

**Nutritional Adequacy of the Low FODMAP Diet Compared to a Diet Based on the Dietary
Guidelines for Americans in Irritable Bowel Syndrome**

THESIS

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Abstract

Introduction: Irritable bowel syndrome (IBS) is the most commonly diagnosed functional gastrointestinal disorder (FGID) defined by characteristics of abdominal pain related to defecation and altered bowel habits. Poor efficacy of medical treatment and reports of dietary factors impacting gastrointestinal symptoms has led to dietary interventions being at the forefront of research. Hypotheses suggest consumption of fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) are the primary culprits of symptom induction in this population. Based on these hypotheses, the low FODMAP diet (LFD) was developed to target gastrointestinal symptoms which has shown efficacy in nearly 75% of sufferers.¹ The LFD requires complete exclusion of high FODMAP food items which excludes many nutrient-dense food groups such as fruits, vegetables, and whole grains. Due to this restrictive approach, investigation of a more liberal dietary approach is warranted.

Objectives: To assess compliance and nutritional adequacy of the LFD compared to an individualized dietary approach based on the Dietary Guidelines for Americans (DGAs) optimizing dietary fiber and minimizing added sugar intake.

Methods: A case presentation of four subjects following either a LFD or individualized dietary approach tailored from the Dietary Guidelines for Americans were assessed for dietary compliance and nutritional adequacy to gain insight into challenges of dietary interventions in those with IBS. Subjects diagnosed with IBS were randomized to either an individualized diet based on the DGAs focused on modulation of added sugar and dietary fiber, or the LFD.

Nutrient analysis, using the Nutrition Data System for Research (NDSR) reported changes in nutrient intakes after the intervention.

Results: The first four consented subjects were randomized to an individualized dietary approach (n=2) or the LFD (n=2) are presented. Macro- and micronutrient intake data was highly variable in both the pre- and post-dietary intervention data. Baseline micronutrient intakes for all participants were poor and consistently fell below the RDA. Vitamin A intake was the only nutrient that consistently increased despite the intervention; however, vitamin A intake post-intervention was below the RDA. Compliance to the LFD was inconsistent.

Conclusions: Recruitment for a dietary intervention in IBS is challenging and future research should explore barriers to participation. Compliance was inconsistent and creates challenges with data interpretation. It is crucial that dietary compliance to the LFD is emphasized in future studies to understand the challenges with nutritional adequacy.

Dedication

I would like to take the time to dedicate this masters' thesis project to my grandmother, my Nana, Betsy Casey. Words cannot express the gratitude and appreciation I have for the innumerable acts of love and support she has provided throughout my entire dietetics journey, always believing in my abilities to the fullest extent. Navigating the road to my Masters' degree has been the most challenging and difficult time in my life, personally and professionally, and I would not be where I am today without her. I love and appreciate you more than I could ever articulate.

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List of Terms

CD – Celiac Disease

CNS – Central Nervous System

DII – Dietary Inflammatory Index

DRI – Daily Recommended Intake

FFQ – Food Frequency Questionnaire

FGID – Functional Gastrointestinal Disorder

FODMAP – Fructose, Oligosaccharides, Disaccharides, Monosaccharides, and Polyols

GHBT – Glucose Hydrogen Breath Test

GI – Gastrointestinal

HMO – Health Maintenance Organization

IBS — Irritable Bowel Syndrome

IBS-C – Irritable Bowel Syndrome, Constipation Predominance

IBS-D – Irritable Bowel Syndrome, Diarrhea Predominance

IBS-M – Irritable Bowel Syndrome, Mixed

IBS-U – Irritable Bowel Syndrome, Unclassified

IBS-SSS – Irritable Bowel Syndrome Symptom Severity Score

LFD – Low FODMAP Diet

LHBT – Lactulose Hydrogen Breath Test

LI – Lactose Intolerance

MMC – Migrating Motor Complex

NCGS – Non-Celiac Gluten Sensitivity

NICE – National Institute of Health and Clinical Excellence

PUFA – Polyunsaturated Fatty Acid

RDA – Recommended Dietary Allowance

RDN – Registered Dietitian Nutritionist

SERT – Serotonin Reuptake Transporter

SGA – Subjective Global Assessment

SIBO – Small Intestinal Bacterial Overgrowth

VAS – Visual Analog Scale

List of Definitions

Bristol Stool Form Scale (BSFS) – A clinical measurement tool used as a visual depiction of stool forms and consistencies, ranging from constipation (type 1) to diarrhea (type 7).

Food Frequency Questionnaire (FFQ) – A dietary assessment tool used to evaluate typical frequency of consumption of certain foods and beverages over a set period of time.

Fermentable oligosaccharide, disaccharide, monosaccharide, and polyols (FODMAPs) – poorly digested and absorbed short-chain carbohydrates.

Functional Gastrointestinal Disorder (FGID) – A class of gastrointestinal disorders characterized with having morphological and physiological abnormalities of the GI tract without anatomical or structural abnormalities.

Irritable Bowel Syndrome (IBS) – A functional gastrointestinal disorder, characterized by symptoms of abdominal pain, bloating, and changes in bowel patterns.

Irritable Bowel Syndrome Severity Scoring System (IBS-SSS) – A clinical measurement tool used to assess a patient's symptom severity.

Lactose Intolerance (LI) – Digestive condition in which lactose maldigestion occurs after lactose ingestion, most commonly as a result of lactase enzyme production deficiency (hypolactasia).

Nutrition Data System for Research (NDSR) – A nutrient data analysis software developed by the Nutrition Coordination Center (NCC) at the University of Minnesota in Minneapolis, MN.

Small Intestinal Bacterial Overgrowth (SIBO) – An increase in gut bacteria load equal to or greater than 10^5 colony forming unit per mL of upper gut aspirate in addition to abdominal pain, discomfort, bloating, flatulence and loose motion.

Visual Analog Scale (VAS) – A tool used to help a person rate the intensity of certain sensations and feelings, such as pain. For pain, it is a straight line with one end meaning no pain and the other end meaning worst pain imaginable. The patient will mark the amount of pain they feel.

Chapter 1: Introduction

Background

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder (FGID) that is the most commonly diagnosed gastrointestinal (GI) disorder defined by characteristics of abdominal pain related to defecation and altered bowel habits.² FGIDs are a classification of GI diseases that have no structural abnormalities or findings yet have presenting symptoms of GI distress with IBS being the most prominent of these. This is diagnosed by the Rome criteria (currently Rome IV) and with the newest update to the criteria, there has begun a shift in terminology towards disorders of the gut-brain interaction due to the significant interaction between them in these disorders.³ In North America, IBS impacts 10-12% of the population.¹ It is most common among women and younger individuals but can affect persons of all demographics. IBS diagnoses are divided among four subtypes: constipation predominant (IBS-C), diarrhea predominant (IBS-D), mixed diarrhea/constipation (IBS-M) and unclassified (IBS-U).¹ Bloating and distension are common symptoms among all subtypes of this disorder.⁴

IBS poses a high encumbrance on the individual, negatively impacting quality of life and impairment of work-related activities. This also poses high burden on the healthcare system, costing upwards of \$10 billion dollars annually, highlighting the necessity of optimal treatment.¹ Treatment is multimodal, involving pharmacological, nutritional and psychological interventions, primarily focusing on symptom management and improving quality of life.¹

Dietary intervention for treatment of IBS has grown significantly within the last decade. Several diets have been trialed with IBS including, but not limited to gluten-free, low-fat,

Mediterranean and the specific carbohydrate diet. Most of these are traditional exclusion diets with unknown efficacy and limited symptom relief. Hypotheses suggest consumption of fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) are the primary culprits of symptom induction in this population.⁴ Based on these hypotheses, the low FODMAP diet (LFD) was developed at Monash University. The LFD is an exclusion diet that requires complete elimination of highly concentrated, fermentable carbohydrates for 2-8 weeks. Over the last decade, substantial research supports the LFD as efficacious and effective treatment for symptom management in those with IBS. However, given the restrictive nature of this dietary intervention understanding the nutritional adequacy is of importance.

The exclusive nature of the LFD which eliminates many whole grains, fruits and vegetables that are nutrient dense has the potential to create nutrient deficiencies. In addition, the exclusionary nature of this diet can be burdensome thus presenting a necessary look into a more liberal dietary pattern approach using the Dietary Guidelines for Americans (DGAs). This study aims to assess these two dietary interventions and the nutritional adequacy of each. The results of this study will help further guide the registered dietitian nutritionist (RDN) delivery of medical nutrition therapy (MNT) for IBS.

Purpose of Study

The primary purpose of this research is to assess the nutritional adequacy of the LFD compared to a diet based on the DGAs. This will allow further insight into the understanding of the nutritional implications for the MNT for IBS.

Research Question

Is there a difference in nutrient intake of vitamin A, vitamin C, vitamin D, calcium, zinc, magnesium and fiber in following a low FODMAP diet versus a diet based on the DGAs?

Hypothesis

There will be no difference in nutrient intake of vitamin A, vitamin C, vitamin D, calcium, zinc, magnesium and fiber for individuals following RDN-led dietary intervention of the LFD and an individualized diet based on the DGAs.

Chapter 2: Background and Literature Review

Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder (FGID) that is the most commonly diagnosed gastrointestinal (GI) disorder defined by characteristics of abdominal pain related to defecation and altered bowel habits.¹ It is currently diagnosed by the Rome IV criteria. Recently, there has been an emphasis on the gut-brain relationship in FGIDs.³ This GI disorder is common in younger adults and women, effecting 10-15% of the world's population. IBS has four subtypes depending on bowel pattern: diarrhea predominant (IBS-D), constipation predominant (IBS-C), mixed and unclassified (IBS-U) subtypes.³ Hypotheses suggest symptoms occur by way of abnormal gut motility, visceral hypersensitivity, altered immune function, varied gut microbiota as well as central nervous system (CNS) processing. Consumption of fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) are thought to be the primary culprits of symptom induction.⁴ Treatment of this disorder is multimodal, inclusive of psychological, pharmacological and nutritional intervention, focusing on symptom management and improving quality of life.⁴ The most efficacious and effective dietary intervention to date is the LFD pioneered at Monash University. Much is still unknown about the mechanisms of this diet and potential long-term concerns including micronutrient inadequacy.

Epidemiology

IBS is the most commonly diagnosed GI disorder.¹ Actual prevalence of IBS has a large reported variation, in part, due to differences in study populations, diagnostic criteria, and study methodology examined. Pooled global prevalence is estimated at 10-15% with the highest prevalence in Western countries including an approximate 12% prevalence in the United

States.⁵⁻⁷ It affects more females than males and those in early adulthood than any other age group.^{1,5} The literature supports a genetic predisposition, physiological stress, and infections of the GI tract as additional risk factors for IBS.¹ Lovell and Ford compiled cross-sectional studies that examined the global prevalence and risk factors of IBS. IBS prevalence according to geographic location had not been well-established prior to this systematic review. Overall pooled prevalence of IBS was 11.2%; the lowest pooled prevalence at 7.0% in Southeast Asia and highest at 21.0% (Rome II) in South America.⁵ Studies of prevalence are nonexistent for Central America at this time. Pooled prevalence among all international regions examined may be found below (Table 1).

| | Number of studies | Number of subjects | Pooled Prevalence (%) |
|-------------------------|-------------------|--------------------|-----------------------|
| All studies | 80 | 260,960 | 11.2 |
| North European studies | 21 | 72,031 | 12.0 |
| Southeast Asian studies | 19 | 55,455 | 7.0 |
| North American studies | 10 | 52,790 | 11.8 |
| South European studies | 9 | 36,577 | 15.0 |
| Middle Eastern studies | 8 | 32,374 | 7.5 |
| South Asian studies | 4 | 5,857 | 17.0 |
| South American studies | 4 | 1,272 | 21.0 |
| Australasian studies | 3 | 3,739 | 14.0 |
| African studies | 2 | 775 | 19.0 |

Table 1. Pooled prevalence of IBS according to geographical location.⁵

When stratifying IBS prevalence by age, gender and socioeconomic status, trends for a decreased prevalence with increasing age was noted, but did not attain statistical significance.⁵ Furthermore, prevalence showed higher in women compared with men (14.0% vs 8.9%, respectively), but did not attain significance and no relationship was found with varying socioeconomic status.⁵

IBS places a high burden on the individual and the healthcare systems costing upwards of \$10 billion annually in direct medical costs.¹ In 2000, patients with IBS whom were enrolled

into a Healthy Maintenance Organization (HMO) were found to have significantly greater amounts of outpatient visits and hospitalizations, more overall prescription use and incurred 51% more in overall healthcare costs ($p < 0.05$).¹ Severity of IBS is associated with this economic burden as well.⁸ Interestingly, in spite of this high economic burden and increase in medical attention, many patients actually feel unsupported by their healthcare providers.⁹ Patients with IBS have reported feelings of insignificance, humiliation, and abandonment by their providers.⁹

As early as 1986, studies have revealed 33% of patients with IBS had a family member who also had IBS demonstrating a strong familial aggregation.¹⁰ Makker and colleagues compiled literature surrounding the notion of familial aggregation which is summarized in Table 2. From this data, familial connections have been identified in both adults and children. Most notably, a large, nationwide study ($N = 51,952$) by Waehrens et al identified a familial connection, finding greater odds of developing IBS if a first-, second-, or third-degree relative diagnosed with IBS.¹⁰ Additionally, according to the literature, Whorwell et al found 33% of individuals with IBS also had a relative with IBS compared to 2% of those without IBS ($p < 0.0001$).¹⁰ When assessing healthcare visits for GI symptoms in children, in addition to the presence of a family member diagnosed with IBS, there were 50% more healthcare visits for GI symptoms in children with parents having a diagnosis of IBS compared to those without ($p = 0.0001$).¹⁰ Genetic studies involving twins have also shown similar findings, noting a significantly higher concordance rate for IBS among monozygotic twins compared to dizygotic twins. Two studies ($N = 3615$ twin pairs) examined this association and reported a 17.2% rate compared to 8.4% rate (monozygotic vs dizygotic, respectively; $p = 0.03$) and a 22.4% compared to 9.1% (monozygotic vs dizygotic, respectively; $p = 0.011$).¹⁰ These further authenticate the notion of shared genes and environmental exposures contributing to IBS onset.

| Author and Year | Patients with IBS | Findings |
|------------------------|-------------------|---|
| Whorwell et al. (1986) | 100 | 33% of those with had another family member with IBS compared to 2% control group |
| Levy et al. (2000) | 373 | Children of parents w/ IBS made 20% more outpatient care visits than those w/o IBS |
| Locke et al. (2000) | 643 | Those w/ FGID had higher odds of reporting a relative w/ GI symptoms (OR=2.3) |
| Kalantar et al. (2003) | 181 | 17% of relatives of patients with IBS had IBS compared to 7% of control group |
| Saito et al. (2008) | 50 | 37% of relatives of patients with IBS had IBS compared to 16% of control group |
| Saito et al. (2010) | 477 | No association between spouses; 50% of patients with IBS had ≥ 1 other relative w/ IBS |
| Waehrens et al. (2015) | 51952 | Higher odds of IBS among first-, second- and third-degree relatives of IBS |

Table 2. Familial aggregation studies reported in the literature from 1986 to 2015.¹⁰ FGID – functional gastrointestinal disorder; OR – odds ratio; IBS – irritable bowel syndrome

Etiology

FGIDs are defined by having morphological and physiological abnormalities of the GI tract without anatomical or structural abnormalities.² FGIDs encompass a multitude of gastrointestinal disorders with IBS being the most common. It has been established that though there are distinct diagnoses for each FGID, significant overlap does occur, and these are therefore considered on a spectrum rather than as isolated entities.² With the updated Rome IV diagnostic criteria, a shift in terminology towards disorders of the brain-gut interaction has occurred, emphasizing the intertwining relationship between the two and influence on these disorders.³ Major symptoms of IBS include abdominal pain, gas and flatulence, alteration in

bowel habits or motility, reflux and noncardiac chest pain. Abdominal pain may be relieved by defecation or it may be constant and chronic in nature. Gas and flatulence are increased in those with IBS due to the pathophysiology of this disease.¹¹ Patients experiencing any of these symptoms may in turn begin aversion of certain foods on their own to minimize or avoid symptoms. This may result in nutrient deficiencies depending on the foods being avoided as well as a lower quality of life with unnecessary dietary restrictions.¹¹

Though there is substantial research on IBS, the exact etiology is still unknown. Hypotheses suggest genetic predisposition, altered immune response related to food sensitivities, altered microbial environment of the GI tract, elevated inflammatory response due to gastroenteritis, small intestinal bacterial overgrowth (SIBO), abnormal serotonin secretion, and increased sensitivity of the nervous system.⁴ These hypotheses remain pertinent due to some of the concurrent diagnoses that are often reported in IBS such as celiac disease, lactose intolerance, and SIBO.⁴

SIBO and IBS

Altered gut flora and gut dysbiosis, including SIBO, are associated with the development or worsening of IBS.^{12–15} SIBO, an increase in bacterial load in the GI tract, is defined as “an increase in bacteria equal to or greater than 10^5 colony forming unit per mL of upper gut aspirate in addition to abdominal pain, discomfort, bloating, flatulence and loose motion”.¹² The proportion of those with IBS also having a SIBO diagnosis is highly variable due to the lack of diagnostic criteria for SIBO. Briefly, three common methods for diagnosis include a quantitative jejunal aspirate culture (gold standard), the hydrogen breath tests (most common) or culturomics (newest technology).¹³ Since the hydrogen breath test is the most commonly used tool to diagnosis SIBO, understanding this tool is important. Diagnosis is substrate specific: the glucose

hydrogen breath test (GHBT) is highly specific yet lacks sensitivity and the other, lactulose hydrogen breath test (LHBT), lacks specificity.¹² Because of this, these tests often lead to false positive diagnoses and consequently an overestimation in frequency of SIBO. Thus, the determined relationship between SIBO and IBS may be overestimated.

Keeping in mind the diagnostic challenges with SIBO, there is a higher prevalence of SIBO diagnosed in IBS compared to those without the syndrome. In a 2009 meta-analysis, Ford and colleagues examined the pooled prevalence of SIBO in individuals with IBS using the lactulose and glucose hydrogen breath tests. From 12 studies examined, results indicated a pooled prevalence of 54% and 31% for lactulose and glucose breath tests, respectively.¹⁴ Shah and colleagues assessed breath testing in IBS in 2010 as well, examining 11 previous studies. In pooling these studies, breath testing was positive more so when an IBS diagnosis was present when compared to their healthy counterparts ($p < 0.0001$).¹⁵ Chen and colleagues compiled prevalence rates of SIBO in those with an IBS diagnosis from 50 case-control and case-series studies and reported an overall pooled prevalence was 38%, ranging from 4% (diagnosed via small intestinal fluid aspirate) to 84% (diagnosed via LHBT).¹² Further analysis suggests the highest pooled prevalence rates among IBS subtypes were that of IBS-D diagnosis (42%) compared to other subtypes (31% in IBS-M, 25% in IBS-C, 17% in IBS-U).¹² Diarrhea predominant bowel patterns could indicate a potential predictor for SIBO among this demographic. Additionally, SIBO had higher odds of occurring among women compared to men.¹² IBS does also have a higher prevalence in women, as previously mentioned, compared to men which could explicate this phenomenon. Though there are clear variations of study design and diagnostic criteria upon examination of SIBO and IBS, prevalence of SIBO has shown to be significantly higher in those with IBS than in those without.

Non-celiac gluten sensitivity and IBS

Non-celiac gluten sensitivity (NCGS) embodies gluten sensitivity, gluten intolerance or non-celiac wheat sensitivity without a concurrent diagnosis of celiac disease (CD) or a wheat allergy.¹⁶ These wheat-reactive individuals present with symptoms similar to that of celiac disease, but serological and histological examination is unfounded.¹⁷ It is theorized that symptoms associated with consumption of gluten may be due to other components in wheat, not the actual gluten protein consumption itself. Other potentially triggering substances for NCGS in wheat are lipopolysaccharides, amylase/trypsin inhibitors, wheat germ agglutinins, and fermentable oligo-, di-, monosaccharides and polyols.¹⁶

NCGS has been associated with IBS since symptoms often present in a similar manner. Understanding the impact of wheat on GI symptoms is challenging as many individuals with reported wheat sensitivity follow a gluten-free diet without medical diagnosis/reason.¹⁶ Carroccio and colleagues reported a retrospective examination of 920 patients with 276 (30%) suffering from gluten sensitivity, including 206 patients having multiple food sensitivities.¹⁷ Those that suffered from gluten sensitivity alone reacted to wheat an average of 3 days (range of 3 hours to 9 days) post-consumption ($p < 0.01$); those that had multiple food sensitivities reacted to wheat an average of 2.5 days (range of 2 hours to 5 days) ($p < 0.01$); no patients reacted to the placebo.¹⁷ Using the visual analog scale (VAS), a tool used to rate intensity of pain, scores for each symptom were found to be significantly higher on a wheat-containing diet when compared to baseline being on a wheat-free diet ($p < 0.0001$).¹⁷ VAS scores on the wheat-containing diet were found to be significantly higher than those on placebo compared to baseline as well ($p < 0.0001$).¹⁷

Lactose intolerance and IBS

Lactose intolerance (LI) is another common concurrent diagnosis in those with IBS. LI is characterized by lactose maldigestion after lactose ingestion, most commonly as a result of hypolactasia (lactase deficiency).¹⁸ Because of this maldigestion, this can lead to colonic fermentation resulting in biproducts that lead to distension, abdominal pain, gas, and diarrhea.¹⁸ Remarkably, with IBS, a lower threshold for lactose dosage yet a more severe symptomatic reaction exists.¹⁸ Often this lactose intolerance is self-reported with no objective measure taken for confirmation.¹⁸

Varjú and colleagues examined three subgroups of lactose ingestion, including 10-18g, 20-25g, and 40-50g, which a cup of cow's milk averages 12-13g of lactose per serving, which they found no significant difference between those with IBS and healthy controls in terms of maldigestion.¹⁸ Additionally, self-reported and objective LI has been associated with IBS.¹⁸ This research suggests IBS could be a contributing factor in LI among those with poor lactose digestion due to the high fermentability in those with IBS.

