dietary intake assessment is necessary to address research questions that investigate diet and disease etiology, disease course, and symptom management. Dietary intake must also be assessed when evaluating the dietary adherence of participants in intervention studies. Researchers have not established one, universally accepted methodology for evaluating dietary intake in any population and in the IBD literature many methodologies have been used to assess dietary intake, including 24-hour recalls,

FFQ, diet histories, and dietary records. In a review of 56 articles investigating diet and IBD course (Table 1), twenty-six implemented FFQs, eight implemented diet recalls, fourteen implemented diet records, four implemented dietary screeners, and six implemented study designed instruments. Some instruments were validated in the study population (Opstelten et al., 2018; Vagianos et al., 2016) while others were validated in populations different from that of the study (Geerling et al., 2000; Gilman, Shanahan, & Cashman, 2006; Vagianos et al., 2007). Some of the instruments were validated in the nutritional outcome relevant to the study (Pedersen et al., 2017; Vernia et al., 2014) and others were novel and not validated outside of their study (Kyaw et al., 2014; Magee et al., 2005). Many studies also collected biochemical samples to verify participant intake of the nutrient of interest and to investigate the nutrient status of participants (Gee, Grace, Wensel, Sherbaniuk, & Thomson, 1985; Geerling et al., 2000; Papada, Amerikanou, Forbes, & Kaliora, 2020; Ripoli, Miszputen, Ambrogini, & Carvalho, 2010; Silvennoinen, Lamberg-Allardt, Karkkainen, Niemela, & Lehtola, 1996; Vagianos et al. 2007). For example, Vagianos et al. (2007) implemented a FFQ, food diary, and biochemical sample to assess the specific nutrient intake and nutrient status of IBD patients. Using this combination of instrumentation, researchers were able to associate dietary intake with serum levels of micronutrients like folate, vitamin B₁₂, and vitamin B₆. While serum levels of specific nutrients do not always reflect accurate nutrient status, when it is feasible and appropriate, biochemical samples can add validation to dietary assessment data. Overall, establishing a study design that gathers accurate, thorough

dietary data is a challenge due to the need to collect extensive, detailed data without overburdening participants.

Table 1. Articles reviewed for dietary assessment literature review, organized by primary outcome of interest.

Author, Year, Country	Outcome	Disease Type (Sample Size)	Study Design	Assessment Method	Assessment Instrument
Antioxidant:					
Geerling, 2000a, the Netherlands	Antioxidant; Fat; Habitual Diet	UC; CD (69)	Cross-sectional	FFQ; Diet History	Validated in pregnant Dutch population. Specific to fat and antioxidant intake.
Calcium:					
Gilman, 2006, Ireland	Calcium; Vitamin D	CD (58)	Cross-sectional	FFQ	Validated in Irish population.
Kuwabara, 2009, Japan	Calcium; Vitamin D; Vitamin K; Habitual Diet	UC; CD (25)	Cross-sectional	1 Day Diet Record	—
Lopes, 2014, Brazil	Calcium; Dairy	UC; CD (65)	Cross-sectional	FFQ	Validated for use in chronic disease intervention studies.
Silvennoinen, 1996, Finland	Calcium; Dairy	UC; CD (152)	Cross-sectional	FFQ	Validated in Finnish population.
Vernia, 2014, Italy	Calcium	UC; CD (187)	Cross-sectional	FFQ	Validated to measure calcium intake in Italian population.
Diet Adherence:					
Berghouse, 1984, UK	Diet Adherence	UC, CD with Ileostomies (10)	Case Cross-over	1 Day Diet Record	—
Chiba, 2010, Japan	Diet Adherence	CD Remission (22)	Prospective	FFQ	Validated in Japanese population.

Table 1 (cont.). Articles reviewed for dietary assessment literature review, organized by primary outcome of interest.					
Author, Year, Country	Outcome	Disease Type (Sample Size)	Study Design	Assessment Method	Assessment Instrument
Kyaw, 2014, UK	Diet Adherence, Habitual Diet	UC (112)	Randomized Control Trial	FFQ	Study designed.
Maagaard, 2016, Denmark	Diet Adherence	UC; CD; IBS (180)	Prospective	Study Designed Questionnaire	Designed to measure adherence to low FODMAP intervention diet.
Marlow, 2013, New Zealand	Diet Adherence	CD (8)	Prospective	Food Diary & Self-Reported Dietary Compliance	—
Olendzki, 2014, USA	Diet Adherence	UC; CD (27)	Case Series	Food Diary	—
Papada, 2020, Greece	Diet Adherence	CD (86)	Cross-sectional	FFQ	MedDiet scoring method
Fat:					
Ferreira, 2010, Portugal	Fat; MUFA; PUFA; Trans FA	CD (99)	Case-Control, Cross-sectional	FFQ	Validated in Portuguese population.
Tanaka, 2007, Japan	Fat; Habitual Diet	CD Remission (76)	Prospective Cohort	FFQ	Validated in Japanese population.
Fiber:					
Bartel, 2007, Austria	Fiber; Diet Adherence	CD Active (18)	Randomized Control Trial	Food Diary	—

Table 1 (cont.). Articles reviewed for dietary assessment literature review, organized by primary outcome of interest.					
Author, Year, Country	Outcome	Disease Type (Sample Size)	Study Design	Assessment Method	Assessment Instrument
Brotherton, 2016, USA	Fiber	UC Remission; CD Remission (1,619)	Prospective	Dietary Screener	Validated 26-item Dietary Screener Questionnaire from the National Cancer Institute.
Dhingra, 2017, India	Fiber; Habitual Diet	UC Remission (97)	Prospective	FFQ; Qualitative Fiber Questionnaire	Pre-tested, open-ended, semi-quantitative FFQ, developed with guidelines from National Institute of Nutrition, Hyderabad, India.
Levenstein, 1985, Italy	Fiber; Diet Adherence	CD Active (52)	Prospective	1 Week Diet Recall	—
Ritchie, 1987, UK	Fiber; Diet Adherence; Sugar	CD (178)	Intervention Study	2 Day Food Diary; Structured Interview	—
FODMAP: Gearry, 2009, Australia	FODMAP; Diet Adherence	UC; CD (52)	Retrospective	Structured Interview	Study-Designed
Halmos, 2016, Australia	FODMAP; Diet Adherence; Fiber; Habitual Diet; Sugar	CD (9)	Randomized Control Trial, Blind, Cross-Over	Food Diary	—
Pedersen, 2017, Denmark	FODMAP; Diet Adherence	UC Remission; CD Remission (89)	Randomized Control Trial	FFQ	Comprehensive Nutrition Assessment Questionnaire