Diagnosis of IBS

The Rome criteria began as the diagnostic criteria for all functional GI disorders in 1990; it reflects expert consensus in the areas of esophageal, gastroduodenal, bowel, biliary and anorectal disease, including diagnostic criteria for IBS.³ Currently in the fourth update (Rome IV), definitive diagnosis for IBS is as follows: abdominal pain associated with defecation or a change in bowel habits present for at least one day per week on the preceding month. If these criteria are met, further classification as diarrhea predominant (IBS-D), constipation predominant (IBS-C), mixed and unclassified (IBS-U) subtypes is given to identify the appropriate treatment options.³ Comparison of Rome III to the updated Rome IV is essential to understanding the literature in IBS and is therefore shown in the table below (Table 3).

| | Duration | Frequency | Symptoms |
|----------|--|--------------------|--|
| Rome IV | ≥3 months of persistent symptoms with symptom onset at ≥ 6 months before diagnosis | ≥1 day per week | Recurrent abdominal pain with at least 2 of the following criteria: <ol style="list-style-type: none"> 1. Related to defecation 2. Associated with change in frequency of stool 3. Associated with change in form of stool |
| Rome III | ≥ 3 months of persistent symptoms with symptom onset ≥ 6 months before diagnosis | ≥ 3 days per month | Recurrent abdominal pain with at least 2 of the following criteria: <ol style="list-style-type: none"> 1. Improvement with defecation 2. Onset associated with change in frequency of stool 3. Onset associated with change in form of stool |

Table 3. Comparison of Rome III and Rome IV criteria for diagnosis of irritable bowel syndrome.⁷

Diagnosis of IBS with the updated criterion have begun to incorporate an emphasis on brain-gut interactions by shifting the classification from “functional GI disorders” to “disorders of the brain-gut interaction”.³ This is partially due to the recognized importance of neural and hormonal interactions between the brain and the gut on producing/modulating symptoms of these disorders. However, periodical update of the criterion poses some challenges. Even slight differentiation in diagnostic nomenclature can present a difference in IBS prevalence. For example, Bai et al examined these differences from Rome III to Rome IV. Researchers found out of 1376 suspected IBS participants, 12.4% were diagnosed with IBS using Rome III and 6.1% were diagnosed using Rome IV.¹⁹ Bai and colleagues noted the main reasoning behind this as the shift of nomenclature from abdominal *discomfort* to abdominal *pain*. When Bai and colleagues analyzed the two criterion, the most commonly diagnosed IBS subtype was IBS-D and least diagnosed was IBS-M for both.¹⁹ Bai and colleagues found Rome IV-diagnosed patients had a significantly higher severity score compared to those not diagnosed with Rome IV

($p < 0.01$). They also noted Rome IV-diagnosed patients had more severe and more frequent abdominal pain, more dissatisfaction with bowel patterns and more interference with quality of life ($p < 0.01$).¹⁹ Despite these changes, the etiologies of these symptoms can be classified similarly.

Pathophysiology

The underlying cause of IBS is not completely understood – it is still being defined and thought to be multifactorial. FGIDs, including IBS, are being referred to as brain-gut disorders due to the complex relationship between the GI system and the CNS which can then result in symptoms. There are generally four main pillars of pathophysiology in IBS that contribute to IBS symptoms: visceral hypersensitivity, gut motility dysregulation, brain-gut communication abnormalities and post-infectious enteritis. Although one or more abnormalities can account for the majority of symptoms in patients with IBS, none are certain to account for all of them.⁶

Visceral hypersensitivity

Increased gastrointestinal permeability has been observed in patients with IBS-D and associated with visceral hypersensitivity.⁶ Major et al proposed two hypotheses on how this phenomenon occurs. With the small bowel hypothesis, it is proposed that fermentable carbohydrates (ie., FODMAPs) are unabsorbed, increasing intraluminal water content in the small intestine, which then leads to distension, causing the symptoms of bloating and abdominal pain or discomfort.²⁰ Increased distension leads to faster intestinal transit, impairing absorption in the small bowel.²⁰ With the large bowel hypothesis, FODMAPs reach the colon unabsorbed where they are then rapidly fermented by colonic bacteria.²⁰ This leads to symptoms of flatulence, bloating and abdominal discomfort via increased gas production and distension of the colon.²⁰ According to Hellström, studies have shown patients with IBS have increased

sensitivity to balloon distension in the colon as well as a higher sensitivity to intestinal contractions compared to healthy counterparts.²¹ Colonic distension mechanisms are depicted in the figure below (Figure 1).

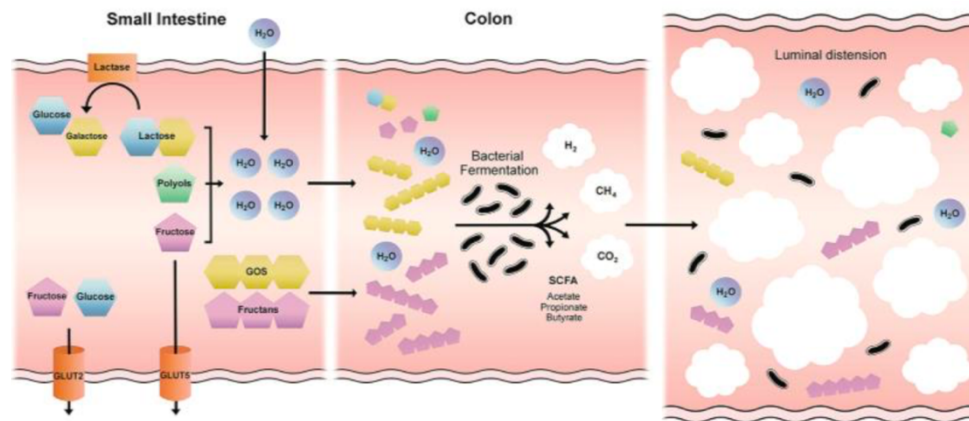


Figure 1. Colonic distension mechanisms.⁵³

Gut motility dysregulation

The migrating motor complex (MMC) is a cyclical process in gastric motility during a fasted state in which gastrointestinal contractions occur.²² There are four phases of the MMC: phase I occurs without contractions, phase II occurs with intermittent and irregular contractions of low amplitude, phase III occurs with short bursts of contractions of high amplitude periodically every 90-120 minutes, phase IV occurs as a transition period back to phase I.²² This process appears to be abnormally regulated in those with IBS. Depending on the predominant subtype, IBS-D has increased levels of MMC contractions and IBS-C has decreased levels of MMC contractions.²² Studies have shown patients with IBS having faster gut motility, primarily following meal consumption and during times of stress.²¹ In this population, contractions of the GI tract have been found to be abnormally prolonged more frequently and of higher amplitude contributing to this increased gut motility.²¹ Those with IBS-D diagnoses have exemplified more rapid GI transit times while patients with IBS-C have exemplified slower GI transit. The

mechanism of abnormal gut motility has not been consistently found throughout the IBS population.²¹ In relation, when examining gut dysmotility, Serra et al found those who received a lipid perfusion and air infusion to the duodenum exhibited increased intestinal gas retention if an IBS diagnosis was present.⁷ Similarly, they also evaluated air infusions alone and found a delayed transit time with gas retention in IBS.⁷

Brain-gut communication

Stress is presented as having a major role in the pathophysiology of IBS, potentially stimulating altered physiologic responses through brain-gut communication. A permanent experience of stress enhances the responsiveness of CNS circuits increasing that individuals' vulnerability in development of functional disorders like IBS.²¹ In about half of IBS cases, IBS originates in the gut, instead of the brain, with IBS symptoms starting first and psychological distress developing later.²³ Patients with IBS report more lifetime stress and daily stress than compared to their healthy counterparts.²¹ Additionally, those with IBS seem to have higher reactivity towards stress than their healthy counterparts.²¹ Psychosocial factors play a major role in this population which could potentially predispose individuals to developing IBS. Forms of abuse and trauma can contribute to the development of IBS through the gut-brain axis as well.⁶ These particular individuals have more symptoms related to IBS and have higher rates of psychological distress, mood disorders, depression and anxiety.⁷ Conversely, those with good social support were found to have lower incidences of symptoms.⁷

Serotonin (5-HT) is a hormone produced endogenously with 95% of this hormone produced in the gut. It has been proposed and studied that there is a defect in serotonin uptake and production in IBS due to the established significant interaction between the gut and brain.²¹ Additionally, the correlation of psychological illness with IBS, such as depression and anxiety,

that also rely heavily on serotonin, also point to a defect in this hormone. The serotonin reuptake transporter (SERT) is present in the brain and gut. The amount of serotonin reuptake that occurs by SERT is genetically predetermined and largely influences the availability of serotonin for stimulation of serotonin receptors.²¹ SERT polymorphisms may be the reason for patient individualization in this area. A study by Coates and colleagues analyzed serotonin transporter activity and immunoreactivity in patients with IBS and healthy controls, finding suggest these to be significantly reduced in those with IBS compared to healthy counterparts.²¹ When analyzing serotonin release, before and after mechanical stimulation, no changes were detected compared to healthy controls, indicating molecular changes in serotonin signaling mechanisms.²¹ This research suggests defects in serotonin signaling could potentially define an etiology behind gut dysmotility, secretion and hypersensitivity in IBS.²¹

Post-infection gastroenteritis

Infectious enteritis (IE) has potential to lead to the development of IBS; this is referred to as post-infectious IBS (PI-IBS) and is found to persist in 10-20% of infected individuals.²³ The onset of PI-IBS is caused mainly by bacterial infections but can also include viral and protozoan infections and food-borne illness.²⁴ A pooled prevalence of PI-IBS in a large sample (N=21,421) 11.5% of cases of PI-IBS were associated with parasitic infections followed by bacterial and viral infections.²⁵ Despite this infectious etiology, symptoms are acute in nature and typically mirrors that of IBS-D symptomology.²⁴ Less commonly, it can present as upper GI dysfunction, IBS-M, or IBS-C. The intestinal inflammation is the predominant etiology whereas the psychiatric component of IBS tends to be less prevalent in this subset (Figure 3).²³ Notably, PI-IBS resolves within 6-8 years whereas traditional IBS is a chronically relapsing condition without resolution.⁶

Treatment for IBS

Pharmacology and Complementary Alternative Medicine

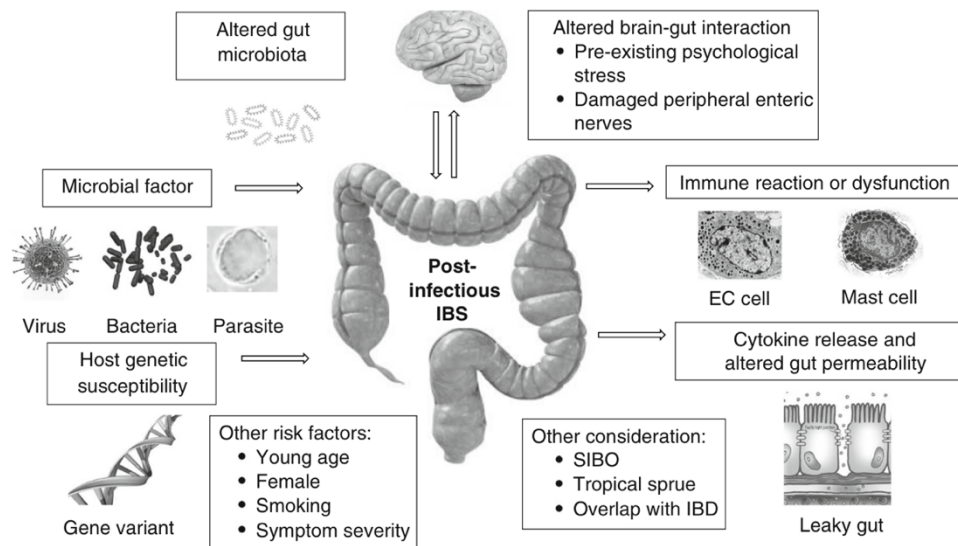


Figure 2. Mechanisms related to the prevalence of post-infectious IBS.²⁴

Management of IBS is complex with treatment being multimodal aforementioned. Pharmacological methods are often combined with complementary, psychological, and nutritional interventions. Medication for IBS has been a therapeutic approach for management of symptoms with little to unknown efficacy and with known side effects. These are prescribed depending on the predominant bowel pattern as well as prevailing symptoms such as abdominal pain or bloating.

Antispasmodics:

Antispasmodics may provide symptom alleviation through the reduction of colonic smooth muscle contraction and transit time, which would provide symptom alleviation of abdominal pain and diarrhea.²⁶ Some examples include hyoscyamine, otilonium, and dicyclomine and are recommended for symptom relief. The American College of Gastroenterology (ACG) monograph on the management of IBS, compiled by Ford and

colleagues, found an overall statistically significant improvement of IBS symptoms with antispasmodics.¹ Overall, 39% of patients assigned to an antispasmodic had persistent symptoms after treatment compared to 56% of those allocated to placebo.²⁷ Side effects reported from taking this included dry mouth, dizziness and blurred vision.²⁷ However, no serious adverse reactions to this medication were reported and is therefore considered a fairly safe treatment option for IBS symptoms.¹

Antidiarrheals:

Antidiarrheals also work to prolong gastrointestinal transit time in addition to increasing water/ion absorption, benefiting stool frequency, consistency and urgency.²⁶ This medication works to decrease bowel movement frequency while increasing the thickness of stools.

Loperamide is one such example of these antidiarrheals. The ACG urges a strong recommendation against the use of this for IBS symptoms at this time.¹ According to the ACG monograph, only two small-scale RCTs have been performed altogether, dating back to 1987, with a very small sample size of 42.¹ Within these studies, no statistically significant effect was found in using loperamide compared to a placebo.¹ Again, due to this low-quality body of evidence and the minimal literature in this area, the ACG recommends against use of this medication.

Prosecretory Agents:

Prosecretory agents can be used when laxative therapy fails for relief of constipation. They work by increasing intestinal fluid secretion thereby accelerating intestinal transit time. Lubiprostone is a prosecretory agent currently approved for adult women with an IBS-C diagnosis at 8 mcg dose twice. Two RCTs (N=1171) examined this drug's effect and found the 8 mcg dose of lubiprostone twice daily had significant symptom relief for abdominal pain and

stool frequency compared to placebo ($p = 0.001$).²⁸ Additionally, three RCTs ($N=651$) shown lubiprostone to superior to placebo for symptom improvement.¹ Linaclotide is a newer prosecretory agent on the market that has shown symptom relief in four RCTs ($N=2867$) compared to placebo ($p < 0.001$).²⁸ Overall, both antiseecretories are recommended by the ACG for overall symptom improvement and abdominal pain in IBS-C. Noted side effects from these prosecretory agents have been diarrhea and nausea due to the underlying mechanism of this drug, though it is generally well-tolerated.¹

Polyethylene glycol (PEG) is an osmotic laxative that could also provide symptom alleviation for constipation; it is easily accessible as an over-the-counter (OTC) medication.¹ Unfortunately, the literature on this laxative has not proven beneficial for IBS-C. The ACG monograph reviewed four RCTs assessing PEG and IBS, showing improvement in frequency of bowel movements, however, with no significant improvement in abdominal pain or discomfort compared to placebo.¹ Given this lack of efficacy for IBS-C, recommendations for using PEG for IBS symptom alleviation cannot be made at this time.¹

Opiate Receptor Agonist and Antagonist:

Opioid receptor antagonists and agonists have potential benefit on visceral hypersensitivity as it works directly on the gut mucosa and enteric nervous system. Eluxadoline an example of this class of medication. The dual nature of this medication may be why diarrhea and abdominal pain-modulating properties exist in this in conjunction with minimal constipation occurrence.²⁸ Several phases of clinical trials have been utilized to evaluate the efficacy of eluxadoline at various doses compared to placebo. One RCT demonstrated significant clinical improvement in groups that adhered to 100 mg and 200 mg twice-daily dosages when compared to placebo.²⁸ Since the 200 mg regimen was found to have more adverse events associated, only

75-100 mg BID regimens were able to move forward to the next phase of the study. In addition, an RCT evaluated a 75-100 mg dose of eluxadoline twice daily for 26 weeks in two separate studies on IBS-D (Rome III) (N=2425).²⁸ A significantly higher proportion of patients experienced improvements in abdominal pain and stool consistency with both dosage interventions compared to placebo and even more symptom relief with the 100mg dose ($p < 0.001$).²⁸ A Sphincter of Oddi spasm and pancreatitis side effects have been found with taking eluxadoline. Therefore, eluxadoline is contraindicated for those without a gallbladder and those who consume more than three alcoholic drinks per day.²⁸

Serotonin Antagonists:

Serotonin receptors can be targeted for medical treatment with serotonin antagonists, particularly in IBS-D. Alosetron is one such drug in this class that has been named as effective for IBS. RCTs by Cremonini et al and Camilleri et al found participants (N=1352) to have significant improvement in quality of life, in terms of workplace productivity and social/leisure hours ($p < 0.05$ and $p < 0.01$, respectively) as well as adequate symptom relief when taking alosetron compared to placebo interventions.²⁸ In 2000, this drug had to be withdrawn from the general population due to reports of severe constipation and ischemic colitis.²⁸ Since then the drug has been put back on the market with strict prescribing protocols. Ramosetron has also been developed in recent years and shows favorable results, though it is not yet FDA approved. It acts similarly to alosetron by decreasing colonic motility and increasing time for fluid absorption and has been shown to improve abdominal pain, bloating and diarrhea.²⁸ In one RCT, 53.2% of patients felt more relief with stool consistency by taking ramosetron compared to 42.0% taking placebo.²⁸ Another study of women with IBS-D (Rome III) (N=576) showed 50.7% patients treated with ramosetron reported significant global symptom improvement

compared to 32% treated with placebo ($p < 0.001$). A meta-analysis of four RCTs (N=1623) demonstrated relief of overall IBS symptoms using ramosetron compared to placebo with no adverse events.²⁸

Antibiotics:

Rifaximin is a gut-specific broad-spectrum antibiotic for use in IBS. Mechanisms of action for symptom relief are currently unknown though hypotheses suggest alterations of the gut microbiome.²⁸ Two large-scale RCTs (N=1260), referred to as TARGET 1 and TARGET 2, have evaluated the efficacy of rifaximin in IBS. A significantly higher proportion of patients experienced adequate symptom relief compared to placebo (41% vs 32% in TARGET 1 and TARGET 2 combined, $p < 0.001$).²⁸ Subsequently, TARGET 3 found two-thirds of responders to an initial course of rifaximin treatment also exemplified a significantly greater response rate when trialed with additional treatments of rifaximin versus placebo.²⁸ Overall, rifaximin was found to be very well-tolerated with no signs of antimicrobial resistance over the course of these studies.²⁸ Following these trials, the FDA approved the use of this medication for IBS-D with a dosage of 550 mg, three times daily for two weeks. It is important to note that rifaximin is also a current treatment option for SIBO and therefore, these studies may be highlighting the connection with the two conditions.

Antidepressants:

Those with IBS-D and IBS-C may also find symptom relief in taking antidepressants. Antidepressants modulate pain perception and can work to treat IBS along with psychological illness, such as depression, that tend to be common in this population.²⁶ Antidepressants are a group of medications that include tricyclics (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), and serotonin-noradrenaline reuptake inhibitors

(SNRIs). Some newer medications in this area are also mirtazapine, reboxetine, bupropion and agomelatine.²⁹ Kułak-Bejda and colleagues analyzed antidepressant effect on IBS to determine the most efficacious line of treatment. Several studies showed improvement in global symptoms with TCAs having greater improvement in symptoms compared to SSRIs.²⁹ All TCA studies analyzed except for one found significant improvement in global symptoms in IBS, with Amitriptyline being particularly effective for relief of abdominal pain and diarrhea.²⁹ A greater improvement in depression scores were noted with TCA use as well as being generally well-tolerated.²⁹ SSRIs produced mixed results with approximately half the RCTs noting significant improvement in IBS symptoms while the other half did not. SSRIs effects examined were not randomized, only had two supporting studies and were produced on small scales. In one of these studies adverse events and therefore withdrawals were reported.²⁹ It is unable to be determined at this time if the IBS symptom relief from SSRIs or TCAs are a result of the concomitant psychological improvement. There are known side effects and many studies have reported adverse events.²⁹

Probiotics and Prebiotics:

Gut dysbiosis in IBS has given reason to trial manipulation of gut flora as a means for symptomatic relief. These modes encompass probiotics, prebiotics and synbiotic supplementation. Probiotics are live microorganisms which, if consumed in adequate amounts, could ascertain a health benefit in humans.³⁰ Prebiotics are undigested, fermentable dietary components, such as fructo-oligosaccharides and inulin, that may incite growth or activity of good bacteria in the gut, which is beneficial to human health.³⁰ Synbiotics are combinations of prebiotics and probiotics that could potentially increase the levels and activity of beneficial microbes in the gut synergistically ultimately improving the gut dysbiosis.³⁰

Probiotics:

Some strains of probiotics have been found to have anti-inflammatory properties with the potential to manipulate visceral hypersensitivity and gut motility, providing rationale for use in IBS.²⁶ Several RCTs have compared the use of probiotics to placebo for treatment of IBS. In the literature analyzed (N=2257), 55.8% of patients reported persistent and unimproved symptoms after probiotic treatment compared to 73.1% of those treated with placebo. The challenge with probiotic trials is the numerous different probiotic strains and species. Researchers have concluded that probiotics do have some beneficial effect on IBS and symptom relief, however, it is still unclear which strains would be best.²⁶

Prebiotics:

Prebiotics are another supplemental option to improve gut dysbiosis. Children with IBS treated with either probiotics, synbiotics, or prebiotics had significant improvements with probiotics and synbiotics, but not with the prebiotic inulin.³¹ Alternatively, when investigating the prebiotic trans-galactooligosaccharides administered at 3.5g/d significant improvements in stool consistency, bloating and gas, and the subjective global assessment (SGA) (all $p < 0.05$).³² Inconclusive findings make recommendations for prebiotics with IBS challenging. Given the nature of prebiotics being fermentable carbohydrates, a substance known to cause symptoms in IBS, this may contribute to conflicting data in this area as they are typically excluded during dietary intervention.

Peppermint Oil:

Peppermint oil (PO) is a naturally occurring compound that contains L-menthol which blocks calcium channels in smooth muscle therefore exhibiting antispasmodic properties.³³ The anti-inflammatory and immune-modulating properties could also present potential benefits for

those with IBS. PO can improve overall IBS symptoms including abdominal pain, bloating, abdominal distension and urgency.²⁶ Cash et al performed a double-blind placebo-controlled trial, testing the efficacy of a PO supplement with IBS symptoms in IBS-D and IBS-M (N=72).³⁴ A reduction in total IBS symptoms was achieved after just 24 hours of treatment compared to placebo.³⁴ At the conclusion of the study, there was a 40% reduction in IBS symptom severity scoring (IBS-SSS) in the PO group compared to a reduction of 24% in the placebo group, however, this did not achieve statistical significance.³⁴ Merat and colleagues performed an RCT, studying the efficacy of PO to reduce abdominal pain and found at 8 weeks post-treatment, the number of patients that were free from abdominal pain was significantly less compared to baseline ($p < 0.001$) and those with residing abdominal pain or discomfort was significantly reduced in the PO intervention group ($p < 0.001$).³⁵ Peppermint oil use has exhibited some benefit on IBS, however, the body of literature is very small and specific limiting true efficacy of this treatment.