Table 1 (cont.). Articles reviewed for dietary assessment literature review, organized by primary outcome of interest.					
Author, Year, Country	Outcome	Disease Type (Sample Size)	Study Design	Assessment Method	Assessment Instrument
Food Avoidance:					
Bergeron, 2018, Canada	Food Avoidance	UC; CD (245)	Cross-sectional	FFQ	Dietary History Questionnaire-II, Adapted for Canada.
Vagianos, 2016, Canada	Food Avoidance; Habitual Diet; Sugar	UC; CD (256)	Longitudinal	FFQ; Food Avoidance Questionnaire; Sugar Intake Questionnaire	Canadian Health Measures Survey; Study Designed Food Avoidance and Sugar Intake Questionnaires
Walton, 2014, UK	Food Avoidance; Habitual Diet	UC (93)	Cross-sectional	24-Hour Recall; Questionnaire	Study-Designed Questionnaire
Habitual Diet:					
Benjamin, 2008, India	Habitual Diet	CD (112)	Cross-sectional	24-Hour Recall; FFQ	Validated to measure energy and fat intake of affluent Northern Indian population.
Bueno-Hernandez, 2015, Mexico	Habitual Diet	UC (233)	Cross-Sectional; Prospective	Study-Designed Questionnaire	Designed and Validated in Study.
Cohen, 2013, USA	Habitual Diet	UC; CD (2,329)	Cross-sectional	Dietary Screener	Validated 26-item Dietary Screener Questionnaire from the National Cancer Institute.
Filippi, 2006, France	Habitual Diet	CD Remission (54)	Cross-sectional	3-Day Food Record	—
Gee, 1985, Canada	Habitual Diet	UC; CD (114)	Cross-sectional	48-Hour Recall	—

Table 1 (cont.). Articles reviewed for dietary assessment literature review, organized by primary outcome of interest.					
Author, Year, Country	Outcome	Disease Type (Sample Size)	Study Design	Assessment Method	Assessment Instrument
Guerreiro, 2007, Portugal	Habitual Diet	CD Remission (78)	Cross-Sectional, Case-Control	FFQ	FFQ validated in Portuguese population.
Han, 2020, USA	Habitual Diet	UC; CD (454)	Cross-sectional	Dietary Screener	Validated 26-item Dietary Screener Questionnaire from the National Cancer Institute.
Imes, 1987, Canada	Habitual Diet	CD (137)	Prospective	48-Hour Recall; Food Diary	122 item food list based on Block FFQ
Joachim, 1999, Canada	Habitual Diet	UC; CD (60)	Cross-sectional	FFQ	
Jowett, 2004, UK	Habitual Diet	UC (183)	Prospective	FFQ	Validated in UK population.
Jowett, 2004, UK	Habitual Diet	UC (183)	Prospective	FFQ	Validated in UK population.
Kakodkar, 2015, USA	Habitual Diet	UC Remission; CD Remission (50)	Case Series	3-Day Food Record	—
Komperød, 2017, Norway	Habitual Diet	CD Remission (12)	Cross-sectional; Prospective	Food List Questionnaire	Study-Designed.
Lim, 2014, Korea	Habitual Diet	UC; CD (41)	Cross-sectional	24-Hour Recall	—
Magee, 2005, UK	Habitual Diet	UC (81)	Cross-sectional	7-Day Validated Diet History	Study-Designed.
Opstelten, 2018, the Netherlands	Habitual Diet	UC; CD (165)	Cross-sectional; Longitudinal	FFQ	Adapted from validated FFQ.
Ripoli, 2010, Brazil	Habitual Diet	UC (65)	Longitudinal	3-Day Food Record; FFQ	No citation for FFQ.

Table 1 (cont.). Articles reviewed for dietary assessment literature review, organized by primary outcome of interest.					
Author, Year, Country	Outcome	Disease Type (Sample Size)	Study Design	Assessment Method	Assessment Instrument
Tasson, 2017, Italy	Habitual Diet	UC; CD (103)	Cross-sectional	FFQ	Adapted from EPIC-Norfolk FFQ. Validated in small group prior to study.
Triggs, 2010, New Zealand	Habitual Diet	CD (446)	Cross-sectional	Food List Questionnaire	Study-Designed.
Urbano, 2013, Brazil	Habitual Diet	UC Remission (59)	Cross-sectional	24-Hour Recall	Multi-pass method.
Vagianos, 2007, Canada	Habitual Diet	UC; CD (126)	Cross-sectional	FFQ; Food Diary	Validated for fat and calcium intake of menopausal women.
Vidarsdottir, 2016, Iceland	Habitual Diet	UC; CD (78)	Cross-sectional	3-Day Food Record; Study-Designed Questionnaire	—
Wada, 2015, Japan	Habitual Diet	UC; CD (388)	Cross-sectional	Diet History Questionnaire	Validated in Japanese population.
Weng, 2019, China	Habitual Diet	UC; CD (322)	Cross-sectional; Case-control	FFQ	Validated in Chinese population.
Iron:					
Lomer, 2004, UK	Iron; Habitual Diet	CD Remission (91)	Cross-sectional; Case-control	7-Day Food Diary	Validated through EPIC study.
Tolkien, 2013, Finland	Iron; Habitual Diet	UC (103)	Cross-sectional	7-Day Food Diary	Validated through EPIC study.

Table 1 (cont.). Articles reviewed for dietary assessment literature review, organized by primary outcome of interest.					
Author, Year, Country	Outcome	Disease Type (Sample Size)	Study Design	Assessment Method	Assessment Instrument
Miscellaneous:					
Albenberg, 2019, USA	Red & Processed Meat; Fiber; Habitual Diet; Iron	CD Remission (213)	Randomized Control Trial	FFQ	Dietary History Questionnaire-II
Chiarello, 2009, Brazil	Folate	UC; CD (10)	Prospective	24-Hour Recall	—
Skolmowska, 2019, Poland	Isoflavone	UC Remission (56)	Cross-sectional	3-Day Food Record	—
Suibhne, 2012, Ireland	Vitamin D	CD (151)	Cross-sectional, Case-control.	FFQ	Validated for calcium and vitamin D intake.
CD: Crohn's Disease; UC: Ulcerative Colitis; FFQ: Food Frequency Questionnaire					

Conclusion

This literature review describes the relationship between IBD and diet and emphasizes the complexity of dietary assessment in the IBD populations. It also highlights the challenge of reproducing generalizable dietary research due to suboptimal dietary assessment methodologies and observational study designs. In order to draw strong, evidence-based conclusions about the role of diet in the treatment and maintenance of IBD, rigorous randomized controlled trials examining the efficacy of diets like the SCD and LFD are necessary. Nevertheless, it is clear that people with IBD hold strong dietary beliefs and alter their dietary intake in an effort to manage their disease status and symptoms.

Due to the prevalence of malnutrition in the IBD population and the associated negative outcomes, it is necessary to assess and quantify the extent to which the dietary beliefs of IBD patients lead to disordered, restrictive eating behaviors and their impact on nutritional status. Currently, there is no research investigating ARFID risk in the IBD population, nor is there any research exploring the association between ARFID risk and nutritional status. Chapter two will describe the prevalence of ARFID risk in the adult, IBD population and it will examine the relationship between ARFID risk and nutritional status. With more information on avoidant and/or restrictive eating behavior and its association with malnutrition, health care professionals can equip themselves with tools to provide targeted screenings, prevention, and treatment for high risk patients going forward.

CHAPTER 2

Journal Article

PREVALENCE OF AVOIDANT/RESTRICTIVE FOOD INTAKE DISORDER AND ASSOCIATION WITH NUTRITION STATUS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES

Abstract

Background: Inflammatory bowel disease (IBD) patients often alter their normal dietary behaviors. The prevalence of avoidant restrictive food intake disorder (ARFID) and its impact on nutritional status among IBD patients are unknown. The purpose of this study was to describe the prevalence of and risk factors for ARFID risk and to examine the relationship between ARFID risk and nutritional status in IBD patients.

Methods: This cross-sectional study recruited adult IBD patients from an outpatient clinic. ARFID risk was measured using the Nine-Item ARFID Screen (NIAS). Nutritional status was measured with the Patient Generated-Subjective Global Assessment (PG-SGA). Patient demographics, disease characteristics, and medical history were abstracted from medical records.

Results: Of the 161 participants, 17% were at ARFID risk. Ninety-two percent avoid food(s) during a flare, while 74% avoid food(s) in the absence of a flare. Participants who avoid food, regardless of disease status had significantly higher ARFID risk scores compared to those who do not avoid food. Patients who reported symptoms of diarrhea, pain, no appetite, and fullness were significantly more likely to be at ARFID risk. There was a positive relationship between ARFID risk and PG-SGA score ($r_s = 0.196$, $P = 0.024$).

Conclusion: Avoidant eating behaviors are prevalent in IBD patients. The positive correlation between ARFID risk score and PG-SGA score indicates that ARFID risk and malnutrition risk are associated. These findings suggest that IBD patients should have

regular visits with registered dietitians who can monitor both disordered eating behaviors and malnutrition risk, directing appropriate nutrition intervention.

Keywords: inflammatory bowel disease, ulcerative colitis, Crohn's disease, avoidant/restrictive food intake disorder, malnutrition

Background

Inflammatory bowel disease (IBD) is a chronic inflammatory illness that encompasses two diagnoses: Crohn's disease (CD) and ulcerative colitis (UC). Both diseases are characterized by periods of heightened activity and remission. Increased disease activity is commonly referred to as a flare, and signs and symptoms include abdominal pain, diarrhea, bloody stool, and/or frequent bowel movements.¹ There is no cure for CD or UC and the best outcome for people with IBD is to remain in remission, while managing uncomfortable and disruptive functional gastrointestinal symptoms. Disease etiology and status in IBD is multifactorial and influenced by a combination of genetic and environmental factors.¹ One of the environmental factors that people with IBD can manipulate is diet. While many diets have been suggested for the management of functional gastrointestinal symptoms and disease management, there is a lack of easily accessible, conclusive, dietary recommendations on which patients can make dietary choices.² Even so, it is well documented that people with IBD believe that their dietary choices influence their disease status.^{3,4} This leads patients with IBD to limit their dietary intake based on advice from the internet or general clinical practitioners.^{4,5} When this independent, unsupervised approach at dietary intake is combined with confusion about what defines the most appropriate diet for IBD, patients may alter their normal dietary choices and behaviors and may run the risk of developing restrictive eating behaviors that can result in deficient nutritional intake, increasing their risk for malnutrition.^{6,7}

In 2013 avoidant/restrictive food intake disorder (ARFID) was introduced into the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) to broaden the scope of

what was previously known as feeding disorder of infancy and early childhood. The new ARFID diagnosis is applicable to individuals of any age whose avoidant/restrictive eating behaviors lead to insufficient caloric and/or nutrient intake and cause at least one of the following symptoms: weight loss, nutritional deficiency, dependence on nutritional supplements, or psychosocial impairment.⁹ The DSM-5 describes three categories that can lead to the symptoms of ARFID: avoidance of many foods based on their sensory properties (“picky eating”); low appetite or limited interest in eating; and fear of negative consequences, such as choking, vomiting, or other painful or uncomfortable symptoms that might be associated with eating, such as abdominal pain and bloating.⁹⁻¹¹ Because of the recency with which ARFID was added to the DSM-5, there have not been any large scale epidemiological studies conducted to measure the prevalence in the general population¹⁰; however, studies have shown that the prevalence of ARFID in patients with gastrointestinal disorders is 12–21%.^{11,12} While these studies demonstrate that ARFID is prevalent in the gastrointestinal disorder population, they do not address how it impacts the nutritional status of patients.

The association between restrictive eating and nutrition status is important to investigate because IBD patients are at a higher risk for malnutrition. Studies have shown that between 29–68% of IBD patients are malnourished^{6,13,14} and have significantly lower mean daily intakes and plasma concentrations of essential micronutrients compared to healthy controls.⁶

These studies demonstrate the prevalence of malnutrition in IBD, but they do not address any association with restrictive eating behaviors. Given the evidence that people

with IBD do restrict their intake, it is reasonable to expect that patients with ARFID may be at an even higher risk for malnutrition. The three aims of this study were to describe the prevalence of ARFID risk in the adult, IBD population, to identify risk factors for ARFID, and to examine the relationship between ARFID risk and nutritional status. With more information on the prevalence of restrictive eating and its association with malnutrition, practitioners can equip themselves with tools to provide targeted screenings, prevention, and treatment for high risk patients going forward.

Materials and Methods

Participant Recruitment

This cross-sectional study was conducted at the University of California, Los Angeles (UCLA) Center for Inflammatory Bowel Diseases from October 2019 to March 2020. English speaking, adult patients receiving care at this outpatient clinic with a confirmed IBD diagnosis (Crohn's disease, ulcerative colitis, or IBD-unknown) were invited to participate in the study. Participants were excluded from the study if they had a medical diagnosis of celiac disease, active anorexia nervosa or bulimia nervosa, an unmanaged psychological disorder, alcohol abuse or if they were pregnant. Written consent was obtained from eligible participants. The study was approved by UCLA's Institutional Review Board and a data sharing agreement was established between San José State University and UCLA.