Fiber:

Soluble fiber supplementation in the form of psyllium has proven to be an effective and easily accessible option that can provide symptom relief for IBS. A recent systematic review performed by Nagarajan and colleagues has shown that soluble fiber can significantly improve global symptoms compared to taking placebo.³⁶ However, analysis on the effects of soluble fiber on abdominal pain did not heed the same results. The literature assessing the effect of soluble fiber and abdominal pain is very limited; few studies were presented in this analysis with small sample sizes (N=187). These results shown no significant difference between taking soluble fiber and a placebo.³⁶ One study examined the effects of soluble fiber on IBS quality of life (QOL) also showing no significant difference in QOL after fiber use.³⁶ In an updated

Cochran systematic review on fiber supplementation and IBS, Ruepert and colleagues found no beneficial effect on abdominal pain or symptom severity compared to a placebo.³⁷ Moayyedi and colleagues found, even more recently, significant benefit associated with soluble fiber supplementation compared to placebo, contradicting Cochran review findings.³⁸ Given these results, consumers may be dissatisfied in using soluble fiber supplementation in attempt to alleviate symptoms. Unfortunately, the mechanisms behind fiber's impact on IBS symptoms is not fully understood and this may explain the mixed results found in the literature. It may be due to the alteration in intestinal transit time or impact on gut dysbiosis, however, additional research would be necessary to understand the mechanisms more clearly.³⁶

Alternative Therapies:

Alternative medicine is another therapeutic approach to help with symptom alleviation in addition to medication and diet. One such alternative, hypnotherapy, works directly on the gut-brain axis providing psychological effects to physiological effects on the GI system and subsequently GI symptom relief. One RCT (N=74) found statistically significant improvements of abdominal pain and psychological well-being after 6 weeks and 6 months of treatment with hypnotherapy compared to the LFD ($p < 0.001$).³⁹ Yoga, another alternative therapy, focuses on symptom relief through the gut-brain axis as well. One small study has examined effects of the LFD or yoga on IBS symptom relief and found a significant reduction in IBS-SSS and IBS-QOL after 12 weeks and 24 weeks of either treatment ($p < 0.001$).⁴⁰ However, research was unable to determine which would be the more effective treatment option. Acupuncture is hypothesized to work by manipulating the visceral system which would result in indirect stimulation of the somatic system therefore providing symptom relief.⁴¹ A systematic review of acupuncture use in IBS compared the effects of this on symptom relief compared to a placebo or medication.⁴² No

differences were found within either comparison to acupuncture in IBS-SSS or IBS-QOL.

However, patients did self-report feeling improvement in symptoms from acupuncture compared to taking medication. The research though is riddled with flaws, most notably unblinded trials with a large possibility of placebo effect occurring here. Though research may appear promising in this area, several flaws with this area of research can be observed: small sample sizes, unblinded participants, large placebo effect, and no true sham or placebo can be implemented. Unfortunately, true effectiveness of these alternative interventions is unable to be determined at this time.

Nutrition Therapy

The majority of patients with IBS, as many as 90%, deem food as a trigger of symptoms warranting dietary intervention as a means for treatment.⁴³ However, without guidance, this can lead to unnecessary food restriction, food aversion and nutritional risk. The RDN is an expert in nutrition and food-related science, translating this expertise to prescribe medical nutrition therapy using an individualized approach. With IBS, the RDN can provide this essential guidance and act as a resource to the patient in navigating their symptom management. In the literature, several nutrition therapies have been trialed such as the Mediterranean diet, low-fat diet, high fiber diet, specific carbohydrate diet and gluten/wheat free diet. These have provided seemingly conflicting results and limited efficacy.^{37,38,44-51} Conversely, one established dietary intervention originating from Monash University – the low FODMAP diet (LFD) – has been noted for significant efficacy for symptom relief in this patient population.

Dietary Guidelines for Americans

Dietary interventions for IBS have been fundamentally exclusionary which can be viewed as a burden on the patient (feeling isolated, time-consuming, expensive, emphasis on

restriction) in seeking symptom improvement. As such, it is worth looking into a more liberalized approach to dietary intervention, through traditional adjustments to the dietary pattern. The Dietary Guidelines for Americans (DGAs) is one such approach: an evidence-based guideline promoting healthy eating patterns and the inclusion of all food groups. Since 1980, there have been a publication of dietary patterns for the general population that are released every five years. Currently, the DGAs are in their 2015-2020 edition with a focus on healthy eating patterns. The DGAs act as recommendations for a healthy, nutritionally adequate diet as well as the prevention of chronic disease.⁵²

The DGAs are developed through the United States Department of Health and Human Services (HHS) and United States Department of Agriculture (USDA) using a 3-step process. Through this process, an advisory report is developed and brought to the HHS and USDA which is comprised of the latest research from meta-analyses and systematic reviews.⁵² Using the previous set of guidelines in conjunction with the advisory report and comments from the public and federal organizations, the new guidelines can be established. There are two particular nutrients, as part of the DGAs, that are of interest here: fiber and added sugar. Both components can significantly impact the gastrointestinal function.

The DGAs themselves do not provide a recommendation for fiber, however, they do present fiber recommendations to the public as food groups (through fruits, vegetables, and whole grains) and recommendations on how to improve daily fiber intake to meet the DRI.⁵² The DRI for fiber ranges from 25g to 38g per day and 95% of Americans do not meet this daily recommendation as we have seen reported through NHANES data.⁵³ According to NHANES data 2009-2010, daily fiber intake for Americans is approximately 16g per day.⁵³ As mentioned, fiber is subdivided into two groups, soluble and insoluble: soluble fiber forms a gel-like material

in the GI tract whereas insoluble fiber increases the bulk of the stool. Both types of dietary fiber contribute individually to gut health and stool regularity. This is especially true in regard to the gut microbiota. Good gut bacteria strains feed on dietary fiber consumed which helps keep beneficial gut bacteria flourishing and gut symbiosis. Fiber clearly impacts gastrointestinal health as does excessive added sugar. Therefore, the DGAs also have an added sugar recommendation of consuming no more than 10% of total calories as added sugar.⁵² According to the DGA data, the average American consumes approximately 71g of added sugar per day.⁵² Similar to the mechanisms behind fiber, an excess of simple sugar in the diet can increase harmful bacteria strains, increasing gut dysbiosis. Having an imbalance of either of these dietary components can produce symptoms like abdominal pain, bloating, distension, and irregular bowel movements.⁵⁴

Utilizing the DGAs as a nutritional intervention, which is a dietary pattern approach, should be less demanding of the patients overall, given the habitual nature within and a goal for a lifetime adherence. The DGAs are an inclusive diet, promoting the inclusion of all food groups and all nutrients. As a result, this could be less psychologically overwhelming, may produce higher compliance and adherence rates, and better quality of life all while ensuring adequate nutrient intakes. Despite the recommendations set forth by the DGAs, many exclusionary diets are popular amongst those with IBS and healthcare providers treating IBS that warrant discussion.

Low Fat Diet

In normal human physiology, postprandial reactions occur in the gastrointestinal tract which induce stimulation of the gastro-colonic reflex.⁴⁴ Among macronutrients, dietary fats/lipids present the most potent effect on this mechanism in addition to a prolonged lag phase

of digestion thereby delaying intestinal transit. This effect from lipids are upregulated in patients with bloating.⁴⁴ Research has found with FGIDs that if the individual has a predominant symptom of bloating, slowed transit time already exists due to inhibited motor activity of the small bowel.⁴⁴ Furthermore, in IBS specifically, IBS-C is noted to experience rectal distension and IBS-D is noted to experience rectal urgency as a result.⁴⁴ This association between dietary fat/lipids and slowing of gastrointestinal transit time leading to an exacerbation of symptoms has warranted a look into low fat recommendations for this patient population.⁴⁴ Simren and colleagues found for those who have food-related symptoms, 63% frequently related those symptoms to higher fat consumption.⁴⁴ Importantly, this has been found among all IBS subtypes, not one particular subtype.⁴⁴ However, several studies have failed to show differences in fat intake between IBS and healthy controls.⁴⁵ Additionally, there are no RCTs to support restriction of dietary fat intake with a result in definitive symptom improvement in IBS. Additionally, it is worth noting that researchers have found a relationship between symptom presentation and consumption of dietary fats potentially dependent on type of fat consumed, in terms of unsaturated and saturated. There is some emerging research suggesting a positive association between polyunsaturated fatty acid (PUFA) intake and IBS symptoms.⁴⁵ The basis for this comes from the low-grade inflammation presence postulated IBS etiology and the anti-inflammatory properties of PUFAs, however, much more research is warranted in this area. Ultimately, the evidence for use of fat restriction in this patient population is conflicting and limited at best. Higher quality research is necessary in this area to determine if modulation of dietary fat intake would actually be beneficial for IBS symptoms.⁴⁶

The Mediterranean Diet

Improving dietary patterns rather than a focus on manipulating certain foods or individual nutrients is a concept that most clearly mimics that of the DGAs. The Mediterranean diet (MD) is one dietary pattern, originating along the coast of the Mediterranean Sea, characterized by higher consumption of olive oil, fiber-rich grains, fruits and vegetables, low fat dairy and a lower consumption of meat or meat-based products.⁴⁷ It is considered a health-protective dietary pattern, associated with cardiovascular health and overall reduction in all-cause mortality. A hypothesis behind this is an increased consumption of antioxidants and reduced consumption of saturated fats. The MD contrasts the Westernized diet in America which is generally characterized by higher consumption of fatty and processed meats, saturated fats, refined grains, sugar, alcohol, salt and corn syrup and lower consumption of fiber, fruits and vegetables.⁵⁵ Literature has shown that a dietary pattern reflective of the Westernized diet directly contributes to obesity, metabolic syndrome and cardiovascular diseases.⁵⁵

Emerging research also proposes the MD as beneficial for gastrointestinal health, including the potential to benefit FGIDs.⁴⁷ Zito and colleagues examined adherence to the MD and the relationship between different levels of adherence with the onset of FGIDs and IBS.⁴⁸ A large study of 1134 participants that were allocated to a control group, dyspepsia group or IBS group were then stratified into different categories of adherence – low, intermediate, or high.⁴⁸ Adherence to the MD was measured using a standardized FFQ in conjunction with an age-specific questionnaire reflective of MD dietary patterns: the Mediterranean Diet Quality index for children and adolescents (KidMed) or the Short Mediterranean Diet Questionnaire. Both assessment tools posed questions surrounding the individual's consumption of specific foods at indicated frequencies, points were given for consuming foods reflective of the MD. Adherence to the MD was defined as follows: >8 optimal, 4-7 intermediate, ≤3 very low adherence (KidMed)

and >7 optimal, 4-6 intermediate, ≤ 3 very low adherence (Short Mediterranean Diet Questionnaire). Total scores were divided by maximum scores to equalize scoring. Zito and colleagues' found significantly lower adherence in the IBS group compared to control ($p < 0.05$).⁴⁸ These results were also found when stratifying participants by age and gender: younger age (17-34 years old) and female were significantly associated with lower adherence to this diet ($p < 0.001$ and $p < 0.05$, respectively).⁴⁸ Based on these findings, an inverse relationship between FGID and MD adherence may be deduced; however, limitations exist in this research including: the limited dietary analysis that focused solely on certain foods consumed and omitted the amounts of these foods, not the whole diet as well as the data originating from a singular region.⁴⁸

IBS has been thought to be a pro-inflammatory condition throughout the literature. Given this proposed ideology, Salari-Moghaddam and colleagues proposed that consumption of proinflammatory foods and nutrients would contribute to the onset or exacerbation of IBS symptoms.⁵¹ To further authenticate this premise, Salari-Moghaddam and colleagues examined the relationship between inflammatory constituents of foods using the dietary inflammatory index (DII), the prevalence of IBS and its severity in a cross-sectional study of 3363 participants.⁵¹ The DII is a very prominent tool in nutrition research used to quantify the overall effect of the diet on inflammatory potential; on its second rendition, it is primarily used in cancer research.⁵⁶ The higher the DII score, the more closely the diet is associated with higher consumption of dairy, refined grains, pizza, soft drinks and lower consumption of whole grains, non-starchy vegetables, fruits, poultry, and legumes.⁵¹ Salari-Moghaddam and colleagues found participants in the highest DII scoring category were 42% more likely to have an IBS diagnosis than those in the lowest scoring category, correlating the consumption of a proinflammatory diet

with an increased risk for IBS.⁵¹ No significant association between DII score and IBS severity occurred in their findings.⁵¹ Though this research seems promising, there are no interventions or randomized control trials with a defined anti-inflammatory diet to determine the actual benefit this type of intervention would have on IBS.

High Fiber Diet

Fiber content of the diet is commonly manipulated in management of GI disorders, including IBS. In respect to fiber's role in GI health, it has characteristically been divided into two subcategories based on its most significant property: soluble and insoluble, which is the ability to dissolve in water. However, more recent literature has determined more appropriate classification of fiber is based on solubility, viscosity and fermentability compared to grouping based on solubility alone. Soluble fibers are viscous and fermentable in nature, though some are non-viscous, and are used as fuel for colonocytes in the gut. These include guar gum, inulin, fructo-oligosaccharides, and pectin. The short-chain fatty acids produced by the fermentation process of these fibers are thought to have an anti-inflammatory role, enhance immune capabilities, and increase the bulk of stool. Insoluble fibers are non-fermentable and non-viscous in nature and include cellulose and lignin. These increase stool bulk and frequency, promoting the passage of stool. Depending on the predominant bowel pattern and type of fiber utilized, this may provide symptom relief for IBS.

Given the physiological effects of fiber, this has led to an interest in providing a fiber-rich diet to this patient population. A high fiber diet does not have a universal definition; this can be defined as a 5-10g/day increase above normal consumption and/or meeting the recommended daily intake (RDI) for fiber, which is 25-38g/day. Most food items contain both types of fibers and, unfortunately, nutrition facts labels are not forced to indicate the amount of each fiber

within. This poses a challenge in recommending specific types of fibers to patients and gives further reasoning behind simply increasing fiber intake altogether. As mentioned previously with fiber supplementation, the beneficial effects of fiber in IBS are very diverse and uncertain. Research in this area is still in its' infancy; recommending this dietary approach for this patient population lacks robust evidence to do so, therefore, should be implemented slowly and cautiously. This is especially important as consuming a diet high in fiber does have the potential to exacerbate IBS symptoms.⁴⁵

Specific Carbohydrate Diet

The specific carbohydrate diet (SCD), is defined as an exclusion diet allowing carbohydrates that contain monosaccharides but exclude disaccharides or polysaccharides. Specifically, this diet is grain-free, soy-free and minimizes sugar in the diet as well.⁴⁹ Originally proposed dietary method for inflammatory bowel disease (IBD), the same ideology is applied for IBS: the SCD would reduce inflammation and possible dysfunction of the gut microbiota. Vincenzi and colleagues evaluated the efficacy and the nutritional adequacy of the SCD compared to the LFD in IBS (Rome IV).⁴⁹ Symptoms were assessed using a food diary, IBS-SSS and VAS. The LFD group exhibited significant improvement in abdominal bloating and distension ($p < 0.0001$) whereas the SCD group did not have statistically significant improvement.⁴⁹ Additionally, this study assessed the nutritional adequacy of vitamin D and folic acid in the SCD compared to the LFD. In terms of these micronutrients, the SCD appears to be of a lessor nutritional adequacy compared to the LFD.⁴⁹ Currently, this is the only RCT comparing the SCD and LFD so little conclusions of efficacy can be made at this time.

Gluten-Free / Wheat-Free Diet

A gluten- or wheat-free diet (WFD), has been investigated for the potential to alleviate IBS symptoms. Over the last decade, there has been a significant increase in awareness of the gluten-free diet (GFD).⁵⁰ Eliminating gluten from the diet is only an established therapy for celiac disease due to the inflammatory response in these individuals. However, it has become an emerging epidemiological issue and trend to eliminate these components of the diet without medical necessity. Catassi and colleagues analyzed the prevalence of this trend, noting a particularly high prevalence in Australia compared to other countries, and a higher percentage of those who exclude wheat and gluten than those diagnosed celiac disease in each country.⁵⁰ Due to NCGS found to be correlated with IBS, eliminating gluten or wheat-containing foods may provide symptom alleviation in these individuals. Several trials have assessed gluten and wheat consumption in association to IBS.⁵⁰ The sample sizes of each are relatively small, however, the recurrent findings in so many studies may support the use of this dietary approach for IBS. Overall, the studies whom provided a gluten challenge experienced more symptoms than those given placebo. Additionally, those who were provided a GFD experienced more symptom relief, with some studies even reaching significant symptom relief.⁵⁰ It is important to note the concurrence that products containing gluten also contain fermentable carbohydrates. This poses a confounding variable when analyzing the efficacy of a WFD or GFD and leaves uncertainty when trialing this diet as a treatment option.

Low FODMAP Diet

Within the last decade, fermentable carbohydrates, collectively termed as FODMAPs (Fermentable, Oligosaccharide, Disaccharide, Monosaccharide, and Polyols), as the culprit for IBS symptoms have taken center stage. As previously mentioned, FODMAPs are poorly absorbed, highly osmotic and rapidly fermented in the colon by bacteria which then manifest into

symptoms such as abdominal pain, bloating, distension, and constipation or diarrhea. Each type of fermentable carbohydrate exhibits their own effect on the gastrointestinal tract, however, there is substantial overlap.^{46,57}

Oligosaccharides, are found as fructans and galactans in foods such as wheat, barley, rye, legumes, onions and garlic.⁵⁸ These nutrients are poorly absorbed in general as humans lack a specific enzyme to break these down and thus are readily fermentable in the GI tract.⁵⁸ According to research by Murray and colleagues, one such oligosaccharide, inulin, substantially increases gas in the colon which leads to distension.⁵⁹

Disaccharides are found in the forms of sucrose, maltose and lactose. The primary disaccharide of interest for this patient population is lactose. Lactose is found in all dairy products that are derived from cow, goat and sheep milk and requires the lactase enzyme for absorption.⁶⁰ The concurrence of lactose intolerance and IBS has been described in length previously. As such, many with IBS tend to avoid lactose-containing products due to symptom exacerbation, such as abdominal pain and diarrhea, being commonly associated with consumption of lactose.⁶⁰ Lactose maldigestion has an osmotic effect on the GI tract and this may be the underlying etiology of symptoms.⁶¹

Monosaccharides are simple carbohydrates found as glucose, fructose and galactose primarily with fructose being the monosaccharide of interest in this patient population. This molecule is the naturally occurring sugar in fruits but is also added to food products such as high fructose corn syrup.⁶² Fructose requires no digestion and is absorbed in the intestines in two ways: through the GLUT-5 transporter and through the GLUT-2 transporter in conjunction with glucose.⁶² The GLUT-2 transporter is the most efficient path for fructose absorption; however, when excess fructose is more present than glucose in the intestine, this leads to poor

absorption.⁶² Generally, about 40% of people have limited ability to absorb free fructose and therefore exhibit fructose malabsorption.⁶²

Polyols, also known as sugar alcohols, are found in a variety of fruits, vegetables, plant products, and used in sugar-free gum, candy and mints, ice cream, baked goods, and fruit spreads.⁵⁸ They can also be used in dental and pharmaceutical products. Polyols are a short-chain carbohydrate that are more osmotically active, are likely to cause diarrhea and are more likely to undergo bacterial fermentation.⁵⁸ Malabsorption of polyols has been shown in up to 70% of both healthy people and individuals with IBS.⁶³

The LFD, founded by Monash University, is posed as the most successful and efficacious dietary intervention with significant symptom reduction. It is important to understand how this dietary intervention is designed. The diet is divided into three distinct phases: elimination, reintroduction and reintegration. The elimination phase is followed anywhere from 2-8 weeks to test for a reduction in symptom severity. If asymptomatic response is achieved, each FODMAP food group is slowly reintroduced into the diet while monitoring reoccurrence of symptoms. After identifying which foods contribute to IBS symptoms, the RDN can assist the patient to construct a well-balanced diet while eliminating trigger foods. This is the final phase of the LFD, reintegration, helps the patient live a well-balanced lifestyle avoiding very specific trigger foods. The ultimate goal is to provide long-term symptom relief while empowering patients to have control over their symptoms.

Because of the significant reduction in symptom severity, numerous trials have tested and examined the efficacy of the LFD in IBS (Table 4). Several RCTs have investigated the efficacy of the LFD for 4-6 weeks in those with IBS and have reported improvements in symptom severity and quality of life.^{39,43,64-71} Halmos et al compared the LFD to a typical Western diet

and reported significant symptom improvement in 70% of participants in the LFD group compared to 0% in the healthy control group ($p < 0.001$).⁴³ However, being that this was a controlled feeding study, it does not reflect real life experiences that patients undergo and limits external validity. Staudacher et al assessed the use of nutrition counseling in conjunction with a LFD for four weeks. Those in the LFD group experienced a 73% response rate in symptom reduction compared to a 43% reduction in the control group ($p = 0.005$).⁶⁶ Böhn et al and Eswaran et al compared the LFD to standard dietary guidelines for IBS (NICE Guidelines).^{65,67} Eswaran et al found a greater number of abdominal pain responders in the LFD group compared to the NICE group (51% vs 23%, respectively; $p = 0.008$).⁶⁷ Böhn et al randomized patients to LFD or NICE dietary advice for four weeks and found a 50% response rate for reduction in symptom severity in the LFD advice group compared with 46% in the NICE advice group though this was not significant.⁶⁵ When comparing a LFD to a high FODMAP diet, it has been identified that the diets low in FODMAPs provide symptom alleviation compared to the diet high in FODMAPs.^{65,67} It is important to note, that with each of these studies there is limited information reported on actual dietary adherence to the interventions implemented which may impact the overall conclusions of these studies (Table 4). Many limitations in the FODMAP literature are of concern. Several studies are conducted from the same laboratory where there is a lack of description of the FODMAP content of the diet and the foods contributing to the FODMAP concentration. Additionally, these studies lack a description of the tools used to assess dietary adherence/compliance. This is critical in determining cause and effect. This information would inform the extent of dietary education required to achieve the desired outcome. These limitations reiterate the necessity for more robust clinical trials aimed at fully

characterizing the dietary FODMAP content and the required adherence (i.e., dose response) to obtain this clinical effect.

| Study | Intervention vs Control (n) | Duration | Symptom Scoring | Key Findings (compliance assessed) | Micronutrient Assessments |
|-------------------------|--|----------|--|--|---|
| Harvie et al (2017) | LFD (23) vs LFD Waiting List (27) | 3 months | IBS-SSS, IBS-QOL | Reduction in IBS-SSS, significantly higher IBS-QOL (no) | None |
| Hustoft et al (2017) | LFD + Placebo (20) vs LFD + fructans (20) | 4 weeks | IBS-SSS, VAS | Reduced IBS-SSS, reduced IBS-SSS (no) | None |
| Staudacher et al (2017) | LFD (51) vs Sham (53) | 4 weeks | AR, IBS-SSS, IBS-QOL | Significantly lower IBS-SSS score, higher IBS-QOL (yes) | None |
| McIntosh et al (2016) | LFD (20) vs HFD (20) | 3 weeks | IBS-SSS | Greater number of responders, reduced IBS-SSS (yes) | None |
| Peters et al (2016) | LFD (24) vs Hypnotherapy (25) vs Combined (25) | 6 weeks | VAS, IBS-QOL | Reduced VAS (no) | None |
| Eswaran et al (2016) | LFD (45) vs modified NICE (39) | 4 weeks | AR | Greater reduction in pain (no) | None |
| Bohn et al (2015) | LFD (38) vs NICE (37) | 4 weeks | IBS-SSS, Stool Frequency, Stool Consistency | No differences (no) | None |
| Pedersen et al (2014) | LFD (42) vs Probiotic (41) vs Habit (40) | 6 weeks | IBS-SSS, IBS-QOL | Reduction in IBS-SSS (no) | None |
| Halmos et al (2014) | LFD (27) vs Typical (27) | 3 weeks | IBS-SSS, VAS, Stool Frequency, Stool Water Content | Significantly reduced overall GI symptoms, reduced stool frequency in IBS-D (yes) | None |
| Staudacher et al (2012) | LFD (19) vs Habit (22) | 4 weeks | AR, GSRS, BSFS | Greater amount of AR, greater frequency of normal stools (yes) | Yes – calcium and iron; calcium intake lower in LFD group |

Table 4. Comparisons of the LFD efficacy through RCTs. Abbreviations: AR – adequate relief, BSFS – Bristol stool form scale, IBS-SSS – irritable bowel syndrome severity scoring system, LFD – low FODMAP diet, NICE – National Institute for Health and Care Excellence VAS – visual analogue scale.

Nutritional Implications

Nutrition implications of following the LFD are extremely limited in the literature. This is relative to the short-term nature of the LFD and the studies available putting more emphasis on symptom relief and efficacy of this diet rather than nutritional impact. Researchers may not envision a necessity in looking into this due to the dietary patterns being similar to that of the general population and as of control groups indicating a low concern for nutrient deficiencies. Elimination diets as a whole have the potential to pose concern for micronutrient deficiencies given the nature of exclusivity. The exclusive nature of the LFD eliminates many fruits, vegetables, whole grains and dairy products. These food groups translate to micronutrient reduction of vitamin A, folic acid, vitamin C, vitamin D, zinc, magnesium and calcium intake.^{65,73} Several RCTs have shown a reduction in total energy/caloric intake for those who followed a LFD compared with a traditional diet which can be detrimental in the long-term.⁷² The impact of this caloric reduction is currently unknown but can pose concerns for micronutrient deficiencies. Literature examining the LFD and assessment of micronutrient intakes is most limited here. Research for IBS tends to solely examine energy, macronutrient and fiber intake, excluding micronutrients. Of ten RCTs analyzed, one had looked into micronutrient assessment and only calcium and iron were considered (Table 4).

Calcium is a micronutrient of concern based on the common exclusion of dairy in those with gastrointestinal conditions. A statistically significant reduction in calcium intake had been shown by Staudacher et al when comparing the LFD to a habitual diet for four weeks.³³ This is likely a result of the significant reduction in dairy products in the LFD, however this information was not reported. At this time, nutrient quantification has only been reported during the strict

elimination phase of the LFD which is short-term in nature.⁷⁴ In general, studies have not shown a severe nutritional impact of these diets on micronutrients.

Gut microbiota alterations have been found in those following the LFD, particularly with *Bifidobacterium* species, which is presumably tied to the low fiber content of the diet. There appears to be a reduction in *Bifidobacterium* concentration, proportion and abundance.⁷² *Bifidobacterium* is a known butyrate producer in the colon, which is a key indicator of colonic health.⁷² Fortunately, Staudacher et al found that a multi-strain probiotic could restore this bacteria in the gut microbiota, potentially solving this negative effect.⁷² It is important to reiterate this decrease in gut bacteria has only been shown in short-term studies and more literature is needed in long-term studies. Overall, an adapted version of the LFD appears to be nutritionally adequate though research is still limited here.⁷⁴

The lack of description of the nutritional intake in the FODMAP literature creates problems for the RDN to deliver a nutrient-rich dietary intervention. It is essential to establish and document the nutritional limitations of the LFD if they exist given the utilization of the LFD for symptom management globally. Although the short-term phase of the elimination likely does not pose severe nutritional risk, there are many factors that are unknown about the long-term use of this diet. Compliance to the LFD is poorly documented in a multitude of ways. Studies reporting compliance in the literature are scarce. The definition for compliance has yet to be universally defined and most studies do not describe compliance measurements. It is uncertain how many patients actually adhere to this for longer than the elimination phase when transitioning into the reintroduction phase or beyond this or the rate at which patients return to RDNs after the strict elimination phase to begin reintroduction. This suggests that some patients do remain in the strict elimination phase for long-term which literature does not expound upon.

Due to these uncertainties, having the ability to describe the nutritional impact and adequacy of the LFD is necessary to bridge the gap in the literature. Consequently, RDNs would be able to identify nutritional risks prior to implementation of the LFD and determine micronutrient supplementation needs.

Conclusion

The etiology of IBS cause remains elusive, immersed in elaborate pathophysiology. Treatment is multimodal, encompassing pharmacological, nutritional and alternative therapeutic approaches, focusing on symptom alleviation. However, despite these medical and nutritional treatment options, little efficacy has been described leading those with IBS to feel abandonment by their healthcare team. The introduction of the LFD has led to numerous publications supporting its' efficacy for treatment of symptom severity, but with the lack of dietary compliance data and an understanding of the nutritional implications of this intervention there is still much to elucidate. Therefore, there is a need for additional investigation into the role of dietary compliance and nutritional adequacy of dietary interventions used to improve symptoms in those with IBS.

Chapter 3: Methods

Introduction

This case report focused on the nutritional adequacy of LFD compared to a diet based on the Dietary Guidelines for Americans after a 2-week intervention. The first four participants are presented as a series of case reports. Assessment for nutritional adequacy of these dietary interventions were analyzed using pre- and post-intervention 3-day diet records. Methodology for this trial was approved by The Ohio State University Institution Review Board (IRB), protocol #2016H0320, for the use of human subjects.

Research Question

Is there a difference in nutrient intake of vitamin A, vitamin C, vitamin D, calcium, zinc, magnesium and fiber after a low FODMAP dietary intervention or a diet based on the DGAs?

Hypothesis

There will be no difference in nutrient intake of vitamin A, vitamin C, vitamin D, calcium, zinc, magnesium and fiber after a low FODMAP dietary intervention or a diet based on the DGAs.

Participants

Men and women (>18 years) with a diagnosis of IBS referred to the RDN within the Division of Gastroenterology, Hepatology and Nutrition (GHN) for individualized counseling for IBS are eligible for recruitment. Patients were offered the opportunity for study participation at the time of RDN referral. Inclusion and exclusion criteria are described below (Table 5).

| |
|---|
| <p><u>Inclusion Criteria:</u></p> <ul style="list-style-type: none"> • 18 years of age or older • Ability to read English • Diagnosis of IBS • RDN referral for nutrition consultation |
| <p><u>Exclusion Criteria:</u></p> <ul style="list-style-type: none"> • Under the age of 18 • Inability to voluntarily provide informed consent for study (including prisoners) • Pregnancy |

Table 5. Inclusion and exclusion criteria included in the recruitment strategy for the RCT.

Study Design

Patients referred to the RDN for a one-on-one appointment that were diagnosed with IBS were contacted via phone to gauge interest in study participation. Those interested, who met inclusion and exclusion criteria, were offered participation in the current study and scheduled for a baseline study visit. Prior to arrival at the baseline study visit, participants were asked to complete a 3-day diet record on non-consecutive days including 1 weekend day. At the baseline study appointment, investigators obtained consent and reviewed Health Information Portability and Accountability Act (HIPAA) documentation. Then, the investigators completed the health questionnaire, the initial IBS-SSS form and reviewed the initial 3-day diet record. Next, the randomization envelope was opened to reveal the assigned dietary intervention for the participants to follow for the subsequent two weeks. Participants completed an additional 3-day diet record and IBS-SSS form after 1 week of the dietary intervention to capture dietary and symptom changes. Those randomized to a LFD were also instructed to complete a daily high FODMAP food checklist if accidental consumption of restricted foods were consumed.

Participants returned to clinic to meet with the RDN after the 2-week intervention and returned the second 3-day diet record, high FODMAP checklists (if applicable) and IBS-SSS. The multiple pass approach was repeated for the additional diet records and another IBS-SSS was completed to end the study. Participants received a \$25 grocery gift card after each one-on-one appointment and all participants received low FODMAP food baskets from FODY Foods Co at the completion of the study.

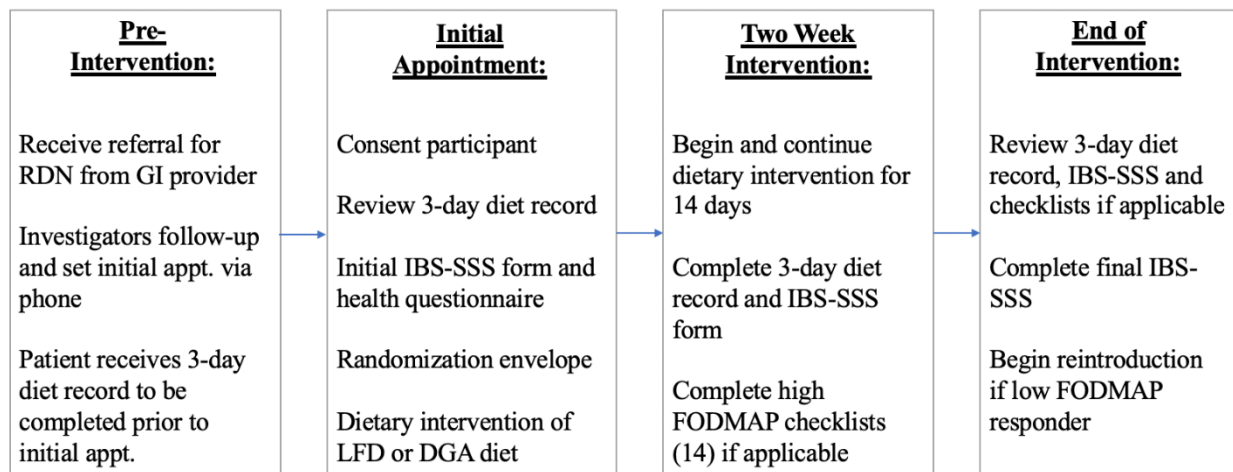


Figure 3. Study flow diagram for all participants enrolled in the RCT

Outcome Measurements and Assessments

Health questionnaire

This is a unique tool created specifically for this study. The questionnaire asks baseline demographic and health information regarding the diagnosis of IBS, current and past medical history, medication, supplements and alternative treatment used, and anthropometric measurements (Appendix A). This was used during the initial counseling appointment to capture medical history, anthropometric data and medication use.

3-Day Diet Record

The 3-day diet is a standardized and well-validated tool for use in nutrition assessment (Appendix B). The data from this will be used to determine changes in the nutrient intake and nutritional adequacy after the given dietary intervention. These records will be collected at baseline and at the end of study to reflect the dietary pattern during the intervention. The multiple pass approach was used to obtain detailed dietary data to facilitate accurate dietary assessment.

IBS Severity Scoring System (IBS-SSS)

Published by Francis et al. in 1997, the IBS-SSS is the most common instrument used in IBS research assessing the severity of participant's symptoms.⁷⁵ Five questions asked evaluate the participant's severity of pain, abdominal pain, distension, satisfaction with bowel habits, and the overall effect of IBS on a person's life (Appendix C).⁷⁵ Each of these questions provide a score of 0-100, adding up to a possible 500 being the highest overall score.⁷⁵ Scores are then subdivided into categories of mild (75-175), moderate (176-300) and severe (>300) IBS.⁷⁵ If a participant has a decreased of ≥ 50 points from baseline, this is associated with clinically significant improvement.⁷⁵ The IBS-SSS was completed at baseline, during the dietary intervention and at the end of study.

Bristol Stool Form Scale (BSFS)

The BSFS was utilized in conjunction with the IBS-SSS to determine the participant's typical stool consistency (Appendix C). It is a numerical and visual depiction of stool ranging from 1-7 with 1 corresponding to hard-to-pass, hard lumps of stool and with 7 corresponding to entirely liquid stool. The BSFS was completed at baseline, during the dietary intervention and at the end of study. This tool was also used to assist in subtyping the diagnosis of IBS: type 1-2

indicated constipation predominance, 3-4 indicated unspecified predominance, and 5-7 indicated diarrhea predominance.

High FODMAP Foods Checklist

For those allocated to the LFD intervention group, they were given *High FODMAP Foods Checklists* to complete each day of the intervention. With this form, participants would check off if they consumed a high FODMAP food item and indicate what that item was. This would assess for compliance to this particular dietary intervention.

Education Materials

The LFD: FODMAP education materials used for this intervention were from Kate Scarlata, MPH, RDN's online resources.⁷⁶ This included *FODMAPs 101*, *High and Low FODMAP Foods Lists*, and *Low FODMAP Grocery List*.⁷⁶ Subjects were educated on following the LFD for 2 weeks. Using the 3-day diet record collected at the baseline study visit, the education on the LFD was tailored to meet the needs of each subject. The subject was educated to replace high FODMAP foods consumed with a similar low FODMAP alternative (i.e. cow's milk was replaced with lactose-free cow's milk) in an effort to maintain the nutritional quality of the diet.

The DGA: Educational materials used for this intervention were resources from OSU Wexner Medical Center's Patient Education Center. This included: *High Fiber Diet*, *Making Sense out of Food Labels*, and *5-day 1800, 1500, 1200 Calorie Menus* (Appendix D). Using the initial 3-day dietary record collected during the baseline study visit, the RDN was able to tailor the education to match the participant needs. Upon review of their initial 3-day diet record, investigators determined which components of the diet should be focused on: increasing fiber intake, decreasing added sugar intake, or both. Specifically, dietary fiber goals were established

to meet the RDI of 25–38 g/day for males and females, respectively. To increase fiber delivery, 1-2 high fiber food items were substituted for a low fiber food item in the participants' diet with the goal of improving fiber delivery towards the goal set for that age and sex of the participant. Reducing added sugar to <10% of total daily calories based on the recommendations set forth through the DGAs, investigators targeted sugar sweetened beverages, candies, cookies and flavored yogurts. When foods associated with added sugars were identified in the 3-day diet records, substitutions for lower sugar alternatives were emphasized during the consultation. Regardless of the participant's need for increased fiber or decreased added sugar, each participant was educated on their assigned dietary intervention with established goals to specifically adjust the diet to comply with the DGAs. Education on reading a food label was provided and kilocalorie specific menus were provided based on their baseline BMI accordingly: 35kcal/kg for BMI of < 18.5, 30 kcal/kg for BMI of 18.5-24.9, 25 kcal/kg for BMI of 25-29.9, 20 kcal/kg for BMI of >30.

Statistical Analysis

Dietary intake collection and analysis was performed using Nutrient Data System for Research (NDSR) software, version 2019, developed by the Nutrition Coordination Center (NCC) of the University of Minnesota. Dietary intake was summarized by means and ranges for continuous variables, including percent of kilocalories from carbohydrates, fats, proteins and percentage of the Recommended Dietary Allowances (RDAs) for micronutrient intake. Demographic and health data were analyzed and summarized using frequencies, means, ranges and percentages. IBS stool type, frequency and severity were analyzed and summarized using frequencies and descriptive, categorical subtyping. Compliance to the dietary intervention was analyzed and summarized using means and percentages.

Chapter 4: Results and Discussion

Results:

A total of eight participants enrolled in this study with six having completed the study (75%); the first four subjects are reported within (Figure 4). The recruitment pool began with 27 potential participants. From the initial pool, 13 were recruited for the study: eight consented to participate while five did not show for their baseline appointment. Of the four participants reported within, one participant did not provide end of study (EOS) data for nutrient intake. Due to the sample size, descriptive statistics will be used to discuss participants using a case study format.

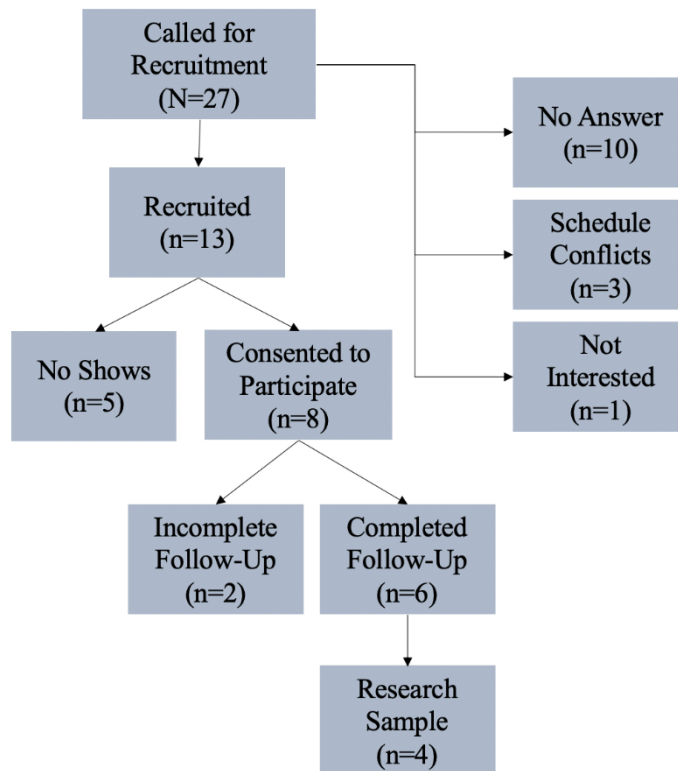


Figure 4. Recruitment flow chart

| Subject | Intervention Group | Compliance |
|---------|--------------------|------------|
| FOD 001 | DGA | - |
| FOD 003 | LFD | 0/12 days |
| FOD 005 | DGA | - |
| FOD 009 | LFD | 14/14 days |

Table 6. Measured daily compliance of subjects recruited.

Cohort Demographics, Lifestyle, and Baseline Characteristics:

Three of the four participants were female. Median age was 46 years (ranging from 39 to 55 years), and median BMI was 32.8kg/m² (ranging from 27.9 to 41.1 kg/m²). Two participants engaged in mild to moderate physical activity. No participants smoked cigarettes, one participant smoked marijuana, and three participants consumed alcohol in moderation. Time since IBS diagnosis ranged from two months to 36 years.

Dietary interventions trialed in this patient population varied. One participant received nutritional counseling or prior nutrition information for management of IBS with instruction for following an elimination of certain food items and also reported several food allergies which led to a number of restricted foods. One participant also had celiac disease and therefore followed a gluten-free diet. Two participants had minor or no food restrictions that were reported at baseline.

Medication use, both prescription and over the counter (OTC), were common in this cohort. Prescription medications were reported by two participants and included anti-cholinergic/anti-spasmodic medications; non-prescription medications were more common, taken by three of four participants, and included pain relief, laxatives and gas relief. Supplement

use was reported by all participants and included multivitamins (MVI), vitamin D, vitamin C, probiotics and fiber. Engagement in alternative therapies were reported by two participants which included yoga and cognitive behavioral therapy (CBT).

| Demographic | |
|-------------------------|------------------|
| Age (years) | 39-55 years |
| Sex (male) | 1 |
| BMI (median) | 27.9-41.1 (32.8) |
| Mild/Moderate Exercise | 50% |
| Smoking | 0% |
| Alcohol | 75% |
| Rx Medication | 50% |
| Non-Rx Medication | 75% |
| Supplement Use | 100% |
| Alternative Therapy Use | 50% |

Table 7. Cohort demographic information.

IBS-SSS was used to determine the severity of IBS symptoms. Based on this scoring system, one participant had severe IBS and three participants had moderate IBS (Table 7). Using the BSFS, one participant had IBS-C, one participant had IBS-D, and two participants had IBS-U.

| Subject | Intervention | Baseline (T₀) | End of Study (T₂) | Change T₀-T₂ |
|----------------|---------------------|---------------------------------|-------------------------------------|---|
| FOD 001 | DGA | 229 | 119 | -110 |
| FOD 003 | FODMAP | 232.5 | 263.5 | +31 |
| FOD 005 | DGA | 323.5 | 272 | -51.5 |
| FOD 009 | FODMAP | 212 | 346 | +134 |

Table 8. Changes in IBS-SSS from Baseline to End of Study (N=4)

Cohort Assessment of Dietary Changes and Diet Adequacy:

Assessment of nutrient intake and dietary changes was performed using NDSR programming. Only three out of four participants were included in this discussion due to one participant not providing their EOS diet records for nutrient analysis. However, significant deficits in nutrient intake were identified in baseline and EPS dietary analysis of 3-day diet records.

Baseline NDSR data showed that daily caloric intake was below recommendations in three of the four participants ranging from 10 to 50% below estimated energy requirements (Table 8). This low caloric intake likely impacted micronutrient intake as all micronutrients of concern were below the RDA with the exception of zinc in three participants, calcium in one participant and vitamin C in another participant (Tables 12, 14, and 16). Regardless of the dietary intervention, micronutrient intake was still suboptimal with the exception of zinc and magnesium in only one participant, respectively, indicating that both the baseline and intervention diets were nutritionally inadequate. Vitamin A and vitamin D intakes did not meet the RDA at baseline or EOS for any of the participants which was concerning given the importance of these fat-soluble vitamins. Overall, vitamin A intake at baseline was below the RDA with two participants falling below 50% of the RDA. Vitamin D intake at baseline was

below 50% of the RDA for all participants, indicating severely depleted dietary intake for both vitamins.

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|----------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 | DGA | 1088 | 923 | -165 |
| FOD 003 | FODMAP | 2890 | - | - |
| FOD 005 | DGA | 1912 | 1963 | +51 |
| FOD 009 | FODMAP | 882 | 1045 | +163 |

Table 9. Changes in Daily Kilocalorie Intake (in kcals) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|----------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 | DGA | 123 | 120 | +77 |
| FOD 003 | FODMAP | 357 | - | - |
| FOD 005 | DGA | 255 | 255 | 0 |
| FOD 009 | FODMAP | 151 | 206 | +55 |

Table 10. Changes in Daily Carbohydrate Intake (in g) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|----------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 | DGA | 16 | 8 | -8 |
| FOD 003 | FODMAP | 21 | - | - |
| FOD 005 | DGA | 23 | 30 | +7 |
| FOD 009 | FODMAP | 8 | 8 | 0 |

Table 11. Changes in Daily Fiber Intake (in g) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 135, (19%) | 332, (47%) | +197 |
| FOD 003 (%RDA) | FODMAP | 563, (63%) | - | - |
| FOD 005 (%RDA) | DGA | 575, (82%) | 617, (88%) | +42 |
| FOD 009 (%RDA) | FODMAP | 121, (17%) | 300, (43%) | +179 |

Table 12. Changes in Daily Vitamin A Intake (in IUs) and percentage of the RDA from Baseline to End of Study (N=4).