Demographic and Medical History Collection

Data were collected from participants by hardcopy survey before scheduled in-clinic appointments. Medical data regarding the age, gender, race, ethnicity, substance use,

disease subtype (CD, UC, IBD-unknown), and disease duration of participants were abstracted from electronic medical records. Current medication use was also identified in electronic medical records and was categorized as aminosalicylates, steroids, immunomodulators or biologics. CD location was classified as ileal, colonic, ileocolonic, upper GI, or unknown and CD behavior was classified as inflammatory, structuring, fistulizing, or perianal. UC extent was classified as rectum, left colon, pancolon, or unknown. Participants were identified as having no flare, recent flare (within 60 days), or active flare and previous small bowel resection, colectomy, or ileoanal anastomosis pouch surgeries were recorded.

Assessment of Avoidant/Restrictive Food Intake Disorder Risk

Avoidant/restrictive food intake disorder (ARFID) risk was measured using a the Nine Item Avoidant/Restrictive Food Intake Disorder Screen (NIAS) which has been validated in a nationally representative subject pool, an undergraduate student population, and in a population selected for eating difficulties.¹⁵ The screening tool is organized into three specific domains of ARFID that have been identified by the DSM-5, each of which is addressed by three questions. The three domains assess eating restriction due to picky eating, poor appetite/limited interest in eating, and fear of negative consequences from eating. Each domain includes three questions and the scores range from 0 to 15 max. When compared to other instruments that measure picky eating, appetite, and fear, the ARFID risk screening tool has high internal consistency (Cronbach's $\alpha = 0.90$), test-retest reliability (ICC = 0.65, 95% CI: 0.56–0.72), and convergent/discriminant validity for adults aged 18–65. Questions are based on a 6-point Likert scale with 0 indicating

“strongly disagree” and 5 indicating “strongly agree.” Survey responses were totaled for an ARFID risk score that ranged from 0–45. Ellis et al.¹⁶ demonstrated that a total cutoff score of 24 showed good sensitivity (0.74) and specificity (0.84) for identifying a positive ARFID diagnosis. Additional questions were added to the survey to provide more detail about the eating behaviors of participants. One question asked whether the participant has consistent access to food and another asked whether they make dietary choices based in specific cultural practices. Participants were also asked “during a flare do you avoid any of the following foods: lactose containing foods, spicy foods, alcohol, wheat products, deep fried/fatty foods, caffeine, or other” and “during remission do you avoid any of the following foods: lactose containing foods, spicy foods, alcohol, wheat products, deep fried/fatty foods, caffeine, or other.” If participants answered yes to one or more foods, they were categorized as avoiding food. If they answered no, they were categorized as not avoiding food.

Assessment of Nutritional Status

Nutritional status risk was measured using an adapted version of the validated Scored Patient-Generated Subjective Global Assessment Short Form (PG-SGA).¹⁷ The PG-SGA is based on self-reported criteria and has been validated to measure nutritional risk in ambulatory oncology settings,¹⁸ an internal medicine ward,¹⁹ and in non-oncology surgery patients.²⁰ The PG-SGA has four sections covering recent weight change, changes in food intake, symptoms with possible nutrition impact, and activities and functions and has been described elsewhere.¹⁷ Of importance to this study was the overall PG-SGA score (0(low risk)–36(high risk)) which indicates malnutrition risk.¹⁷ Gabrielson

et al.²¹ found that a cutoff score of six or greater had high sensitivity (0.938) and specificity (0.776) and was optimal for capturing patients with confirmed malnutrition. Percent weight loss over past month was calculated from the patient report of current weight and weight from one-month prior on the PG-SGA. To determine nutrition impact symptoms, responses to the third section of the PG-SGA were used. Participants were asked to select symptom(s) that kept them from eating enough during the past two weeks and were instructed to select all symptoms that apply. IBD related symptoms were reviewed for this study and included: no appetite, just did not feel like eating; vomiting; nausea; diarrhea; constipation; smells bother me; feel full quickly; fatigue; pain; and other.

Data Analysis

All statistical analyses were performed using SPSS and results were considered statistically significant when $P < 0.05$. Continuous variables were tested for normalcy using the Shapiro-Wilk test. Parametric data were summarized as means ($\pm$ standard deviation (SD)) or percentages and non-parametric data were summarized as median (interquartile range (IQR)). To test for significant differences between ARFID domains, the Kruskal-Wallis test was performed. The Kruskal-Wallis test was also used to test for differences in ARFID risk score across clinical characteristics (BMI, flare status, gender, IBD type). Any significant differences were analyzed post-hoc using a Mann-Whitney U test, adjusted with a Bonferroni correction. Multiple linear regression was used to evaluate associations between clinical characteristics and ARFID risk score. Correlations between total ARFID risk score, and measures of nutritional status were evaluated using

the Spearman correlation coefficient. Nominal results were tested for dependence using the chi-square test. If criteria for the chi-square test were not met the Fisher's Exact test was used.

Ethical Considerations

Consent was obtained from all participants and the ethics committee at UCLA approved the study.

Results

Participant Demographics

One hundred and sixty-one patients were enrolled in the study, completed the ARFID risk questions, and were included in this study. Of the 161 participants, 73 had CD (45.3%), 83 had UC (51.6%), and 5 had IBD-unclassified (3.1%). Eighty-eight participants were female (54.7%) and 73 were male (45.3%). The average age of participants was 41.1 years (SD $\pm$ 15.5). The majority of participants were white (n = 114, 70.8%), 14 were Hispanic (8.7%), 3 were Asian (1.9%), and 6 were black (3.7%) (Table 1). The mean duration of IBD diagnosis was 13.0 years (SD $\pm$ 11.6). The majority of patients had no recent flare (n = 110, 68.3%), 11 (6.8%) patients had a flare within 60 days, and 40 (24.8%) patients had an active flare. Twenty-two (13.7%) participants reported that they make dietary choices based in cultural practices. Fifty-four percent of participants had a BMI in the normal range, 5.6% were underweight, and 40.4% of participants were overweight/obese (mean 24.7; SD $\pm$ 4.6). BMI did not differ between IBD types (Kruskal-Wallis H: 2.395, P = 0.302) (Table 2).

TABLE 2. Demographic and Clinical Characteristics

	n, (%)	Mean ($\pm$ SD)	Median (IQR)
Age	161 (100)	41.1 (15.5)	38.3 (21.2)
Gender	161 (100)		
Female	88 (54.7)		
Male	73 (45.3)		
BMI	161 (100)	24.7 (4.6)	23.8 (5.5)
Underweight	9 (5.6)	17.2 (1.2)	17.5 (1.3)
Normal	87 (54.0)	22.2 (1.6)	22.3 (2.4)
Overweight	47 (29.2)	27.1 (1.5)	27 (2.4)
Obese	18 (11.2)	34.0 (3.4)	33 (5.1)
Disease Duration	159 (98.8)	13.0 (11.6)	10.0 (10.0)
IBD Type	161 (100)		
Crohn's disease	73 (45.3)		
Ulcerative colitis	83 (51.6)		
IBD-U	5 (3.1)		
Race	161 (100)		
Asian	3 (1.9)		
Black	6 (3.7)		
White	114 (70.8)		
Other	38 (23.6)		
Hispanic	161 (100)		
Yes	14 (8.7)		
No	147 (91.3)		
CD Location	73 (45.3)		
Ileal	21 (28.8)		
Colon	16 (21.9)		
Ileocolonic	35 (47.9)		
Upper Gastrointestinal	1 (1.4)		
CD Behavior	73 (45.3)		
Inflammatory	36 (49.3)		
Stricturing	17 (23.3)		
Fistulizing	21 (28.8)		
Perianal	25 (15.5)		
Number of EIM	161 (100)		
0	121 (62.1)		
1	27 (16.8)		
2+	13 (8.1)		
Flare Status	161 (100)		
No Recent Flare	110 (68.3)		
Recent Flare within 60 Days	11 (6.8)		
Active Flare	40 (24.8)		

TABLE 2 (cont.). Demographic and Clinical Characteristics			
	n, (%)	Mean ($\pm$ SD)	Median (IQR)
Current Medications			
Aminosalicylates	64 (39.8)		
Steroids	38 (23.6)		
Immunomodulators	49 (30.4)		
Biologics	88 (54.7)		
Number of Prior Biologics	161 (100)		
0	109 (67.8)		
1	23 (14.3)		
2+	29 (18.0)		
Number of Surgeries	161 (100)		
0	134 (83.2)		
1	18 (11.2)		
2	9 (5.6)		
Surgical History			
None	134 (83.2)		
Small Bowel Resection	15 (9.3)		
Colectomy	14 (8.7)		
Ileal Pouch-Anal Anastomosis	7 (4.3)		
Current Substance Use			
Smoking	6 (3.7)		
Drugs	20 (12.8)*		
Alcohol	73 (45.3)		
CD: Crohn's disease; UC: ulcerative colitis; IBD-U: inflammatory bowel disease-unclassified; EIM: extraintestinal manifestation			
*n=156			

Avoidant/Restrictive Food Intake Disorder Risk

The first aim of this study was to describe the prevalence of ARFID risk indicated by a score of $\geq 24^{16}$ in an IBD population in Southern California. The median overall ARFID risk score was 12 (IQR 7–20) with 17% of participants scoring ≥ 24 (Table 3). Of the three domains that were assessed by the ARFID risk screening questionnaire, the fear of negative consequences domain scored the highest with a median score of 5 (IQR 3–9) and was significantly higher than the poor appetite domain which had a median score of 3

(IQR 0–6, $P < 0.001$) (Table 3). ARFID risk score was greater for participants who make dietary choices based in cultural practices (median 18, IQR 9–26) compared to participants who do not make dietary choices based in cultural practices (median 12, IQR 7–19, $P = 0.49$) (Table 3). Ninety-two percent of participants ($n = 148$) avoid one or more foods when they are having a flare, while 74% ($n = 119$) avoid one or more foods in the absence of a flare. In a flare, 54% ($n = 87$) of participants reported that they avoid lactose containing foods, 71% ($n = 114$) reported that they avoid spicy foods, 70% ($n = 112$) reported that they avoid alcohol, 38% ($n = 61$) reported that they avoid wheat products, 67% ($n = 108$) reported that they avoid deep fried/fatty foods, and 45% ($n = 73$) reported that they avoid caffeine. In absence of a flare, 37% ($n = 60$) of participants reported that they avoid lactose containing foods, 43% ($n = 70$) reported that they avoid spicy foods, 40% ($n = 64$) reported that they avoid alcohol, 23% ($n = 37$) reported that they avoid wheat products, 39% ($n = 62$) reported that they avoid deep fried/fatty foods, and 22% ($n = 36$) reported that they avoid caffeine. In both flare and no flare, participants commonly wrote in that they avoid meat and vegetables.

The second aim of this study was to identify risk factors for ARFID. There were no significant differences in ARFID risk score across IBD type, flare status, or gender (Table 3). Participants who reported avoiding food during a flare and in the absence of a flare had significantly higher ARFID risk scores ($P < 0.001$, $P = 0.030$, respectively) (Table 3). Forty-six percent of participants reported one or more symptom that prevented eating enough over the past two weeks. The most frequently reported problems were fatigue (17%); no appetite, just did not feel like eating (16%); diarrhea (16%); pain

(15%); feel full quickly (14%); and nausea (13%). Participants who responded affirmatively to symptoms of diarrhea, pain, no appetite, and fullness were significantly more likely to have an ARFID risk score above 24 ($P = 0.009$, $P = 0.002$, $P \leq 0.001$, $P \leq 0.001$, respectively). In the multiple linear regression analysis, participants with prior biologic use were found to have an ARFID score 3.3 points higher than participants with no prior biologic use (95% confidence interval 0.30–6.3, $P = 0.033$). Age, gender, alcohol consumption, disease activity, flare status, steroid use, and colon resection were not found to be associated with higher ARFID risk scores.

TABLE 3. Comparison of Avoidant/Restrictive Food Intake Disorder (ARFID) Risk Score by Domain and Total ARFID Risk Score Across IBD Patient Characteristics

	Sample Size (%)	Median (IQR)	Test Statistic	<i>P</i>
Total ARFID Risk Score (minimum: 0 maximum: 45)	161 (100)	12 (7–20)		
Picky Eating Score (minimum: 0 maximum: 15)	161 (100)	4 (2–7) ^{ab}	18.5	< 0.001
Poor Appetite Score (minimum: 0 maximum: 15)	161 (100)	3 (0–6) ^a		
Fear of Negative Consequences Score (minimum: 0 maximum: 15)	161 (100)	5 (3–9) ^b		
IBD Type				
Crohn’s disease	73 (45.3)	11.5 (7–19)	0.013	0.994
Ulcerative colitis	83 (51.6)	13 (7–20)		
IBD-unclassified	5 (3.1)	11 (9–15)		
Flare Status				
No Recent Flare	110 (68.3)	12 (6.25–17)	5.212	0.074
Recent Flare within 60 Days	11 (6.8)	10 (8–15)		
Active Flare	40 (24.8)	18.5 (8.75–26)		

TABLE 3 (cont). Comparison of Avoidant/Restrictive Food Intake Disorder (ARFID) Risk Score by Domain and Total ARFID Risk Score Across IBD Patient Characteristics

	Sample Size (%)	Median (IQR)	Test Statistic	<i>P</i>
Gender				
Female	88 (54.7)	14.5 (9–20)	3.623	0.057
Male	73 (45.3)	11 (6–18)		
Makes Dietary Choices Based in Cultural Practices				
Yes	22 (13.7)	18 (9–26)	3.874	0.49
No	139 (86.3)	12 (7–19)		
Avoids Food During Flare				
Yes	148 (91.9)	13 (8–20)	4.712	0.030
No	13 (8.1)	6 (5–11)		
Avoids Food in Absence of Flare				
Yes	119 (73.9)	15 (9–20)	12.405	< 0.001
No	42 (26.1)	8 (5–12.75)		

Kruskal-Wallis test was used to test for differences in ARFID risk score across clinical characteristics and across domains.