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 22, (29%) | 16, (21%) | -5.6 |
| FOD 003 (%RDA) | FODMAP | 149, (165%) | - | - |
| FOD 005 (%RDA) | DGA | 40, (53%) | 51, (68%) | +10.8 |
| FOD 009 (%RDA) | FODMAP | 25, (33%) | 51, (68%) | +26.3 |

Table 13. Changes in Daily Vitamin C Intake (in mg) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 3, (19%) | 5 (33%) | +2.0 |
| FOD 003 (%RDA) | FODMAP | 7, (47%) | - | - |
| FOD 005 (%RDA) | DGA | 5, (33%) | 8 (53%) | +2.9 |
| FOD 009 (%RDA) | FODMAP | 0.2 (1%) | 0 (0%) | -0.2 |

Table 14. Changes in Daily Vitamin D Intake (in IUs) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 454, (45%) | 594, (59%) | +140 |
| FOD 003 (%RDA) | FODMAP | 1098, (110%) | - | - |
| FOD 005 (%RDA) | DGA | 807, (81%) | 945, (95%) | +138 |
| FOD 009 (%RDA) | FODMAP | 480, (48%) | 198, (20%) | -282 |

Table 15. Changes in Daily Calcium Intake (in mg) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 164, (51%) | 145, (45%) | -19 |
| FOD 003 (%RDA) | FODMAP | 386, (92%) | - | - |
| FOD 005 (%RDA) | DGA | 312, (98%) | 373, (117%) | +61 |
| FOD 009 (%RDA) | FODMAP | 74, (23%) | 90, (28%) | +16 |

Table 16. Changes in Daily Magnesium Intake (in mg) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 7.9, (99%) | 5.6, (70%) | -2.3 |
| FOD 003 (%RDA) | FODMAP | 12.1, (110%) | - | - |
| FOD 005 (%RDA) | DGA | 11.7, (146%) | 16.9, (211%) | +5.2 |
| FOD 009 (%RDA) | FODMAP | 3.1, (39%) | 3.0, (38%) | -0.1 |

Table 17. Changes in Daily Zinc Intake (in mg IUs) from Baseline to End of Study (N=4).

FOD 001

FOD 001 was a 50-year-old female, with moderate IBS-D that was diagnosed two months prior to this intervention with a BMI of 27.9 kg/m². This participant had not received previous nutritional counseling for management of IBS and without following any special diet. However, prior to this initial appointment the participant had been regularly decreasing rice intake and simultaneously increasing water intake to help with symptom alleviation. Prior to this intervention, the participant also engaged in physical activity in the form of walking for 20 minutes, 3x per week. She did not endorse smoking or consumption of alcohol. The participant did not take any prescription medications for IBS symptom relief; however, endorsed use of OTC ibuprofen approximately 3x per week for pain relief from IBS. The participant took a MVI supplement daily.

Nutrient Intake Changes

Participant FOD 001 was randomized to an individualized approach to the DGAs. Upon review of the participant's initial 3-day diet record, it was determined that the participant consumed foods with little to no added sugar, however, fiber intake appeared suboptimal at baseline. Therefore, dietary instruction to increase fiber intake was the primary goal. Specifically, this participant was educated to substitute white rice and cornflakes with brown rice and whole grain cereals, and increase pinto bean consumption, which would increase the amount of fibrous foods as the academy of nutrition and dietetics recommends. It was estimated that this would increase her dietary fiber from 16 g/day to 25 g/day meeting the RDA for age and sex. Analysis of pre-intervention diet records indicated the participant was below the RDA for kilocalories, carbohydrates, fiber, vitamin A, vitamin C, vitamin D, calcium, and magnesium. The participant consumed 100% of the RDA for zinc prior to intervention (Table 17). At the conclusion of the study, post-intervention dietary analysis indicated a further decline in overall nutrient intake which was likely related to her decline in overall kilocalorie consumption by 166 kcals/day (Table 17). Specifically, kilocalorie, carbohydrate and fiber decreased from baseline to the end of study (see Table 17). A decrease in vitamin C, from 29% of the RDA to 21% of the RDA and magnesium, from 51% to 45% of the RDA occurred. Zinc intake had been the only micronutrient that had reached the RDA, but this micronutrient also decreased after the dietary intervention to 75% of the RDA. The appropriate dietary substitution of white rice to brown rice was achieved despite the decrease in fiber intake by 50%, meeting only 21-32% of the RDA.

| Nutrient | RDA* | Intake at Baseline | % RDA Met | Intake at EOS | % RDA Met |
|--------------------------------|-------------|---------------------------|------------------|----------------------|------------------|
| Kilocalories (kcal/day) | 1718-2148 | 1088 | 51-63% | 922 | 43-54% |
| Carbohydrate (g/day) | 130 | 123 | 94% | 120 | 92% |
| Fiber (g/day) | 25-38 | 16 | 42-64% | 8 | 21-32% |
| Vitamin A (mcg/day) | 700 | 135 | 19% | 332 | 47% |
| Vitamin C (mg/day) | 75 | 22 | 29% | 16 | 21% |
| Vitamin D (mcg/day) | 15 | 3 | 20% | 5 | 33% |
| Calcium (mg/day) | 1000 | 454 | 45% | 594 | 59% |
| Magnesium (mg/day) | 320 | 164 | 51% | 145 | 45% |
| Zinc (mg/day) | 8 | 8 | 100% | 6 | 75% |

Table 18. Changes in Nutrient Intakes for FOD001 from Baseline to End of Study

FOD 003

FOD 003 was a 55-year-old male, with moderate IBS-U that was diagnosed 35 years prior with a BMI of 28.5 kg/m². This participant had not received previous nutritional counseling for management of IBS and did not follow any particular diet or restrictions prior to the initial appointment. Prior to this intervention, the participant also engaged in physical activity in the form of swimming and biking approximately 2-3 miles, twice per day, 3-4x per week. He endorsed having a previous smoking history, with cessation occurring in June of 2007; he endorsed drinking alcohol in the form of beer, approximately 3-4x per week. This participant did not take any prescription or OTC medications for IBS symptom relief; however, endorsed taking MVI, fiber, and probiotic supplements once daily. He also participated in yoga as an alternative therapy 4x per week.

Nutrient Intake Changes

Participant FOD 003 was randomized to the LFD intervention. Upon review of the participant's initial 3-day diet record, it was observed that the participant did consume a diet with a plethora high FODMAP foods. The participant was instructed to follow the LFD and educated on how to do so, emphasizing the importance of restricting the high FODMAP food items the participant regularly consumed (i.e. apples). This participant did not provide a completed 3-day diet record at the end of the intervention, therefore, only pre- diet analysis occurred. Analysis of the diet record indicated an average caloric intake and carbohydrate intake above the estimated energy requirements which likely contributed to fiber intake being 84% of the minimum RDA range. Several micronutrients were also above the RDA, including vitamin C (165%), calcium (110%), and zinc (110%). Despite the higher caloric intake, magnesium, vitamin A, and vitamin D still were below the RDA at 92%, 63%, and 47%, respectively. Although there was not a 3-day intervention diet record, the participant did return the FODMAP checklists which revealed consumption of high FODMAP food items daily during the intervention indicating poor compliance.

| Nutrient | RDA* | Intake at Baseline | % RDA Met | Intake at EOS |
|--------------------------------|-------------|---------------------------|------------------|----------------------|
| Kilocalories (kcal/day) | 1846-2308 | 2890 | 125-157% | - |
| Carbohydrate (g/day) | 130 | 357 | 275% | - |
| Fiber (g/day) | 25-38 | 21 | 55-84% | - |
| Vitamin A (mcg/day) | 900 | 563 | 63% | - |
| Vitamin C (mg/day) | 90 | 149 | 165% | - |
| Vitamin D (mcg/day) | 15 | 7 | 47% | - |
| Calcium (mg/day) | 1000 | 1098 | 110% | - |
| Magnesium (mg/day) | 420 | 386 | 92% | - |
| Zinc (mg/day) | 11 | 12.1 | 110% | - |

Table 19. Changes in Nutrient Intakes for FOD003 from Baseline to End of Study

FOD 005

FOD 005 was a 40-year-old female, with severe IBS-U that was diagnosed 22 years prior with a BMI of 41.1 kg/m². This participant had not received previous nutritional counseling for management of IBS, however, was following a gluten free diet due to their underlying celiac disease diagnosis. They also chose to limit overall food consumption to help with IBS symptom alleviation. Prior to this intervention, the participant did not engage in regular physical activity. She endorsed smoking of medical marijuana up to 3x per day as well as consumption of alcohol on occasion but was unable to quantify the amount or type of alcohol consumed. This participant endorsed use of a prescription medication, dicyclomine, twice daily which is an antispasmodic. Reported use of several OTC medications included: omeprazole 3x per day, polyethylene glycol 1-2x per day, and Roloids brand antacids on occasion. Supplement use consisted of vitamin D, vitamin C, prenatal MVI and melatonin daily. Alternative therapies were utilized by this patient in the form of CBT 1x per week.

Nutrient Intake Changes

Participant FOD 005 was randomized to the individualized approach to the DGAs. Upon review of the participant's initial 3-day diet record, it was determined that the participant consumed many foods that contained added sugar (i.e. sugar-sweetened creamers, cereals and granola bars) while also including low fiber food sources in their diet. Consequently, the participant was instructed to both decrease added sugar intake to <10% of total calories and increase dietary fiber intake to 25 g/day based on the recommendation for age and sex. The participant was encouraged to increase fresh fruit, vegetable and legume intake to 2.5 cups/day by incorporating new vegetables (i.e. beans) to meet fiber goals. Additionally, sugar-sweetened creamers, drinks, cereals and granola bar consumption were emphasized to limit. Analysis of pre-intervention dietary records indicated this participant consumed nutrients below the RDA on all nutrients of interest with the exception of carbohydrates (196% of the RDA) and zinc (150% of the RDA). Post-intervention analysis indicated no relevant changes in kilocalorie or carbohydrate consumption (see Table 19). Mean fiber intake increased from a mean intake of 23g/day to 30g/day post-intervention, meeting recommendations of 25 g/day despite mean carbohydrate intake remaining the same. Evaluation of the 3-day diet records at baseline showed implementation of high fiber recommendations daily. Micronutrient intake increased for vitamin A, vitamin C, vitamin D, calcium, magnesium and zinc. Magnesium and zinc exceeded the RDA (117% and 213%, respectively), while vitamin A, vitamin C, vitamin D, and calcium remained below the RDA despite these increasing from baseline.

| Nutrient | RDA* | Intake at Baseline | % RDA Met | Intake at EOS | % RDA Met |
|--------------------------------|-------------|---------------------------|------------------|----------------------|------------------|
| Kilocalories (kcal/day) | 2180-2725 | 1912 | 70-88% | 1963 | 72-90% |
| Carbohydrate (g/day) | 130 | 255 | 196% | 255 | 196% |
| Fiber (g/day) | 25-38 | 23 | 61-92% | 30 | 79-120% |
| Vitamin A (mcg/day) | 700 | 575 | 82% | 617 | 88% |
| Vitamin C (mg/day) | 75 | 40 | 53% | 51 | 68% |
| Vitamin D (mcg/day) | 15 | 5 | 33% | 8 | 53% |
| Calcium (mg/day) | 1000 | 807 | 81% | 945 | 95% |
| Magnesium (mg/day) | 320 | 312 | 98% | 373 | 117% |
| Zinc (mg/day) | 8 | 12 | 150% | 17 | 213% |

Table 20. Changes in Nutrient Intakes for FOD005 from Baseline to End of Study

FOD 009

FOD 009 was a 39-year-old female, with moderate IBS-C that was diagnosed 9 years prior with a BMI of 33.5 kg/m². This participant had received nutritional counseling and tried the LFD in the past; however, this did not seem to alleviate symptoms. In addition, this participant had multiple food allergies, like wheat and egg whites, and would restrict these allergens “as best as I can” as well as avoiding seasonings. Prior to this intervention, the participant did not engage in physical activity. They did not endorse smoking and would consume alcohol in the form of sherry, sipping this approximately 2x per week. This participant took the antispasmodic, dicyclomine, and the antidepressant, sertraline, as prescription medications to help with IBS symptom relief. In addition, the participant took a half dose of hydrocodone as a pain reliever 3x per day. The participant did not take any non-prescription medications, however, endorsed taking vitamin D 10,000 IU daily, probiotics daily, and thyme

and fenugreek supplements in unknown amounts once daily. They did not participate in any alternative therapies.

Nutrient Intake Changes

Participant FOD 009 was randomized to the LFD intervention. The participant was instructed to follow the LFD and educated on how to do so, emphasizing the importance of restricting the high FODMAP food items the participant regularly consumed. Analysis of both pre- and post-intervention diet records shown the participant's overall caloric intake was well below recommended energy needs, meeting only about 50% for both pre- and post- dietary analysis. At baseline, fiber, vitamin A, vitamin C, vitamin D, calcium, magnesium and zinc all fell below the RDA (Table 20). At baseline carbohydrate intake met the RDA at 116% which increased to 158% of the RDA post-intervention despite the low caloric intake. Vitamin A, vitamin C, and magnesium all increased from baseline, but still to suboptimal levels. NDSR did not detect any sources of vitamin D from either 3-day diet record; however, the subject was consuming a high-dose vitamin D supplement orally. This participant completed all FODMAP checklists and the intervention 3-day diet record which both indicated 100% compliance to the dietary intervention.

| Nutrient | RDA* | Intake at Baseline | %RDA Met | Intake at EOS | % RDA Met |
|--------------------------------|-------------|---------------------------|-----------------|----------------------|------------------|
| Kilocalories (kcal/day) | 1780-2225 | 882 | 40-50% | 1045 | 47-59% |
| Carbohydrate (g/day) | 130 | 151 | 116% | 206 | 158% |
| Fiber (g/day) | 25-38 | 8 | 21-32% | 8 | 21-32% |
| Vitamin A (mcg/day) | 700 | 121 | 17% | 300 | 43% |
| Vitamin C (mg/day) | 75 | 25 | 33% | 51 | 68% |
| Vitamin D (mcg/day) | 15 | 0.2 | 0% | 0 | 0% |
| Calcium (mg/day) | 1000 | 480 | 48% | 198 | 20% |
| Magnesium (mg/day) | 320 | 74 | 23% | 90 | 28% |
| Zinc (mg/day) | 8 | 3 | 38% | 3 | 38% |

Table 21. Changes in Nutrient Intakes for FOD009 from Baseline to End of Study

Discussion:

Assessing the nutritional composition of usual dietary consumption to that after an RDN-led dietary education and connecting these dietary patterns to those with IBS requires acknowledgement of the comparisons of these four subjects with that of the typical IBS population. Fortunately, demographic data and medical management of these participants was consistent with what is identified in the literature. Additionally, IBS is a female predominant condition in which patients tend to be of normal weight BMI presenting between the ages of 39 to 55 which was also consistent with these four participants.^{77,78} Most importantly, we were able to portray the challenges that may present with different IBS subtypes as this case study presentation provides representation of each IBS subtype.

Each of these participants were referred to the RDN for nutrition counseling yet most were restricting or limiting various foods before the baseline visit highlighting the need for the RDN to assess the nutritional adequacy of their diet before and after an RDN-led intervention.

It is well-understood that the patients' perception of food is the number one contributor to symptoms and consequently assert food restrictions as self-management.⁷⁹⁻⁸² The most common foods that are self-eliminated from a patient's diet are typically dairy and gluten-containing products which are rich sources of calcium, vitamin D, B vitamins and iron.^{80,81} Logically, extensive restriction for an unknown length of time would lead to high risk of micronutrient deficiencies. This was exactly what was seen in the results reported within.

Baseline Dietary Patterns

The overall consensus that can be deduced about this cohort was the inability to meet the RDA for most nutrients across the board despite dietary intervention and encouragement to meet guidelines and recommendations. This was not exactly surprising when we look at dietary patterns for Americans. According to the most recent edition of the DGAs, calcium, vitamin D and fiber have been recognized as nutrients of public health concern due to the negative consequences seen in consuming too little of these, such as poor colon health.⁵² To become a public health concern acknowledged by the DGAs, a significant proportion of the American population is not meeting the recommended intakes set forth by these guidelines.⁵² It was hypothesized that those with IBS might have similar challenges adhering to the concepts outlined in the DGAs with perhaps additional challenges due to the self-restrictions of various food groups (i.e. dairy and wheat). As evidenced by the nutrient intake data for this cohort, caloric intake was optimal in two participants. In those unable to meet their estimated energy intake, we expected challenges meeting micronutrient needs as well. However, mean nutrient intake for most nutrients did fall below the RDA at baseline despite caloric intake.

Dietary fiber intake was suboptimal in three of the four participants. During participant interviews, most expressed perceiving fiber to be the cause of all IBS symptoms. Literature

supports that food groups that are heavily restricted are naturally fibrous food sources: legumes, whole grains, fruits, and vegetables.⁶⁵ As mentioned previously, optimal dietary fiber intake is linked with a diverse microbiome and is associated with a reduced risk of many chronic illnesses including colorectal cancer. Therefore, education is necessary for the American population to increase fiber intake, but this may be even a greater concern for those with IBS that are self-restricting fibrous foods as well. Food group analysis was unavailable for the cases presented within; however, this could be an area to gain insight into baseline dietary patterns in those with IBS.

Vitamin A and vitamin D intakes were suboptimal for all participants at baseline. Vitamin A intake did not attain even 50% of the RDA at baseline for two of the participants whereas vitamin D intake did not attain 50% of the RDA for all participants at baseline. These fat-soluble vitamins in combination with calcium (also well-below the RDA for three participants at baseline) are critical for bone health. The level at which these were deficient are doubly concerning given two of the participants also transitioned to a restrictive dietary intervention. An RDN-led intervention should help to reduce these micronutrient shortcomings, however, post-dietary analysis was still concerning for nutritional inadequacies.

Post-intervention Dietary Analysis

Post-intervention nutrient data was heterogeneous as it relates to nutrient intake with some participants increasing their nutrient intake and others decreasing intake. Only two participants met their estimate energy needs which reemphasized the importance of bringing caloric intake into context as this is expected to be associated with inadequate nutrient intakes. Despite dietary intervention led by an RDN, the RDAs for nutrients were seldom achieved by participants. Nutrient intakes meeting the RDA decreased across the board after the RDN-led

intervention. As mentioned, lower nutrient intake was expected when participants are unable to meet estimated energy needs. Carbohydrate intake for all three participants remained relatively consistent with little increase or decrease post-intervention. Most participants (two of three) achieved the RDA for carbohydrates while one decreased intake remaining below the RDA. Only one participant managed to achieve the RDI for fiber intake post-intervention. The other two participants either kept fiber intake consistent at 50% of recommendations or decreased their fiber intake by an additional 50%.

| Subject | Intervention | Baseline (T₀) | End of Study (T₂) | Change T₀-T₂ |
|-----------------------|---------------------|---------------------------------|-------------------------------------|---|
| FOD 001 (%RDA) | DGA | 454, (45%) | 594, (59%) | +140 |
| FOD 003 (%RDA) | FODMAP | 1098, (110%) | - | - |
| FOD 005 (%RDA) | DGA | 807, (81%) | 945, (95%) | +138 |
| FOD 009 (%RDA) | FODMAP | 480, (48%) | 198, (20%) | -282 |

Table 22. Changes in Daily Calcium Intake (in mg) from Baseline to End of Study (N=4)

At post-intervention, magnesium recommendations were only met by one participant. The other two participants fell below 50% of the RDA post-intervention. Zinc appeared to be the most abundant nutrient in this cohort, however, at post-intervention, zinc intake decreased for two of three participants while one participant continued to exceed the recommendations for zinc intake. Vitamin C intake did not achieve the RDA for any participants post-intervention. Similarly, as with the pre-intervention diets, vitamin D and vitamin A were two nutrients that were a challenge for all participants. Interestingly, vitamin A intake did increase for all participants after the intervention but were still at suboptimal intakes. Vitamin D was similar in that intake also increased for the majority of participants (two out of three), though also remaining below the RDA. This may be due to the common restriction of dairy products in this

patient population for symptom management, however, dairy consumption was reported for most participants in the form of milks or cheeses. Additionally, when dairy consumers are starting on the LFD they were educated on calcium and vitamin D rich food substitutes to prevent suboptimal intake. It was clear from this subset of participants that micronutrient intake is likely a greater concern than previously identified in the literature. The literature on micronutrient intake in those with IBS varies considerably. According to recent literature by Torres et al, lower intakes of micronutrients, including calcium and zinc, have been observed in this patient population.⁸³ Previous literature, such as that of Williams et al, had indicated opposite results in that this patient population had adequate micronutrient consumption.⁸⁴ Note that there are two studies highlighted in this discussion as most LFD research does not report micronutrient intake in pre- or post-intervention diets.

Examination between the two dietary intervention subgroups show subtle differences between them. This was particularly hard to assess as each cohort included only two participants and with the LFD subgroup missing nutrient intake data at EOS. Mean nutrient intake data for the DGA subgroup demonstrated that two nutrients (carbohydrate and zinc intake) exceeded the RDA. Mean nutrient intake data for the LFD subgroup shown none of the nutrients meeting the RDA. Again, the LFD subgroup extrapolations are challenging due to only one participant having EOS data reported as a mean. Based on the nutrient intake data for both subgroups, it seems as though the DGA dietary intervention had overall better results from this than did the LFD dietary intervention. This is particularly interesting as the DGA intervention was less restrictive and reflective of a dietary pattern approach.

The DGA intervention was designed to compare a standard dietary education to improve the nutritional quality of the diet without a restrictive approach aiming to provide fewer

nutritional challenges in meeting the RDA for most micronutrients. Several RCTs have shown a reduction in total energy, or kilocalorie, intake for those who followed a LFD compared with a traditional diet which can be detrimental in the long-term.⁷² Regardless of the intervention, caloric intake was a challenge and requires the RDN to address. However, with the exclusive nature of the LFD, eliminating many fruits, vegetables, whole grains and dairy products, we hypothesized that this would correlate with lower intakes of vitamin A, vitamin C, vitamin D, zinc, magnesium and calcium intake.^{65,73} Data presented here does not support that the LFD creates more of a nutritional deficit than a standard dietary intervention based on the DGAs. Both groups struggled to meet micronutrient needs. This may be related to the cohort consuming fewer fruits, vegetables, whole grains and dairy products, but food group analysis was not assessed. Presently, nutrient quantification has only been reported in few studies and only during the strict elimination phase of the LFD which is short-term in nature.⁷⁴ Suboptimal fiber intake in all participants may impact *Bifidobacterium* species, a known butyrate producer in the colon, which is a key indicator of colonic health.⁷² From these cases, the RDN must consider methods for improving fiber and/or probiotic delivery to combat this risk as seen in work from Staudacher et al.⁷¹ As mentioned, their work shown the abundance of *Bifidobacterium* species was lower in those on the LFD than those on the sham diet but higher in those given a probiotic supplement.⁷¹ Additional research emphasizing the dietary impact of the LFD on the microbiome needs highlighted in future studies especially given the overlap of SIBO and IBS.

Compliance

Understanding differences between these dietary interventions must be discussed in the context of dietary compliance to ensure we are actually comparing the LFD to a standard dietary approach based on the DGAs. The assessment of compliance to dietary intervention were

implemented for the LFD subgroup for this study. Current literature has not achieved a universal definition for compliance to the LFD. To take the most conservative approach for this study, investigators defined compliance to this dietary intervention as no intake of high FODMAP food items for any day of the intervention. In previous literature, compliance can also be defined as following this diet anywhere between 50-100% of the time. Higher compliance to this diet did not yield improvement in IBS-SSS scores in this study cohort. Compliance to the individualized dietary approach based on the DGAs was not defined in any capacity given this approach is more aimed at long-term dietary pattern changes. Healthy eating index (HEI) scores are a means of assessing adherence to the DGAs, however, these were not utilized given the nature of this individualized approach.

Out of 10 RCTs, only four incorporated compliance and adherence data (Table 21). The definition of compliance and adherence to the interventions varied from study to study, never establishing one cohesive definition. One study, by McIntosh et al, relayed that they looked at compliance, however, did not report how they had planned to assess this nor how they were defining compliance. Results of this were reported as “good” compliance to the intervention yet it is difficult to determine what exactly that means. A study by Staudacher et al in 2012 defined compliance as having a lower consumption of short-chain fermentable carbohydrates at the EOS with results showing all participants being compliant to this definition. Another study by Staudacher et al in 2017 defined compliance as self-reporting following the assigned diet greater than 50% of the time with all participants being compliant to this definition. Similarly, Halmos et al defined compliance as following the intervention as greater than 81% of the time or 17/21 days of the intervention and all participants were compliant to this definition. The occurrence of examining compliance is scarce and when this does occur, the definition is completely

heterogeneous. Consequently, the results pertaining to compliance are also variable and difficult to interpret. The majority of these studies also include feeding studies which, unfortunately, are not realistic to what an actual patient would encounter in their own daily lives. These results and unclear definition of compliance also gives uncertainty to the interpretation of nutrient intake analysis from these few studies.

The cases presented within this study provide a most conservative definition of compliance while incorporating two 3-day diet records reviewed for accuracy by study investigators to provide clear assessment of the nutritional adequacy of the LFD compared to DGAs. It is important to reiterate that implementation of the DGAs are designed more for the purposes of adherence rather than compliance. This study did not utilize HEI scores, however, this would give the ability to test for adherence to the DGAs in future studies.

| Study | Intervention vs Control (n) | Duration | Compliance Assessed and Means of Assessment | Compliance Results |
|-------------------------|--|----------|--|---|
| Harvie et al (2017) | LFD (23) vs LFD Waiting List (27) | 3 months | None | None |
| Hustoft et al (2017) | LFD + Placebo (20) vs LFD + fructans (20) | 4 weeks | None | None |
| Staudacher et al (2017) | LFD (51) vs Sham (53) | 4 weeks | Yes – defined as following diet >50% of the time, self-reported | All participants reported compliance to LFD |
| McIntosh et al (2016) | LFD (20) vs HFD (20) | 3 weeks | Yes – Did not define compliance or means of assessment | Good compliance to dietary intervention |
| Peters et al (2016) | LFD (24) vs Hypnotherapy (25) vs Combined (25) | 6 weeks | None | None |
| Eswaran et al (2016) | LFD (45) vs modified NICE (39) | 4 weeks | None | None |
| Bohn et al (2015) | LFD (38) vs NICE (37) | 4 weeks | None | None |
| Pedersen et al (2014) | LFD (42) vs Probiotic (41) vs Habit (40) | 6 weeks | None | None |
| Halmos et al (2014) | LFD (27) vs Typical (27) | 3 weeks | Yes – defined as >81% (17/21 days) | All participants were compliant to LFD |
| Staudacher et al (2012) | LFD (19) vs Habit (22) | 4 weeks | Yes – defined as lower consumption of short-chain fermentable carbohydrates at EOS | All participants were compliant to LFD |

Table 23. Comparisons of the LFD RCTs and measured compliance. Abbreviations: LFD – low FODMAP diet, NICE – National Institute for Health and Care Excel, EOS – end of study.

Strengths and Limitations

First and foremost, an in-depth analysis of the first four participants through case series descriptive statistics did allow for greater insight to the challenges of following these two diets. One strength found within this study was the high participant retention rate and low drop-off rate. Though study accrual was not as fast as would have been desired, once participants consented to the study, they were retained and completed the study. As with all investigative research, limitations can always be found. The sample size and heterogeneity within this study

population hindered the ability for external validity and generalization of findings. Recruitment in human studies is a challenge for most investigators. Traveling to OSUMC and navigating campus parking is likely a deterrent to participation. Therefore, this is another potential area of burden the researchers could address for participants for future studies. Additionally, keeping dietary intake data utilizing a three-day diet record was also another challenge faced by participants. Upon return of the three-day diet records, detail was lacking which impacted the 60-minute appointment for all study-related tasks. Study investigators were unable to capture all details needed to provide a complete record for analysis which is a limitation of this tool for dietary analysis. Additionally, evidence of the Hawthorne Effect was suspected as pre- and post-dietary analysis revealed subtle differences, yet our participants felt symptom changes.

Recommendations for Future Studies

Throughout this discussion, many strengths and limitations have come to light. The primary focus areas for future studies should be in improving recruitment and addressing compliance. As mentioned, compliance and adherence to LFD was assessed utilizing *High FODMAP Foods Checklists*. Unfortunately, this is still not considered a universal measure of adherence as it has yet to be defined in the literature. Additionally, moderate FODMAP food items are not included as part of these checklists. As indicated in the literature, FODMAPs have a concentration or additive effect on the GI tract. Those whom consume a large enough portion of a moderate FODMAP food item would then be considered a high FODMAP food item and noncompliant with a LFD. In regard to the individualized dietary approach based on the DGAs, measurements of compliance or adherence to this intervention were not feasible. HEI scores could be utilized, however, this would not have been appropriate for this study for numerous reasons. Firstly, the DGAs are not a dietary pattern that all components must meet 100% of

compliance, nor is it necessarily feasible; the DGAs act as a guideline for improving healthy eating patterns in all areas for the prevention of chronic disease. Secondly, the individualized approach in this study had a primary purpose of improving symptoms within the GI tract via fiber intake and added sugar intake. Investigators in this study took the time to consider which nutrients would be the most impactful on GI health, hopefully improving symptoms while remaining nutritionally adequate. Continued focus and improvement in this area, including explicitly definitions of adherence, would be necessary to produce more robust literature and replicability for studies in IBS. The amount of information and instruction for the participants to follow and understand can bit quite overwhelming to them despite encouragement and education from providers. Implementation of an initial grocery store tour with participants may be helpful to show them foods they should be considering for purchase and give additional time for participants to ask more nuanced questions about their assigned diets. Given the connection of the gut-brain interaction in this patient population, additional assessment tools, such as a food insecurity screener and perceived stress scale screener would be best to implement as well. This would provide a holistic perspective into the participant's life rather than based solely on food intake. An exit survey would also be useful for the participant to fill out to let researchers know of the challenges and benefits they felt they faced by having to do these diets. Given the difficulties or challenges the participants may have faced in attending the individual counseling sessions at OSUWMC, providing the option for Telehealth appointments has the potential to alleviate this burden from participants and should be considered for future studies.

Conclusion

The body of literature on the nutritional adequacy of the LFD is extremely limited and in its' infancy. This study assessed this in those following the LFD and those following an

individualized approach to the DGAs. We hypothesized that there would be no difference in nutrient intakes for those following the LFD and for those following the DGA diet. Though it has been hypothesized that adequate nutrient intake could be at risk, we did not find this to be the case through this study. Rather it was shown that majority of participants in this patient population did not consume adequate nutrient intake as is. Post-intervention data shown that regardless of a RDN-led dietary intervention, participants were not able to meet the RDA for most nutrients of interest. Generally, those who consumed an adequate or surplus number of calories were able to meet more RDA guidelines for micronutrients more readily and that following a restrictive or particular diet did not affect this. The outcomes of this RCCT, once completed, should provide key understandings of dietary compliance, nutritional adequacy and symptom improvement between those on a LFD and those encouraged to adhere to the DGAs. However, more studies to determine the long-term nutritional impact of these diets and the impact of the dietary pattern on the intestinal microbiome must be included in future research alongside dietary compliance.

The Low FODMAP Diet: A case-based approach to reviewing the nutritional adequacy compared to a standardized dietary approach in irritable bowel syndrome

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Abstract: *Introduction:* Irritable bowel syndrome (IBS) is the most commonly diagnosed functional gastrointestinal disorder (FGID) defined by characteristics of abdominal pain related to defecation and altered bowel habits. Hypotheses suggest consumption of fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) being the primary culprits of symptom induction in this population. Despite the reported high efficacy in nearly 75% of sufferers, the low FODMAP diet requires exclusion of many nutrient-dense food groups such as fruits, vegetables, and whole grains. Due to this restrictive approach, investigation of a more liberal dietary approach is warranted. *Objectives:* The primary objective was to assess compliance and nutritional adequacy of the low FODMAP diet compared to a standardized dietary approach. *Methods:* The first four subjects enrolled in this case report aimed at understanding the nutritional adequacy and symptom improvement in IBS when following a low FODMAP diet are presented within. Nutrient analysis, using the Nutrition Data System for Research (NDSR) was completed on two sets of three-day diet records during a two-week intervention. *Results:* The first 4 consented subjects randomized to an individualized dietary approach (n=2) or the LFD (n=2) are presented. Macro- and micronutrient intake data was highly variable in both the pre- and post-dietary intervention data. Baseline micronutrient intakes for all participants were poor and consistently fell below the RDA. Vitamin A intake was the only nutrient that consistently increased despite the intervention; however, vitamin A intake post-intervention was below the RDA. Compliance to the LFD was inconsistent. *Conclusions:* Nutritional inadequacy is of concern in those with IBS despite dietary intervention. Dietary compliance is likely a larger problem than currently discussed in the literature and must be included in the methodology of all future publications in this area. Recruitment for a dietary intervention in IBS is challenging and future research should explore barriers to participation.

Introduction:

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder (FGID) that is the most commonly diagnosed gastrointestinal (GI) disorder defined by characteristics of abdominal pain related to defecation and altered bowel habits.² FGIDs are a classification of GI diseases that have no structural abnormalities or findings yet have presenting symptoms of GI distress with IBS being the most prominent of these. This is diagnosed by the Rome criteria (currently Rome IV) and with the newest update to the criteria, there has begun a shift in terminology towards disorders of the gut-brain interaction due to the significant interaction between them in these disorders.³ In North America, IBS impacts 10-12% of the population.¹ It is most common among women and younger individuals but can affect persons of all demographics. IBS diagnoses are divided among four subtypes: constipation predominant (IBS-C), diarrhea predominant (IBS-D), mixed diarrhea/constipation (IBS-M) and unclassified (IBS-U).¹ Bloating and distension are common symptoms among all subtypes of this disorder.⁴

IBS poses a high encumbrance on the individual, negatively impacting quality of life and impairment of work-related activities. This also poses high burden on the healthcare system, costing upwards of \$10 billion dollars annually, highlighting the necessity of optimal treatment.¹ Treatment is multimodal, involving pharmacological, nutritional and psychological interventions, primarily focusing on symptom management and improving quality of life.¹

Dietary intervention for treatment of IBS has grown significantly within the last decade. Several diets have been trialed with IBS including, but not limited to gluten-free, low-fat, Mediterranean and the specific carbohydrate diet. Most of these are traditional exclusion diets with unknown efficacy and limited symptom relief. Hypotheses suggest consumption of fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) are the

primary culprits of symptom induction in this population.⁴ Based on these hypotheses, the low FODMAP diet (LFD) was developed at Monash University. The LFD is an exclusion diet that requires complete elimination of highly concentrated, fermentable carbohydrates for 2-8 weeks. Over the last decade, substantial research supports the LFD as efficacious and effective treatment for symptom management in those with IBS. However, given the restrictive nature of this dietary intervention understanding the nutritional adequacy is of importance.

The exclusive nature of the LFD which eliminates many whole grains, fruits and vegetables that are nutrient dense has the potential to create nutrient deficiencies. In addition, the exclusionary nature of this diet can be burdensome thus presenting a necessary look into a more liberal dietary pattern approach using the Dietary Guidelines for Americans (DGAs). This study aims to assess the nutritional adequacy and dietary compliance of the LFD as compared to a standardized dietary approach using the DGAs as the basis for education. Specifically, assessment of vitamin A, vitamin C, vitamin D, calcium, zinc, magnesium and fiber before and after intervention will be explored.

Methods

This case series focuses on the nutritional adequacy of LFD compared to a standardized dietary education, four participants are presented within as a series of case reports. Methodology for this trial was approved by The Ohio State University Institution Review Board (IRB), protocol #2016H0320, for the use of human subjects.

Men and women (>18 years) with a diagnosis of IBS referred to the RDN within the an ambulatory gastroenterology clinic at a large academic institution were considered eligible for

recruitment if meeting the following inclusion and exclusion criteria are described below (Table 5).

| |
|---|
| <u>Inclusion Criteria:</u> <ul style="list-style-type: none">• 18 years of age or older• Ability to read English• Diagnosis of IBS• RDN referral for nutrition consultation |
| <u>Exclusion Criteria:</u> <ul style="list-style-type: none">• Under the age of 18• Inability to voluntarily provide informed consent for study (including prisoners)• Pregnancy |

Table 24. Inclusion and exclusion criteria included in the recruitment strategy for the RCT.

Study Design

Patients referred to the RDN for a one-on-one appointment that were diagnosed with IBS were contacted via phone to gauge interest in study participation. Those interested, who met inclusion and exclusion criteria, were offered participation in the current study and scheduled for a baseline study visit. Prior to arrival at the baseline study visit, participants were asked to complete a 3-day diet record completed on non-consecutive days including 1 weekend day. At the baseline study appointment, investigators obtained consent and reviewed Health Information Portability and Accountability Act (HIPAA) documentation. Then, the investigators completed the health questionnaire, the initial IBS-SSS form and reviewed the initial 3-day diet record. Next, the randomization envelope was opened to reveal the assigned dietary intervention for the participants to follow for the subsequent two weeks. Two weeks was selected based on prior

research suggesting maximum symptom reduction after 2-weeks compared to 4- and 6-weeks (unpublished). Participants completed an additional 3-day diet record and IBS-SSS form after 1 week of the dietary intervention to capture dietary and symptom changes. Those randomized to a LFD were also instructed to complete a daily high FODMAP food checklist if accidental consumption of restricted foods were consumed. Participants returned to clinic to meet with the RDN after the 2-week intervention and returned the second 3-day diet record, high FODMAP checklists (if applicable) and IBS-SSS. The multiple pass approach was repeated for the additional diet records and another IBS-SSS was completed to end the study. Participants received a \$25 grocery gift card after each one-on-one appointment and all participants received low FODMAP food baskets from FODY Foods Co at the completion of the study.

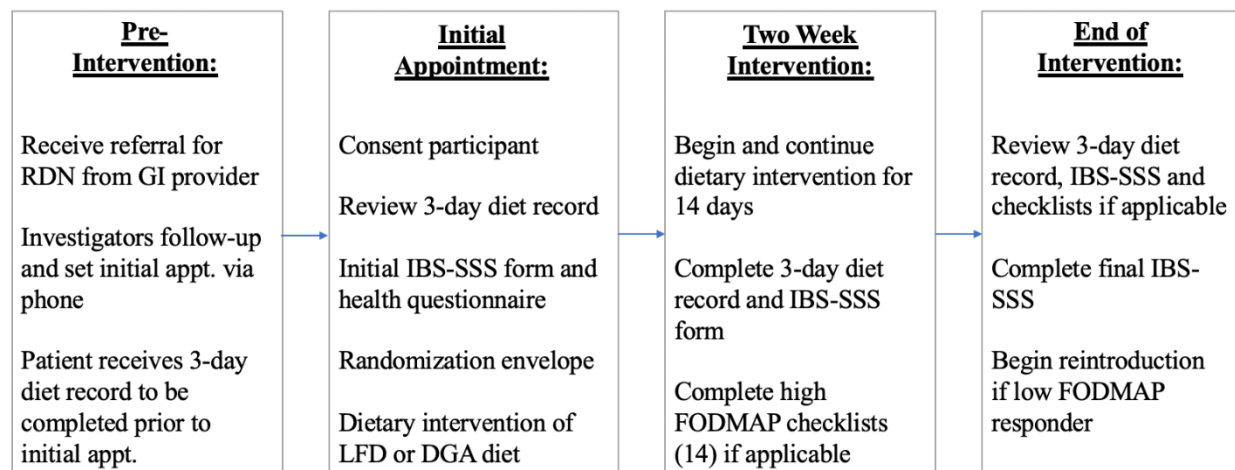


Figure 5. Study flow diagram for all participants enrolled in the RCT

Study Tools

A health questionnaire was utilized to collect baseline demographic and health information regarding the diagnosis of IBS, current and past medical history, medication, supplements and

alternative treatment used, and anthropometric measurements. Three-day diet records were collected at baseline and the end of study to assess nutrient intake and measure dietary compliance to the intervention. Additionally, symptom severity was captured at baseline and the end of study using the IBS-SSS. Bristol Stool Form Scale (BSFS) was utilized in conjunction with the IBS-SSS to determine the participant's typical stool consistency to allow for IBS-subtyping as diarrhea-, constipation-, mixed- or unclassified-IBS. To provide daily data on dietary compliance without requiring daily food records, high FODMAP checklists were created. With this form, participants would check if they consumed a high FODMAP food item and indicate what that item was. Kate Scarlata, MPH, RDN's online resources⁷⁶ were used for all LFD education. Standard of care nutritional education was focused on dietary fiber goals (to meet recommendations of 25–38 g/day for females and males, respectively) to increase fiber delivery by emphasizing 1-2 high fiber food items daily and reducing added sugar to <10% of total daily calories based on the recommendations. Education on reading a food label was provided and kilocalorie specific menus were provided based on their baseline BMI accordingly: 35kcal/kg for BMI of < 18.5, 30 kcal/kg for BMI of 18.5-24.9, 25 kcal/kg for BMI of 25-29.9, 20 kcal/kg for BMI of >30.

Statistical Analysis

Dietary intake collection and analysis was performed using Nutrient Data System for Research (NDSR) software, version 2016, developed by the Nutrition Coordination Center (NCC) of the University of Minnesota. Dietary intake was summarized by means and standard deviations for continuous variables, including percent of kilocalories from carbohydrates, fats, proteins and percentage of the Recommended Dietary Allowances (RDAs) for micronutrient intake. Frequencies and percentages were used to summarize categorical data.

Results:

The first four subjects are reported within (Figure 4). The recruitment pool, in which patients were eligible to participate from, began with 27 potential participants. From the initial pool, 13 were recruited for the study: eight consented to participate while five did not show for their baseline appointment. Of the four participants reported within, one participant did not provide end of study (EOS) data for nutrient intake. Due to the sample size, descriptive statistics was used to discuss participants using a case study format.

Cohort Demographics, Lifestyle, and Baseline Characteristics:

Three of the four participants were female (75%). Median age was 46 years (ranging from 39 to 55 years), and median BMI was 32.8kg/m² (ranging from 27.9 to 41.1 kg/m²). Two participants (50%) engaged in mild to moderate physical activity. No participants smoked cigarettes, one participant smoked marijuana, and three participants consumed alcohol in moderation. Time since IBS diagnosis ranged from 2 months to 36 years.

Dietary interventions trialed in this patient population varied. One participant received nutritional counseling or prior nutrition information for management of IBS with instruction for following an elimination of certain food items and also reported several food allergies which led to a number of restricted foods. One participant also had celiac disease and therefore followed a gluten-free diet. Two participants had minor or no food restrictions that were reported at baseline.

Medication use, both prescription and over-the-counter (OTC), were common in this cohort. Prescription medications were reported by two participants (50%) and included anti-cholinergic/anti-spasmodic medications; non-prescription medications were more common (75%) and included pain relief, laxatives and gas relief. Supplement use was reported by all

participants and included multivitamins (MVI), vitamin D, vitamin C, probiotics and fiber.

Engagement in alternative therapies were reported by two participants (50%) which included yoga and cognitive behavioral therapy (CBT).

IBS-SSS was used to determine the severity of IBS symptoms. Based on this scoring system, one participant (25%) had severe IBS and three participants (75%) had moderate IBS (Table 7). Using the BSFS, this supported predominant bowel patterns of one participant (25%) having IBS-C, one participant (25%) having IBS-D, and two participants (50%) having IBS-U.

Cohort Assessment of Dietary Changes and Diet Adequacy:

Assessment of nutrient intake and dietary changes were performed using NDSR programming. When assessing these, it was important to note that only three out of four participants were included in this discussion due to one participant not providing their EOS diet records for nutrient analysis. However, significant deficits in nutrient intake were identified in baseline and EPS dietary analysis of 3-day diet records.

Baseline NDSR data shows that daily caloric intake was below recommendations in three of the four participants ranging from 10 to 50% below estimated energy requirements (Table 8). This low caloric intake likely impacted micronutrient intake as all micronutrients of concern were below the RDA with the exception of zinc in three participants, calcium in one participant and vitamin C in another participant (Tables 12, 14, and 16). Regardless of the dietary intervention, micronutrient intake was still suboptimal with the exception of zinc and magnesium in only one participant, respectively, indicating that both the baseline and intervention diets were nutritionally inadequate. Vitamin A and vitamin D intakes did not meet the RDA at baseline or EOS for all participants which was concerning given the importance of these fat-soluble vitamins. Vitamin A intake at baseline was below the RDA with two participants falling below

50% of the RDA. Vitamin D intake at baseline was below 50% of the RDA for all participants supporting severely depleted dietary intake for both vitamins.

FOD 001

FOD 001 was a 50-year-old female, with moderate IBS-D that was diagnosed two months prior to this intervention with a BMI of 27.9 kg/m². This participant had not received previous nutritional counseling for management of IBS and without following any special diet. However, prior to this initial appointment the participant had been regularly decreasing rice intake and simultaneously increasing water intake to help with symptom alleviation. Prior to this intervention, the participant also engaged in physical activity in the form of walking for 20 minutes, 3x per week. She did not endorse smoking or consumption of alcohol. The participant did not take any prescription medications for IBS symptom relief; however, endorsed use of OTC ibuprofen approximately 3x per week for pain relief from IBS. The participant takes a MVI supplement daily.

Nutrient Intake Changes

Participant FOD 001 was randomized to an individualized approach to the DGAs. Upon review of the participant's initial 3-day diet record, it was determined that the participant consumed foods with little to no added sugar, however, fiber intake appeared suboptimal at baseline. Therefore, dietary instruction to increase fiber intake was the primary goal. Specifically, this participant was educated to substitute white rice and cornflakes with brown rice and whole grain cereals, and increase pinto bean consumption, which would increase the amount of fibrous foods as the academy of nutrition and dietetics recommends. It was estimated that this would increase her dietary fiber from 16 g/day to 25 g/day meeting the recommendations for age and sex. Analysis of pre-intervention diet records indicated the participant was below

recommendations for kilocalories, carbohydrates, fiber, vitamin A, vitamin C, vitamin D, calcium, and magnesium. The participant consumed 100% of the RDA for zinc prior to intervention (Table 17). At the conclusion of the study, post-intervention dietary analysis indicated a further decline in overall nutrient intake which was likely related to her decline in overall kilocalorie consumption by 166 kcals/day (Table 17). Specifically, kilocalorie, carbohydrate and fiber decreased from baseline to the end of study (see Table 17). A decrease in vitamin C, from 29% of the RDA to 21% of the RDA and magnesium, from 51% to 45% of the RDA occurred. Zinc intake had been the only micronutrient that had reached the RDA, but this micronutrient also decreased after the dietary intervention to 75% of the RDA. The appropriate dietary substitution of white rice to brown rice was achieved despite the decrease in fiber intake by 50%, meeting only 21-32% of the recommendations.