^{ab}Values without a common superscript are significantly different as determined by Mann-Whitney U test and adjusted with Bonferroni's correction.

Nutritional Status

The third aim of the study was to determine the relationship between ARFID risk and nutritional status. The PG-SGA questionnaire was completed by 133 participants and nutritional risk was quantified. Twenty-nine percent of participants scored ≥ 6 . The median nutritional risk score was 2 (IQR 1–6) (Table 4). Results indicated a positive linear relationship ($r_s(131) = 0.196$, $P = 0.024$) between ARFID risk score and PG-SGA score, indicating that participants who scored higher for ARFID risk also scored higher

for nutritional status risk (Table 4). BMI was inversely correlated to ARFID risk score ($r_s(159) = -0.161, P < 0.042$); participants with a lower BMI score had a significantly higher ARFID risk score (Table 4). Percent weight loss (median = 0, IQR -1.8–0.91) did not differ based on IBD type ($P = 0.549$) or flare status ($P = 0.062$) and there was no correlation between ARFID risk score and percent weight loss ($r_s(153) = 0.081, P = 0.821$) (Table 4).

TABLE 4. Correlation of Avoidant/Restrictive Food Intake Disorder (ARFID) Risk Score to Measures of Nutritional Status

	Sample Size	Median (IQR)	Rho	P
Overall Nutritional Risk Score (minimum: 0 maximum: 36)	133	2 (1–6)	0.196	0.024
BMI	161	23.8 (21.6–27.1)	-0.161	0.042
Percent Weight Loss	154	0 (-1.8–0.91)	0.018	0.821
Intake Score (minimum: 0 maximum: 4)	133	1 (0–1)	0.039	0.654
Spearman's Rho was used to measure correlation between ARFID risk score and measures of nutritional status.				

Discussion

The primary aim of this study was to describe the prevalence of ARFID risk, a feeding disorder characterized by avoidant and/or restrictive eating behaviors in an outpatient IBD population in Southern California. This study found that 17% of IBD patients were at risk for ARFID, specifically, 16.4% of CD patients and 19.3% of UC patients were at ARFID risk. No difference in ARFID risk was found between type of IBD, sex, or flare status. In the general gastrointestinal disorder population, ARFID risk has been reported between 12–21%.^{11,12} ARFID is associated with co-occurring anxiety

disorders, gastrointestinal complications, and malnutrition and proper diagnosis can help direct treatment and prevent nutritional and psychological complications.²² This was the first cross-sectional study to look at the prevalence of ARFID risk in an IBD specific population using a validated questionnaire. In line with previous research in the gastrointestinal population⁸ and because the Nine-Item ARFID Screen has not previously been used in the IBD population, a cutoff of 24 was selected for this study; however, in a population selected for eating disturbances, researchers found that a score of 28 was necessary to achieve adequate sensitivity and specificity.¹⁶ Future validation in the IBD population would improve the utility of the screener in clinical practice.

Results show that 92% of IBD patients avoid foods when they are having a flare compared to 74% who avoid foods in the absence of a flare. Cross-sectional studies have found that between 49–90% of IBD patients avoid or restrict foods.^{3–5} This avoidance is likely due to patient beliefs that certain foods exacerbate IBD symptoms.^{23,24} One-half of our participants reported a nutrition impact symptom. The participants who reported that at least one of the symptoms—diarrhea, pain, no appetite, or fullness—prevented them from eating normally in the prior two weeks, were significantly more likely to have an ARFID risk score of 24 or higher compared to those who did not. Previous research has shown that IBD symptoms impact dietary intake⁵; however, this is the first study to draw associations between IBD symptoms and ARFID risk score. Of the variables included in the multilinear regression analysis, prior biologic use was the only clinical characteristic that was associated with higher ARFID risk score. It is possible that the sample size in this study was not large enough to detect a significant impact of the other variables that

were included in the model. Although the majority of IBD patients are demonstrating food avoidance, there is no evidence-based guideline recommending the avoidance of any specific food to prevent or treat IBD flares.²⁵ Based on clinical experience, the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline development group agreed that all IBD patients should be regularly screened for malnutrition and micronutrient deficiencies and that impairments should be corrected individually when necessary.²⁵ Evidence supports the monitoring and supplementation of serum calcium and vitamin D levels for IBD patients in active disease and/or on steroid-treatments to help prevent low bone mineral density.²⁵ For UC patients in remission, there is also evidence to support the use of probiotic therapy for the maintenance of remission; however, probiotic therapy should not be used for maintenance of remission in CD.²⁵ There was a strong consensus, based on the clinical expertise of the ESPEN guideline group, that all IBD patients in remission should undergo counseling by a dietitian to improve nutritional therapy and to avoid malnutrition and nutrition-related disorders; although, the Academy of Nutrition and Dietetics could not draw conclusions about the optimal frequency, duration of nutrition professional visits, or medical nutrition therapy effectiveness for gastrointestinal disorders.²⁶

In the absence of strong evidence, the Academy of Nutrition and Dietetics Nutrition Care Manual (NCM) offers some guidance to practicing clinicians, advising that the primary goals of nutrition intervention should be to identify impediments to adequate oral intake, correct or compensate for malabsorption, and meet increased nutritional requirements, while correcting for nutritional deficiencies and losses.²⁷ The NCM

recommends IBD patients in active disease eat small, frequent meals that are low in fat and fiber and high in protein and calories, and IBD patients in disease remission should prioritize weight management and nutrient intake while making individualized adjustments for gastrointestinal function.²⁸ In a clinical practice expert review on the treatment of functional gastrointestinal symptoms in patients with IBD, Colombel et al.²⁹ endorse the implementation of a diet low in fermentable oligo-, di-, mono-saccharides and polyols (FODMAP) for IBD patients in remission. The recommendation specifies that because undernutrition is common in the IBD population and the low FODMAP diet is restrictive, it should be introduced and monitored by a dietitian with special attention placed on the provision of nutritional adequacy.²⁹ This type of dietary management requires the expertise of medical professionals to address patient-specific intolerances while mitigating the risk of energy and nutrient deficiencies.