FOD 003

FOD 003 is a 55-year-old male, with moderate IBS-U that was diagnosed 35 years prior with a BMI of 28.5 kg/m². This participant had not received previous nutritional counseling for management of IBS and did not follow any particular diet or restrictions prior to the initial appointment. Prior to this intervention, the participant also engaged in physical activity in the form of swimming and biking approximately 2-3 miles, twice per day, 3-4x per week. They endorsed previous smoking history, having quit in June of 2007, as well as drinking alcohol in the form of beer, approximately 3-4 per week. This participant did not take any prescription or OTC medications for IBS symptom relief; however, endorsed taking MVI, fiber, and probiotic supplements once daily. They also participated in yoga as an alternative therapy 4x per week.

Nutrient Intake Changes

Participant FOD 003 was randomized to the LFD intervention. Upon review of the participant's initial 3-day diet record, it was observed that the participant did consume a diet with a plethora high FODMAP foods. The participant was instructed to follow the LFD and educated on how to do so, emphasizing the importance of restricting the high FODMAP food items the participant regularly consumed (i.e. apples). This participant did not provide a completed 3-day diet record at the end of the intervention, therefore, only pre- diet analysis occurred. Analysis of the diet record indicated an average caloric intake and carbohydrate intake above the estimated energy requirements which likely contributed to fiber intake being 84% of the minimum recommendations. Several micronutrients were also above the RDA, including vitamin C (165%), calcium (110%), and zinc (110%). Despite the higher caloric intake, magnesium, vitamin A, and vitamin D still were below the RDA at 92%, 63%, and 47%, respectively. Although there was not a 3-day intervention diet record, the participant did return the FODMAP checklists which revealed consumption of high FODMAP food items daily during the intervention indicating poor compliance.

FOD 005

FOD 005 was a 40-year-old female, with severe IBS-U that was diagnosed 22 years prior with a BMI of 41.1 kg/m². This participant had not received previous nutritional counseling for management of IBS, however, was following a gluten free diet due to their underlying celiac disease diagnosis. They also chose to limit overall food consumption to help with IBS symptom alleviation. Prior to this intervention, the participant did not engage in regular physical activity. She endorsed smoking of medical marijuana up to 3x per day as well as consumption of alcohol on occasion but was unable to quantify the amount or type of alcohol consumed. This participant endorsed use of a prescription medication, dicyclomine, twice daily which is an

antispasmodic. Reported use of several OTC medications included: omeprazole 3x per day, polyethylene glycol 1-2x per day, and Roloids brand antacids on occasion. Supplement use consisted of vitamin D, vitamin C, prenatal MVI and melatonin daily. Alternative therapies were utilized by this patient in the form of CBT 1x per week.

Nutrient Intake Changes

Participant FOD 005 was randomized to the individualized approach to the DGAs. Upon review of the participant's initial 3-day diet record, it was determined that the participant consumed many foods that contained added sugar (i.e. sugar-sweetened creamers, cereals and granola bars) while also including low fiber food sources in their diet. Consequently, the participant was instructed to both decrease added sugar intake to <10% of total calories and increase dietary fiber intake to 25 g/day based on the recommendation for age and sex. The participant was encouraged to increase fresh fruit, vegetable and legume intake to 2.5 cups/day by incorporating new vegetables (i.e. beans) to meet fiber goals. Additionally, sugar-sweetened creamers, drinks, cereals and granola bar consumption were emphasized to limit. Analysis of pre-intervention dietary records indicated this participant consumed nutrients below the RDA on all nutrients of interest with the exception of carbohydrates (196% of the RDA) and zinc (150% of the RDA). Post-intervention analysis indicated no relevant changes in kilocalorie or carbohydrate consumption (see Table 19). Mean fiber intake increased from a mean intake of 23g/day to 30g/day post-intervention, meeting recommendations of 25 g/day despite mean carbohydrate intake remaining the same. Evaluation of the 3-day diet records at baseline showed implementation of high fiber recommendations daily. Micronutrient intake increased for vitamin A, vitamin C, vitamin D, calcium, magnesium and zinc. Magnesium and zinc exceeded the RDA

(117% and 213%, respectively), while vitamin A, vitamin C, vitamin D, and calcium remained below the RDA despite these increasing from baseline.

FOD 009

FOD 009 was a 39-year-old female, with moderate IBS-C that was diagnosed 9 years prior with a BMI of 33.5 kg/m². This participant had received nutritional counseling and tried the LFD in the past; however, this did not seem to alleviate symptoms. In addition, this participant had multiple food allergies, like wheat and egg whites, and would restrict these allergens “as best as I can” as well as avoiding seasonings. Prior to this intervention, the participant did not engage in physical activity. They did not endorse smoking and would consume alcohol in the form of sherry, sipping this approximately 2x per week. This participant took the antispasmodic, dicyclomine, and the antidepressant, sertraline, as prescription medications to help with IBS symptom relief. In addition, the participant took a half dose of hydrocodone as a pain reliever 3x per day. The participant did not take any non-prescription medications, however, endorsed taking vitamin D 10,000 IU daily, probiotics daily, and thyme and fenugreek supplements in unknown amounts once daily. They did not participate in any alternative therapies.

Nutrient Intake Changes

Participant FOD 009 was randomized to the LFD intervention. The participant was instructed to follow the LFD and educated on how to do so, emphasizing the importance of restricting the high FODMAP food items the participant regularly consumed. Analysis of both pre- and post-intervention diet records shown the participant’s overall caloric intake was well below recommended energy needs, meeting only about 50% for both pre- and post- dietary analysis. At baseline, fiber, vitamin A, vitamin C, vitamin D, calcium, magnesium and zinc all

fell below recommendations (Table 20). At baseline carbohydrate intake met the RDA at 116% which increased to 158% of the RDA post-intervention despite the low caloric intake. Vitamin A, vitamin C, and magnesium all increased from baseline, but still to suboptimal levels. NDSR did not detect any sources of vitamin D from either 3-day diet record; however, the subject was consuming a high-dose vitamin D supplement orally. This participant completed all FODMAP checklists and the intervention 3-day diet record which both indicated 100% compliance to the dietary intervention.

Discussion

Assessing the nutritional composition of usual dietary consumption to that after an RDN-led dietary education and connecting these dietary patterns to those with IBS requires acknowledgement of the comparisons of these four subjects with that of the typical IBS population. Fortunately, demographic data and medical management of these participants was consistent with what is identified in the literature. Additionally, IBS is a female predominant condition in which patients tend to be of normal weight BMI presenting between the ages of 39 to 55 which was also consistent with these four participants.^{77,78} Most importantly, we were able to portray the challenges that may present with different IBS subtypes as this case study presentation provides representation of each IBS subtype.

Each of these participants were referred to the RDN for nutrition counseling yet most were restricting or limiting various foods before the baseline visit highlighting the need for the RDN to assess the nutritional adequacy of their diet before and after an RDN-led intervention. It is well-understood that the patients' perception of food is the number one contributor to symptoms and consequently assert food restrictions as self-management.⁷⁹⁻⁸² The most common

foods that are self-eliminated from a patient's diet are typically dairy and gluten-containing products which are rich sources of calcium, vitamin D, B vitamins and iron.^{80,81} Logically, extensive restriction for an unknown length of time would lead to high risk of micronutrient deficiencies. This is exactly what was seen in the results reported within.

Baseline Dietary Patterns

The overall consensus that can be deduced about this cohort is the inability to meet the RDA for most nutrients across the board despite dietary intervention and encouragement to meet guidelines and recommendations. This is not exactly surprising when we look at dietary patterns for Americans. According to the most recent edition of the DGAs, calcium, vitamin D and fiber had been recognized as nutrients of public health concern due to the negative consequences seen in consuming too little of these, such as poor colon health.⁵² To become a public health concern acknowledged by the DGAs, a significant proportion of the American population is not meeting the recommended intakes set forth by these guidelines.⁵² It is hypothesized that those with IBS might have similar challenges adhering to the concepts outlined in the DGAs with perhaps additional challenges due to the self-restrictions of various food groups (ie., dairy and wheat). As evidenced by the nutrient intake data for this cohort, caloric intake was optimal in two participants. In those unable to meet their estimated energy intake, we would expect challenges meeting micronutrient needs as well. However, mean nutrient intake for most nutrients did fall below the RDA at baseline despite caloric intake.

Dietary fiber intake was suboptimal in three of the four participants as participants expressed perceiving fiber to be the cause of all IBS symptoms. Literature supports that food groups that are heavily restricted are naturally fibrous food sources: legumes, whole grains, fruits, and vegetables.⁶⁵ As mentioned previously, optimal dietary fiber intake is linked with a

diverse microbiome and is associated with a reduced risk of many chronic illnesses including colorectal cancer. Therefore, education is necessary for the American population to increase fiber intake, but this may be even a greater concern for those with IBS that are self-restricting fibrous foods as well. Food group analysis is unavailable for the cases presented within; however, this could be an area to gain insight into baseline dietary patterns in those with IBS.

Vitamin A and vitamin D intakes were suboptimal for all participants at baseline. Vitamin A intake did not attain even 50% of the RDA at baseline for two of the participants whereas vitamin D intake did not attain 50% of the RDA for all participants at baseline. These fat-soluble vitamins in combination with calcium (also well-below the RDA for three participants at baseline) are critical for bone health. The level at which these were deficient are doubly concerning given two of the participants then had to adhere to a restrictive dietary intervention. An RDN-led intervention should help to reduce these micronutrient shortcomings, however, post-dietary analysis was still concerning for nutritional inadequacies.

Post-intervention Dietary Analysis

Post-intervention nutrient data was heterogeneous as it relates to nutrient intake with some participants increased their nutrient intake and others decreased intake. Again, caloric intake must be discussed as only two participants met their estimated energy needs which we would expect inadequate caloric intake to be associated with suboptimal nutrient intakes. Despite dietary intervention led by an RDN, the RDAs for nutrients were seldom achieved by participants. Nutrient intakes meeting the RDA decreased across the board after the RDN-led intervention. As mentioned, lower nutrient intake is expected when participants are unable to meet estimated energy needs. Carbohydrate intake for all three participants remained relatively consistent with little increase or decrease post-intervention. Most participants (two of three)

achieved the RDA for carbohydrates while one decreased intake remaining below the RDA. Only one participant managed to achieve the recommendations for fiber intake post-intervention. The other two participants either kept fiber intake consistent at 50% of recommendations or decreased their fiber intake by an additional 50%.

At post-intervention, magnesium recommendations were only met by one participant. The other two participants fell below 50% of the RDA post-intervention. Zinc appeared to be the most abundant nutrient in this cohort, however, at post-intervention, zinc intake decreased for two of three participants while one participant continued to exceed the recommendations for zinc intake. Vitamin C intake did not achieve the RDA for all participants post-intervention. Similarly, as with the pre-intervention diets, vitamin D and vitamin A were two nutrients that were a challenge for all participants. Interestingly, vitamin A intake did increase for all participants after the intervention but were still at suboptimal intakes. Vitamin D was similar in that intake also increased for the majority of participants (two out of three), though also remaining below the RDA. This may be due to the common restriction of dairy products in this patient population for symptom management, however, dairy consumption was reported for most participants in the form of milks or cheeses. Additionally, when dairy consumers were starting on the LFD they were educated on calcium and vitamin D rich food substitutes to prevent suboptimal intake. It is clear from this subset of participants that micronutrient intake is likely a greater concern than previously identified in the literature. The literature on micronutrient intake in those with IBS varies considerably. According to recent literature by Torres et al, lower intakes of micronutrients, including calcium and zinc, have been observed in this patient population.⁸³ Previous literature, such as that of Williams et al, had indicated opposite results in that this patient population did not tend to inadequately consume micronutrients.⁸⁴ Note that

there are two studies highlighted in this discussion as most LFD research does not report micronutrient intake in pre- or post-intervention diets.

Examination between the two dietary intervention subgroups shown subtle differences between them. This was particularly hard to assess due to each cohort only being comprised of two participants and with the LFD subgroup missing nutrient intake data at EOS. Mean nutrient intake data for the DGA subgroup shown two nutrients (carbohydrate and zinc intake) exceeded the RDA. Mean nutrient intake data for the LFD subgroup shown none of the nutrients meeting the RDA. Again, the LFD subgroup extrapolations are challenging due to only one participant having EOS data reported as a mean. Based on the nutrient intake data for both subgroups, it seems as though the DGA dietary intervention had overall better results from this than did the LFD dietary intervention. This is particularly interesting as the DGA intervention was less restrictive and reflective of a dietary pattern approach.

The DGA intervention was designed to compare a standard dietary education to improve the nutritional quality of the diet without a restrictive approach aiming to provide fewer nutritional challenges in meeting the RDA for most micronutrients. Several RCTs have shown a reduction in total energy, or kilocalorie, intake for those who followed a LFD compared with a traditional diet which can be detrimental in the long-term.⁷² Regardless of the intervention, caloric intake was a challenge and requires the RDN to address. However, with the exclusive nature of the LFD, eliminating many fruits, vegetables, whole grains and dairy products, we hypothesized that this would correlate with lower intakes of vitamin A, vitamin C, vitamin D, zinc, magnesium and calcium intake.^{65,73} Data presented here does not support that the LFD creates more of a nutritional deficit than a standard dietary intervention based on the DGAs. Both groups struggled to meet micronutrient needs. This may be related to the cohort consuming

fewer fruits, vegetables, whole grains and dairy products, but food group analysis is unavailable. Presently, nutrient quantification has only been reported in few studies and only during the strict elimination phase of the LFD which is short-term in nature.⁷⁴ Suboptimal fiber intake in all participants may impact Bifidobacterium species, a known butyrate producer in the colon, which is a key indicator of colonic health.⁷² From these cases, the RDN must consider methods for improving fiber and/or probiotic delivery to combat this risk as seen in work from Staudacher et al.⁷¹ As mentioned, their work shown the abundance of Bifidobacterium species was lower in those on the LFD than those on the sham diet but higher in those given a probiotic supplement.⁷¹ Additional research emphasizing the dietary impact of the LFD on the microbiome needs highlighted in future studies especially given the overlap of SIBO and IBS.

Compliance

Understanding differences between these dietary interventions must be discussed in the context of dietary compliance to ensure we are actually comparing a LFD to a standard dietary approach based on the DGAs. Compliance and assessment of adherence to dietary intervention were implemented for the LFD subgroup for this study. Current literature has not achieved a universal definition for compliance to the LFD. To take the most conservative approach for this study, investigators defined compliance to this dietary intervention as no intake of high FODMAP food items for any day of the intervention. In previous literature, compliance can also be defined as following this diet anywhere between 50-100% of the time. Higher compliance to this diet did not yield improvement in IBS-SSS scores in this study cohort. Compliance to the individualized dietary approach based on the DGAs was not defined in any capacity given this approach is more aimed at long-term dietary pattern changes.

Out of 10 RCTs, only four incorporated compliance and adherence data (Table 21). The definition of compliance and adherence to the interventions varied from study to study, never establishing one cohesive definition. One study, by McIntosh et al, relayed that they looked at compliance, however, did not report how they had planned to assess this nor how they were defining compliance. Results of this were reported as “good” compliance to the intervention yet it is difficult to determine what exactly that means. A study by Staudacher et al in 2012 defined compliance as having a lower consumption of short-chain fermentable carbohydrates at the EOS with results showing all participants being compliant to this definition. Another study by Staudacher et al in 2017 defined compliance as self-reporting following the assigned diet greater than 50% of the time with all participants being compliant to this definition. Similarly, Halmos et al defined compliance as following the intervention as greater than 81% of the time or 17/21 days of the intervention and all participants were compliant to this definition. The occurrence of examining compliance is scarce and when this does occur, the definition is completely heterogeneous. Consequently, the results pertaining to compliance are also variable and difficult to interpret. The majority of these studies also include feeding studies which, unfortunately, are not realistic to what an actual patient would encounter in their own daily lives. These results and unclear definition of compliance also gives uncertainty to the interpretation of nutrient intake analysis from these few studies.

The cases presented within this study provide a most conservative definition of compliance while incorporating two 3-day diet records reviewed for accuracy by study investigators to provide clear assessment of the nutritional adequacy of the LFD compared to DGAs. It is important to reiterate that implementation of the DGAs are not for purposes of

compliance but more so as a means of adherence. This study did not utilize HEI scores, however, this would give the ability to test for adherence to the DGAs in future studies.

Strengths and Limitations

First and foremost, an in-depth analysis of the first four participants through case series descriptive statistics did allow for greater insight to the challenges of following these two diets. One strength found within this study was the high participant retention rate and low drop-off rate. Though study accrual was not as fast as would have been desired, once participants consented to the study, they were retained and completed the study. As with all investigative research, limitations can always be found. The sample size and heterogeneity within this study population hindered the ability for external validity and generalization of findings. Recruitment in human studies is a challenge for most investigators. Traveling to OSUMC and navigating campus parking is likely a deterrent to participation. Therefore, this is another potential area of burden the researchers could address for participants for future studies. Additionally, keeping dietary intake data utilizing a three-day diet record was also another challenge faced by participants. Upon return of the three-day diet records, detail was lacking which impacted the 60-minute appointment for all study-related tasks. Study investigators were unable to capture all details needed to provide a complete record for analysis which is a limitation of this tool for dietary analysis. Additionally, evidence of the Hawthorne Effect was suspected as pre- and post-dietary analysis revealed subtle differences, yet our participants felt symptom changes.

Recommendations for Future Studies

Throughout this discussion, many strengths and limitations have come to light. The primary focus areas for future studies should be in improving recruitment and addressing compliance. As mentioned, compliance and adherence to LFD was assessed utilizing *High*

FODMAP Foods Checklists. Unfortunately, this is still not considered a universal measure of adherence as it has yet to be defined in the literature. Additionally, moderate FODMAP food items are not included as part of these checklists. As indicated in the literature, FODMAPs have a concentration or additive effect on the GI tract. Those whom consume a large enough portion of a moderate FODMAP food item would then be considered a high FODMAP food item and noncompliant with a LFD. In regard to the individualized dietary approach based on the DGAs, measurements of compliance or adherence to this intervention were not feasible. HEI scores could be utilized, however, this would not have been appropriate for this study for numerous reasons. Firstly, the DGAs are not a dietary pattern that all components must meet 100% of compliance, nor is it necessarily feasible; the DGAs act as a guideline for improving healthy eating patterns in all areas for the prevention of chronic disease. Secondly, the individualized approach in this study had a primary purpose of improving symptoms within the GI tract via fiber intake and added sugar intake. Investigators in this study took the time to consider which nutrients would be the most impactful on GI health, hopefully improving symptoms while remaining nutritionally adequate. Continued focus and improvement in this area, including explicitly definitions of adherence, would be necessary to produce more robust literature and replicability for studies in IBS. The amount of information and instruction for the participants to follow and understand can bit quite overwhelming to them despite encouragement and education from providers. Implementation of an initial grocery store tour with participants may be helpful to show them foods they should be considering for purchase and give additional time for participants to ask more nuanced questions about their assigned diets. Given the connection of the gut-brain interaction in this patient population, additional assessment tools, such as a food insecurity screener and perceived stress scale screener would be best to implement as well. This

would provide a holistic perspective into the participant's life rather than based solely on food intake. An exit survey would also be useful for the participant to fill out to let researchers know of the challenges and benefits they felt they faced by having to do these diets. Given the difficulties or challenges the participants may have faced in attending the individual counseling sessions at OSUWMC, providing the option for Telehealth appointments has the potential to alleviate this burden from participants and should be considered for future studies.

Conclusion

The body of literature on the nutritional adequacy of the LFD is extremely limited and in its' infancy. This study assessed this in those following the LFD and those following an individualized approach to the DGAs. We hypothesized that there would be no difference in nutrient intakes for those following the LFD and for those following the DGA diet. Though it has been hypothesized that adequate nutrient intake could be at risk, we did not find this to be the case through this study. Rather it was shown that majority of participants in this patient population did not consume adequate nutrient intake as is. Post-intervention data shown that regardless of a RDN-led dietary intervention, participants were not able to meet the RDA for most nutrients of interest. Generally, those who consumed an adequate or surplus number of calories were able to meet more RDA guidelines for micronutrients more readily and that following a restrictive or particular diet did not affect this. The outcomes of this RCCT, once completed, should provide key understandings of dietary compliance, nutritional adequacy and symptom improvement between those on a LFD and those encouraged to adhere to the DGAs. However, more studies to determine the long-term nutritional impact of these diets and the impact of the dietary pattern on the intestinal microbiome must be included in future research alongside dietary compliance.