Due to the prevalence of malnutrition in the IBD population^{13,14} and the self-reported evidence that IBD patients avoid or restrict foods in their diets³⁻⁵, this study sought to investigate whether ARFID was relevant in the IBD population and if it was associated with risk for compromised nutritional status. Malnutrition in IBD patients increases the risk of non-elective surgery, increased length of stay, and mortality.²⁵ Because malnutrition is challenging to measure, this study investigated multiple markers of nutritional status including weight status, percent weight loss, and the PG-SGA malnutrition screener. One-third of the IBD patients in this study were found to be at risk of malnutrition which aligns with previous reported prevalence rates of 29–68%.^{6,13,14} Unique to this study, higher ARFID risk was associated with higher malnutrition risk and

lower BMI status; although, only 6% of patients had a BMI low enough to be categorized as underweight and there was no association with recent weight loss and ARFID risk score. This study did not evaluate all six characteristics that can be used to diagnose malnutrition.³⁰ Future studies should include a nutrition focused physical exam to determine loss of muscle mass, subcutaneous fat, and fluid accumulation that may mask malnutrition.³¹

Regardless of flare status, participants reported that they avoid lactose containing foods, wheat products, meat, and vegetables, supporting avoidant dietary intake patterns that have been identified in previous studies.^{32,33} Common nutritional deficiencies in IBD patients that have been associated with food avoidance include vitamin D, calcium, iron, zinc, vitamin B₆, vitamin B₁₂, and vitamin C.^{32,33} Foods that are avoided by IBD patients such as dairy, meat, and raw fruits and vegetables are good sources of these essential nutrients and patients who avoid these foods may be at an increased risk for nutrient deficiencies.³⁴ Nutrient deficiencies have been associated with increased risk of osteoporosis, surgery, and hospitalization.^{35,36} In this study, dietary assessments were not collected, thus the nutrient intake and adequacy of participants could not be determined.

The majority of participants in this study avoid one or more foods during a flare or in remission. Our findings also show that IBD patients who report avoiding foods, whether in a flare or in the absence of a flare, have significantly higher ARFID risk scores compared to those who do not avoid foods. This indicates that IBD patient care should include discussion about food avoidance and ARFID risk assessment. If a patient avoids entire food groups, such as dairy, they should be referred to a registered dietitian as diet

counseling has been shown to have an impact on the nutritional status of IBD patients³⁷ and is recommended by the European Society for Clinical Nutrition and Metabolism.²⁵ It is well established that registered dietitian nutritionists are critical to the nutrition care of individuals with eating disorders³⁹ as they can perform nutrition focused physical examinations, assess biochemical results, and interpret weight status, implementing clinical judgement to direct interventions and mitigate impairments. According to registered dietitians, Scarlata et al.⁴⁰ in the irritable bowel syndrome population, restrictive dietary interventions, such as the low FODMAP diet, are not universally appropriate and are particularly risky for patients who are at risk for eating disorders. They suggest that irritable bowel syndrome patients should be screened for eating disorders and that patients who have maladaptive food avoidance would benefit from coordinated care between registered dietitians and mental health providers. The results from this study that demonstrate the prevalence of ARFID risk in the IBD population show that maladaptive food avoidance is relevant and that the clinical practice recommendation from Scarlata et al.⁴⁰ is applicable to IBD patients as well. While this may be time and resource intensive, individualization of dietary interventions is required to ensure their appropriateness, minimize nutritional risk, improve disease outcomes, and reduce the likelihood that maladaptive eating patterns and the associated risks are exacerbated.

In the future, researchers should confirm the prevalence of ARFID in the IBD population through clinical verification, assessing participants psychosocial impairment such as work or school interference, social interference, and family interference as well

as medical consequences such as ARFID related weight loss, reliance on supplemental feeding, and ARFID related nutritional deficiency.⁹ There is also a need for controlled, prospective studies to evaluate how ARFID impacts nutritional status or deficiencies. Finally, evidence-based practices for the treatment of ARFID should also be established through rigorous clinical trials.

In conclusion, this study establishes that IBD patients are at risk for ARFID and that there is an association between ARFID risk and nutritional status. With this knowledge, IBD patients should be screened for factors that were found to be associated with higher ARFID risk score such as avoidant eating behaviors, low BMI, IBD symptoms like diarrhea, pain, lack of appetite, and early satiety, and prior biologic treatment. Regular ARFID screening of IBD patients would help direct appropriate dietary interventions for disease and symptom management and could help identify early malnutrition risk, leading to earlier intervention and reduced negative outcomes.

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CHAPTER 3

Summary and Recommendations

Summary

Previous research has explored the relationship between diet, inflammatory bowel disease (IBD) etiology, and disease course; however, strong evidence-based practices for IBD prevention or disease management are limited due to inconsistent, poor-quality research (Forbes et al., 2017). As explored in chapter one, it is challenging to draw generalizable conclusions about the impact of diet on IBD from studies that implement inconsistent dietary assessment methodologies and observational study designs. Based on the lack of high-quality research, experts do not endorse the universal application of one diet pattern or the elimination of any specific foods for IBD prevention or management (Forbes et al., 2017); however, previous research and this study demonstrate that IBD patients do avoid or restrict foods (Limdi et al., 2016; Zallot et al., 2013). While avoidant or restrictive dietary behaviors may be effective and safe for the symptom management of some IBD patients, they could also increase their risk of malnutrition and/or nutrient deficiency. It is also possible that avoidant eating behaviors could indicate or portend the development of the feeding disorder avoidant/restrictive food intake disorder (ARFID), making the recommendation of a restrictive diet like the low fermentable oligo-, di-, mono-saccharides and polyols (FODMAP) diet, specific carbohydrate diet, or the anti-inflammatory diet inappropriate.

This study aimed to describe the prevalence of ARFID risk, identify risk factors for ARFID risk, and evaluate the relationship between ARFID risk and nutritional status in

the IBD population. While this study could not diagnose ARFID, it was the first study to demonstrate that a proportion of the IBD population is at risk for ARFID, with 17% of the 161 participants scoring equal to or above the cutoff value on the Nine-Item ARFID Screener instrument. Low body mass index (BMI), food avoidance regardless of disease status, and prior biologic treatment were identified as possible ARFID risk factors based on their association with higher ARFID risk scores. Participants who reported a nutritional impact symptom of diarrhea, pain, no appetite, or feeling full quickly were also significantly more likely to be at risk for ARFID. While these results do not demonstrate the direction of the relationship between IBD symptoms and ARFID risk, they do suggest a possible bi-lateral relationship between disease symptoms and restrictive eating behaviors. This was the first study to investigate the relationship between ARFID risk and nutritional status, finding that a higher ARFID risk score was associated with a higher malnutrition risk score.

Recommendations

The prevalence of ARFID risk in the IBD population and its association with increased nutritional risk, supports the recommendation that patients with IBD should be automatically referred to registered dietitians. Regular malnutrition screenings for the IBD population have been recommended elsewhere (Forbes et al., 2017) and this study augments that recommendation, proposing that if there is evidence that a patient has avoidant eating behaviors, the adequacy of their nutritional intake should be monitored closely. Implementing regular ARFID screenings in clinical practice could help practitioners easily identify patients with avoidant eating behavior and also help direct the

most appropriate nutrition interventions from registered dietitians. Patients who demonstrate avoidant eating behaviors may not be appropriate candidates for highly restrictive dietary interventions as a highly restrictive diet could exacerbate avoidant behaviors, leading to further food avoidance and increasing the risk for inadequate nutritional provision, nutrient deficiencies, and/or malnutrition.

Due to the novelty of this area of research, there are many outstanding research questions. First future research should confirm the prevalence of ARFID in the IBD population through clinical verification, assessing psychosocial impairments and medical consequences. There is also a need for controlled, prospective studies to evaluate how ARFID diagnosis or risk impacts the nutritional status or specific nutrient deficiencies of IBD patients. Finally, further research is necessary to establish strong evidence-based guidelines for when it is appropriate to implement restrictive diets in the IBD population and to determine evidence-based alternatives.

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APPENDIX A

University of California Los Angeles
10889 Wilshire Blvd, Suite 830
Los Angeles, CA 90095-1406

<http://ora.research.ucla.edu/ohrpp>
General Campus IRB: (310) 825-7122
Medical IRB: (310) 825-5344

APPROVAL NOTICE New Study

DATE:	9/5/2019
TO:	Berkeley Limketkai, MD, PhD MEDICINE-GASTROENTEROLOGY
FROM:	DANIEL CLEMENS, MD, PhD Chair, MIRB1
RE:	IRB#19-001299 Dietary Patterns of Patients with Inflammatory Bowel Diseases

The UCLA Institutional Review Board (UCLA IRB) has approved the above-referenced study. UCLA's Federalwide Assurance (FWA) with Department of Health and Human Services is FWA00004642.

Submission and Review Information

Type of Review	Expedited Review
Approval Date	9/5/2019
Expiration Date of the Study	9/4/2020

Regulatory Determinations

– **Waiver of Signed Informed Consent** - The UCLA IRB waived the requirement for signed informed consent for the research under 45 CFR 46.117(c)(2). An information sheet will be provided to the subjects.

Documents Reviewed included, but were not limited to:

Document Name	Document Version #
19-001299_MinRisk Information Sheet - Dietary Patterns in IBD v1 (clean).pdf.pdf	0.01

Important Note: Approval by the Institutional Review Board does not, in and of itself, constitute approval for the implementation of this research. Other UCLA clearances and approvals or other external agency or collaborating institutional approvals may be required before study activities are initiated. Research undertaken in conjunction with outside entities, such as drug or device companies, are typically contractual in nature and require an agreement between the University and the entity.

General Conditions of Approval

As indicated in the PI Assurances as part of the IRB requirements for approval, the PI has ultimate responsibility for the conduct of the study, the ethical performance of the project, the protection of the rights and welfare of human subjects, and strict adherence to any stipulations imposed by the IRB.

The PI and study team will comply with all UCLA policies and procedures, as well as with all applicable Federal, State, and local laws regarding the protection of human subjects in research, including, but not limited to, the following:

- Ensuring that the personnel performing the project are qualified, appropriately trained, and will adhere to the provisions of the approved protocol,
- Implementing no changes in the approved protocol or consent process or documents without prior IRB approval (except in an emergency, if necessary to safeguard the well-being of human subjects and then notifying the IRB as soon as possible afterwards),
- Obtaining the legally effective informed consent from human subjects of their legally responsible representative, and using only the currently approved consent process and stamped consent documents, as appropriate, with human subjects,
- Reporting serious or unexpected adverse events as well as protocol violations or other incidents related to the protocol to the IRB according to the OHRPP reporting requirements.
- Assuring that adequate resources to protect research participants (i.e., personnel, funding, time, equipment and space) are in place before implementing the research

APPENDIX B

DocuSign Envelope ID: 38A8D5F2-E307-40DD-B94D-71BFBD7E52DA

February 2019

FDP Data Transfer and Use Agreement

Agreement ID: MTA2020-00000579

FDP Data Transfer and Use Agreement ("Agreement")	
Provider: The Regents of the University of California, Los Angeles	Recipient: San Jose State University
Provider Scientist Name: Berkeley Limketkai Email: blimketkai@mednet.ucla.edu	Recipient Scientist Name: Emily Yelencich Email: emily.yelencich@gmail.com
Agreement Term Start Date: Date of last signature below End Date: One (1) Years after the Start Date	Project Title: Attachment 2 Type: De-identified Data about Human Subjects
<p style="text-align: center;">Terms and Conditions</p> <ol style="list-style-type: none"> 1) Provider shall provide the data set described in Attachment 1 (the "Data") to Recipient for the research purpose set forth in Attachment 1 (the "Project"). Provider shall retain ownership of any rights it may have in the Data, and Recipient does not obtain any rights in the Data other than as set forth herein. 2) If applicable, reimbursement of any costs associated with the preparation, compilation, and transfer of the Data to the Recipient will be addressed in Attachment 1. 3) Recipient shall not use the Data except as authorized under this Agreement. The Data will be used solely to conduct the Project and solely by Recipient Scientist and Recipient's faculty, employees, fellows, students, and agents ("Recipient Personnel") and Collaborator Personnel (as defined in Attachment 3) that have a need to use, or provide a service in respect of, the Data in connection with the Project and whose obligations of use are consistent with the terms of this Agreement (collectively, "Authorized Persons"). 4) Except as authorized under this Agreement or otherwise required by law, Recipient agrees to retain control over the Data and shall not disclose, release, sell, rent, lease, loan, or otherwise grant access to the Data to any third party, except Authorized Persons, without the prior written consent of Provider. Recipient agrees to establish appropriate administrative, technical, and physical safeguards to prevent unauthorized use of or access to the Data and comply with any other special requirements relating to safeguarding of the Data as may be set forth in Attachment 2. 5) Recipient agrees to use the Data in compliance with all applicable laws, rules, and regulations, as well as all professional standards applicable to such research. 6) Recipient is encouraged to make publicly available the results of the Project. Before Recipient submits a paper or abstract for publication or otherwise intends to publicly disclose information about the results of the Project, the Provider will have thirty (30) days from receipt to review proposed manuscripts and ten (10) days from receipt to review proposed abstracts to ensure that the Data is appropriately protected. Provider may request in writing that the proposed publication or other disclosure be delayed for up to thirty (30) additional days as necessary to protect proprietary information. 	