Figures and Tables

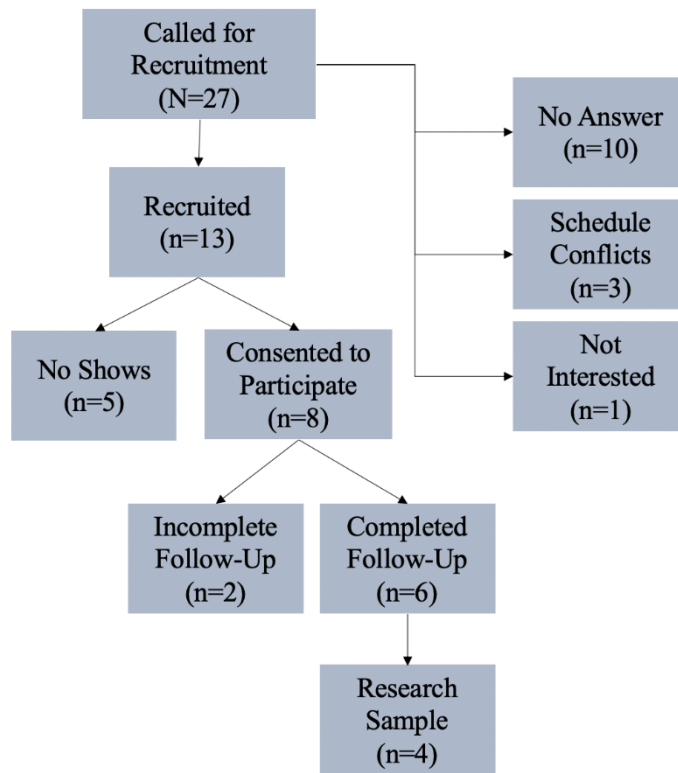


Figure 6. Recruitment flow chart

| Subject | Intervention Group | Compliance |
|---------|--------------------|------------|
| FOD 001 | DGA | - |
| FOD 003 | LFD | 0/12 days |
| FOD 005 | DGA | - |
| FOD 009 | LFD | 14/14 days |

Table 25. Measured daily compliance of subjects recruited.

| | |
|-------------------------|------------------|
| Demographic | |
| Age (years) | 39-55 years |
| Sex (male) | 1 |
| BMI (median) | 27.9-41.1 (32.8) |
| Mild/Moderate Exercise | 50% |
| Smoking | 0% |
| Alcohol | 75% |
| Rx Medication | 50% |
| Non-Rx Medication | 75% |
| Supplement Use | 100% |
| Alternative Therapy Use | 50% |

Table 26. Cohort demographic information.

| Subject | Intervention | Baseline (T₀) | End of Study (T₂) | Change T₀-T₂ |
|----------------|---------------------|---------------------------------|-------------------------------------|---|
| FOD 001 | DGA | 229 | 119 | -110 |
| FOD 003 | FODMAP | 232.5 | 263.5 | +31 |
| FOD 005 | DGA | 323.5 | 272 | -51.5 |
| FOD 009 | FODMAP | 212 | 346 | +134 |

Table 27. Changes in IBS-SSS from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T₀) | End of Study (T₂) | Change T₀-T₂ |
|----------------|---------------------|---------------------------------|-------------------------------------|---|
| FOD 001 | DGA | 1088 | 923 | -165 |
| FOD 003 | FODMAP | 2890 | - | - |
| FOD 005 | DGA | 1912 | 1963 | +51 |
| FOD 009 | FODMAP | 882 | 1045 | +163 |

Table 28. Changes in Daily Kilocalorie Intake (in kcals) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|----------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 | DGA | 123 | 120 | +77 |
| FOD 003 | FODMAP | 357 | - | - |
| FOD 005 | DGA | 255 | 255 | 0 |
| FOD 009 | FODMAP | 151 | 206 | +55 |

Table 29. Changes in Daily Carbohydrate Intake (in g) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|----------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 | DGA | 16 | 8 | -8 |
| FOD 003 | FODMAP | 21 | - | - |
| FOD 005 | DGA | 23 | 30 | +7 |
| FOD 009 | FODMAP | 8 | 8 | 0 |

Table 30. Changes in Daily Fiber Intake (in g) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 135, (19%) | 332, (47%) | +197 |
| FOD 003 (%RDA) | FODMAP | 563, (63%) | - | - |
| FOD 005 (%RDA) | DGA | 575, (82%) | 617, (88%) | +42 |
| FOD 009 (%RDA) | FODMAP | 121, (17%) | 300, (43%) | +179 |

Table 31. Changes in Daily Vitamin A Intake (in IUs) and percentage of the RDA from Baseline to End of Study (N=4).

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 22, (29%) | 16, (21%) | -5.6 |
| FOD 003 (%RDA) | FODMAP | 149, (165%) | - | - |
| FOD 005 (%RDA) | DGA | 40, (53%) | 51, (68%) | +10.8 |
| FOD 009 (%RDA) | FODMAP | 25, (33%) | 51, (68%) | +26.3 |

Table 32. Changes in Daily Vitamin C Intake (in mg) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 3, (19%) | 5 (33%) | +2.0 |
| FOD 003 (%RDA) | FODMAP | 7, (47%) | - | - |
| FOD 005 (%RDA) | DGA | 5, (33%) | 8 (53%) | +2.9 |
| FOD 009 (%RDA) | FODMAP | 0.2 (1%) | 0 (0%) | -0.2 |

Table 33. Changes in Daily Vitamin D Intake (in IUs) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 454, (45%) | 594, (59%) | +140 |
| FOD 003 (%RDA) | FODMAP | 1098, (110%) | - | - |
| FOD 005 (%RDA) | DGA | 807, (81%) | 945, (95%) | +138 |
| FOD 009 (%RDA) | FODMAP | 480, (48%) | 198, (20%) | -282 |

Table 34. Changes in Daily Calcium Intake (in mg) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 164, (51%) | 145, (45%) | -19 |
| FOD 003 (%RDA) | FODMAP | 386, (92%) | - | - |
| FOD 005 (%RDA) | DGA | 312, (98%) | 373, (117%) | +61 |
| FOD 009 (%RDA) | FODMAP | 74, (23%) | 90, (28%) | +16 |

Table 35. Changes in Daily Magnesium Intake (in mg) from Baseline to End of Study (N=4)

| Subject | Intervention | Baseline (T ₀) | End of Study (T ₂) | Change T ₀ -T ₂ |
|-----------------------|--------------|----------------------------|--------------------------------|---------------------------------------|
| FOD 001 (%RDA) | DGA | 7.9, (99%) | 5.6, (70%) | -2.3 |
| FOD 003 (%RDA) | FODMAP | 12.1, (110%) | - | - |
| FOD 005 (%RDA) | DGA | 11.7, (146%) | 16.9, (211%) | +5.2 |
| FOD 009 (%RDA) | FODMAP | 3.1, (39%) | 3.0, (38%) | -0.1 |

Table 36. Changes in Daily Zinc Intake (in mg IUs) from Baseline to End of Study (N=4).

| Nutrient | RDA* | Intake at Baseline | % RDA Met | Intake at EOS | % RDA Met |
|--------------------------------|-------------|---------------------------|------------------|----------------------|------------------|
| Kilocalories (kcal/day) | 1718-2148 | 1088 | 51-63% | 922 | 43-54% |
| Carbohydrate (g/day) | 130 | 123 | 94% | 120 | 92% |
| Fiber (g/day) | 25-38 | 16 | 42-64% | 8 | 21-32% |
| Vitamin A (mcg/day) | 700 | 135 | 19% | 332 | 47% |
| Vitamin C (mg/day) | 75 | 22 | 29% | 16 | 21% |
| Vitamin D (mcg/day) | 15 | 3 | 20% | 5 | 33% |
| Calcium (mg/day) | 1000 | 454 | 45% | 594 | 59% |
| Magnesium (mg/day) | 320 | 164 | 51% | 145 | 45% |
| Zinc (mg/day) | 8 | 8 | 100% | 6 | 75% |

Table 37. Changes in Nutrient Intakes for FOD001 from Baseline to End of Study

| Nutrient | RDA* | Intake at Baseline | % RDA Met | Intake at EOS |
|--------------------------------|-------------|---------------------------|------------------|----------------------|
| Kilocalories (kcal/day) | 1846-2308 | 2890 | 125-157% | - |
| Carbohydrate (g/day) | 130 | 357 | 275% | - |
| Fiber (g/day) | 25-38 | 21 | 55-84% | - |
| Vitamin A (mcg/day) | 900 | 563 | 63% | - |
| Vitamin C (mg/day) | 90 | 149 | 165% | - |
| Vitamin D (mcg/day) | 15 | 7 | 47% | - |
| Calcium (mg/day) | 1000 | 1098 | 110% | - |
| Magnesium (mg/day) | 420 | 386 | 92% | - |
| Zinc (mg/day) | 11 | 12.1 | 110% | - |

Table 38. Changes in Nutrient Intakes for FOD003 from Baseline to End of Study

| Nutrient | RDA* | Intake at Baseline | % RDA Met | Intake at EOS | % RDA Met |
|--------------------------------|-------------|---------------------------|------------------|----------------------|------------------|
| Kilocalories (kcal/day) | 2180-2725 | 1912 | 70-88% | 1963 | 72-90% |
| Carbohydrate (g/day) | 130 | 255 | 196% | 255 | 196% |
| Fiber (g/day) | 25-38 | 23 | 61-92% | 30 | 79-120% |
| Vitamin A (mcg/day) | 700 | 575 | 82% | 617 | 88% |
| Vitamin C (mg/day) | 75 | 40 | 53% | 51 | 68% |
| Vitamin D (mcg/day) | 15 | 5 | 33% | 8 | 53% |
| Calcium (mg/day) | 1000 | 807 | 81% | 945 | 95% |
| Magnesium (mg/day) | 320 | 312 | 98% | 373 | 117% |
| Zinc (mg/day) | 8 | 12 | 150% | 17 | 213% |

Table 39. Changes in Nutrient Intakes for FOD005 from Baseline to End of Study

| Nutrient | RDA* | Intake at Baseline | %RDA Met | Intake at EOS | % RDA Met |
|--------------------------------|-------------|---------------------------|-----------------|----------------------|------------------|
| Kilocalories (kcal/day) | 1780-2225 | 882 | 40-50% | 1045 | 47-59% |
| Carbohydrate (g/day) | 130 | 151 | 116% | 206 | 158% |
| Fiber (g/day) | 25-38 | 8 | 21-32% | 8 | 21-32% |
| Vitamin A (mcg/day) | 700 | 121 | 17% | 300 | 43% |
| Vitamin C (mg/day) | 75 | 25 | 33% | 51 | 68% |
| Vitamin D (mcg/day) | 15 | 0.2 | 0% | 0 | 0% |
| Calcium (mg/day) | 1000 | 480 | 48% | 198 | 20% |
| Magnesium (mg/day) | 320 | 74 | 23% | 90 | 28% |
| Zinc (mg/day) | 8 | 3 | 38% | 3 | 38% |

Table 40. Changes in Nutrient Intakes for FOD009 from Baseline to End of Study

| Study | Intervention vs Control (n) | Duration | Compliance Assessed and Means of Assessment | Compliance Results |
|-------------------------|--|-----------------|--|---|
| Harvie et al (2017) | LFD (23) vs LFD Waiting List (27) | 3 months | None | None |
| Hustoft et al (2017) | LFD + Placebo (20) vs LFD + fructans (20) | 4 weeks | None | None |
| Staudacher et al (2017) | LFD (51) vs Sham (53) | 4 weeks | Yes – defined as following diet >50% of the time, self-reported | All participants reported compliance to LFD |
| McIntosh et al (2016) | LFD (20) vs HFD (20) | 3 weeks | Yes – Did not define compliance or means of assessment | Good compliance to dietary intervention |
| Peters et al (2016) | LFD (24) vs Hypnotherapy (25) vs Combined (25) | 6 weeks | None | None |
| Eswaran et al (2016) | LFD (45) vs modified NICE (39) | 4 weeks | None | None |
| Bohn et al (2015) | LFD (38) vs NICE (37) | 4 weeks | None | None |
| Pedersen et al (2014) | LFD (42) vs Probiotic (41) vs Habit (40) | 6 weeks | None | None |
| Halmos et al (2014) | LFD (27) vs Typical (27) | 3 weeks | Yes – defined as >81% (17/21 days) | All participants were compliant to LFD |
| Staudacher et al (2012) | LFD (19) vs Habit (22) | 4 weeks | Yes – defined as lower consumption of short-chain fermentable carbohydrates at EOS | All participants were compliant to LFD |

Table 41. Comparisons of the LFD RCTs and measured compliance. Abbreviations: LFD – low FODMAP diet, NICE – National Institute for Health and Care Excel, EOS – end of study.

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Appendix A: Health Questionnaire

Demographics and Health Questionnaire

The following questionnaire will help us evaluate your health status. Please fill out and mail back to us in the stamped envelope we provided or bring it with you on day of your class session.

If you have any questions, please contact: Kristen M Roberts, PhD, RDN 614-366-7191

1. Name: _____

2. Gender: M F Other

3. Age: _____

4. Weight: _____

5. Height: _____

6. When were you diagnosed with IBS?: _____

7. Have you previously received information about nutrition therapy for your IBS from a health care provider or met with a Registered Dietitian to discuss diet for managing your IBS symptoms?
Yes No

If yes, please indicate the type of nutrition recommendation made for you:

8. Do you currently follow a special diet to help with your IBS symptoms? Yes No
If yes, please specify or describe the diet:

9. Do you currently exclude any foods to help with your IBS symptoms? Yes No
If yes, please indicate which foods you avoid:

10. Do you engage in physical activity? Yes No
If yes, please indicate:

Type of exercise (example: walking, running, etc.): _____

Length of physical activity period (example: 10 minutes): _____

Three Day Food Record Form

Instructions for Completing the Food Record:

Choose three typical days (2 weekdays and 1 weekend day). Try to eat the way you usually do while you are keeping the food record. Please follow the instructions below as carefully as you can. If you have questions, please e-mail Kristen Roberts, PhD, RD (Kristen.Roberts@osumc.edu) or all 614-292-4758.

1. Record all the food you eat or drink for each day you choose to record. Most people find it helpful to do this as soon after the meal or snack as they can.
2. Write only one food item on a line.
3. Describe the **type of food** eaten as clearly as you can. Use the sample provided as a guide.
 - o List ingredients to help describe any unusual casserole or salad.
 - o Indicate whether the food is canned, fresh, frozen or diet.
 - o List the brand names of foods if you know them.
4. Describe how the food was prepared.
 - o Baked, broiled, fried, raw are examples
5. Remember to include all condiments such as pickles, catsup, tartar sauce, salad dressings, gravies and sauces.
6. Be sure to include any snacks such as gum or candy.
7. If you take a vitamin/mineral or other supplement consistently (at least once per week), please return the package label with your food records if it is available. Please list brand name, how many, how often you take them at the top of the first food record.
 - o Ex: Centrum plus 1 tablet 5 days per week
8. Describe the **amounts** of food you eat and drink as clearly as you can. Use the following examples as a guide.

Practical guide to estimating portions

This is like:

| | |
|------------------------------------|---------------------------|
| Thumb | 1 ounce cheese |
| 4 stacked dice | 1 ounce cheese |
| Thumb tip to 1 st joint | 1 tsp |
| Bar of soap or deck cards | 3 ounces meat |
| Palm of hand | 3 ounces |
| 1 ice cream scoop | ½ cup |
| Fist or baseball | 1 cup |
| Handful | 1 or 2 ounces snack chips |
| Tennis ball | 1 medium fruit serving |
| Computer mouse | ½ to ¾ cup |
| Ping pong or golf ball | 2 TBSP |
| Yo-yo or hockey puck | 1 bagel serving |

Specific information for estimating portions and recording

Liquids – list as *cups, parts of cups or fluid ounces

Meat, fish, cheese, eggs – list in ounces, by number, or size. Specify if the amount given is in cooked or raw weight. List bacon or sausage by number of slices or links.

| | | | |
|-----|------------------------|---------------------------|-------------|
| Ex: | Chicken breast | Baked, boneless, skinless | 3 oz. |
| | Lean ground beef patty | Broiled | ¼ pound raw |
| | American cheese | Kraft singles | 1 slice |

Fruits – list as cups*, parts of cups, or by number. If possible, include the size (diameter and/or length) of fresh fruits

| | | |
|-----|--------|--------------------------------|
| Ex: | Banana | 1 small (6 inches long) |
| | Apple | 1 medium (size of tennis ball) |

Vegetables - list as cups*, parts of cups, or by number.

| | | | |
|-----|--------------|------------------|------------|
| Ex: | Green beans | Del Monte canned | ½ cup |
| | Baby carrots | fresh | 10 carrots |

| | | | |
|---|--|---|---|
| Bread, rolls, crackers – list by number or size. | | | |
| Ex: | whole wheat bread Triscuits | Pepperidge Farm Nabisco | 1 slice 4 crackers |
| Cereal, rice, noodles, potato - list by cups*, parts of cups, or by number. | | | |
| Ex: | spaghetti Potato | cooked, San Giorgio baked | 1 cup 1 medium (about 4 inches long) |
| Pancakes, waffles – list by number and size | | | |
| Ex: | pancakes | Betty Crocker, buttermilk | 2 (5" diameter) |
| Jam, jelly, honey, syrup, sugar – list by teaspoons or tablespoons, one tablespoon is three teaspoons | | | |
| Ex: | syrup | Aunt Jemima Lite | 3 TBSP |
| Candy – list by number and size of bar (bite size, mini, regular or king) or pieces | | | |
| Ex: | Sno Caps Baby Ruth | 3.1 ounce package 1 regular size candy bar | |
| Jello, puddings, ice cream – list as cups or parts of cups. Please indicate if pre-packaged or homemade. | | | |
| Cookies – list by number and size | | | |
| Ex: | cookies, Choc chip | Mrs. Fields | 5 cookies (2 1/2" diameter) |
| Pie, cake – list by number and size (length and width at the longest end). | | | |
| Ex: | Ice cream cone, strawberry Choc cake with chocolate icing | Ben & Jerry's Homemade | 1/2 cup 1/10 of 9" layer Cake |

Miscellaneous – list by teaspoons, tablespoons, parts of cups, or pats. Include butter, margarine, oil, sauces, dressings, gravies, dessert toppings added in cooking or at the table.

Eating Out

Give the name of the restaurant so that we may call for more info if necessary. Describe food items eaten as carefully as you can.

Ex: Pizza Hut Pizza Sausage and cheese 1 slice of medium 4" x 6"
 McDonalds Quarter pounder with cheese 1 sandwich
 French fries, McD's 1 small package about 30 fries

Example food record

| Date/Time | Kind of Food | How Prepared or Brand Name | Amount or Size of Serving |
|-----------|------------------------|----------------------------|---------------------------|
| 9/17/2006 | | | |
| 7:30 AM | Cheerios | General Mills | 1 cup |
| | 2% milk | Kroger Brand | 1/2 oz |
| | Banana | | 1/2 small |
| | One-A-Day vitamin | Women's formula | One pill |
| 12:00 PM | Turkey sandwich | | |
| | Bread | Home Pride, whole wheat | 2 slices |
| | Turkey breast | Butterball | 3 deli slices |
| | Reduced Fat Mayonnaise | Kraft | 1 Tbsp |
| | Lettuce | Romaine | 1 leaf |
| | Tomato | Fresh | 2 slices |
| 3:45 PM | String cheese | Maptown, | 1 oz |
| | Pepsi | Regular | 12 oz (1 can) |
| | Corn Chips | Frito Lay | 1 package (1.5 oz) |
| 6:30 | Spaghetti | Mueller's | 1 cup (cooked) |
| | Spaghetti sauce | Ragu, meat-flavored | 3/4 cup |
| | String beans | DelMonte, canned | 1/3 cup |
| | Lettuce | Iceberg, chopped | 1 cup |
| | Tomato | Fresh | 1/2 small |
| | French dressing | Kraft Fat Free | 2 Tbsp |
| | 2% milk | Kroger Brand | 1 cup |
| 8:30 PM | Ice cream | Breyer's strawberry | 1/2 cup |

Food Record

Subject Number in study: _____
Date: _____ Weekday/Weekend

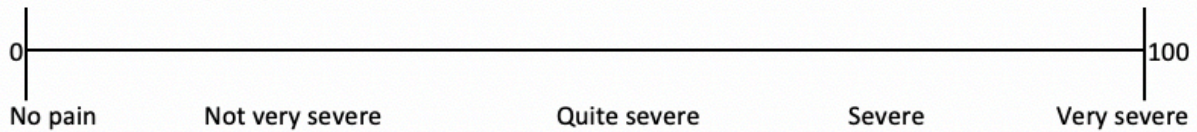
[illegible]

Appendix C: IBS-SSS and BSFS

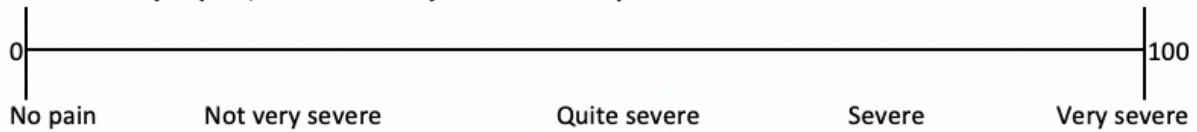
IBS Severity Score

Place an X anywhere on the line between 0 and 100 to indicate as accurately as possible the severity of your symptoms

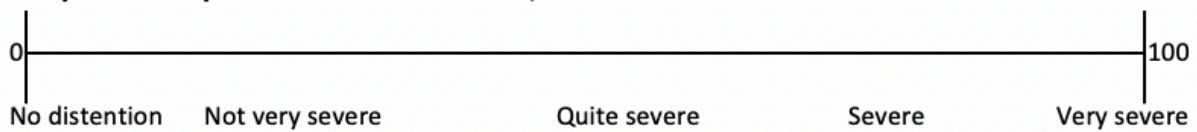
1. How severe is your pain?



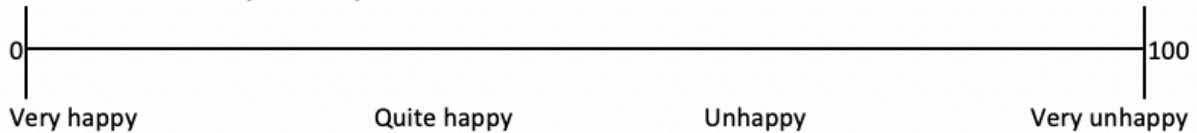
2. If currently in pain, how severe is your abdominal pain?



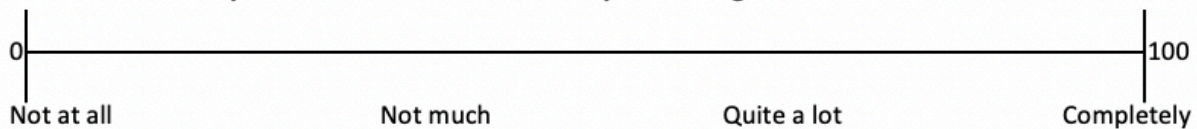
3. If you currently have abdominal distention, how severe is it?



4. How satisfied are you with your bowel habits?



5. How much does your IBS affect or interfere with your life in general?



6. Currently, how often do you pass a bowel action? (please check one box)

Once a week ☐

Once every 4-6 days ☐

Once every 2-3 days ☐

Once a day ☐








2-3 times a day ☐

4-6 times a day ☐

7 or more times a day ☐

7. Please check the box that best describes your current stool:

Bristol Stool Chart

| | | | |
|--------|---|--|--------------------------|
| Type 1 |  | Separate hard lumps, like nuts (hard to pass) | <input type="checkbox"/> |
| Type 2 |  | Sausage-shaped but lumpy | <input type="checkbox"/> |
| Type 3 |  | Like a sausage but with cracks on its surface | <input type="checkbox"/> |
| Type 4 |  | Like a sausage or snake, smooth and soft | <input type="checkbox"/> |
| Type 5 |  | Soft blobs with clear-cut edges (passed easily) | <input type="checkbox"/> |
| Type 6 |  | Fluffy pieces with ragged edges, a mushy stool | <input type="checkbox"/> |
| Type 7 |  | Watery, no solid pieces. Entirely Liquid | <input type="checkbox"/> |



Making Sense Out of Food Labels

Claims on food packages can be confusing. Knowing what is in food may help you to make healthier choices. Reading food labels is the best way to get information about what is in your foods. This can help you make better choices and eat healthier overall.

Nutrition Facts

- 1. Look for the Nutrition Facts on the food label.** The numbers on this illustration match the numbers in the Nutrition Facts section of this handout. Refer back to this page as you learn what each item means.
- 2. Serving Size:** The amount of food recommended to be eaten at one time. All of the following nutrition information is based on this serving size. For instance, if you ate 2 servings, you would need to double the numbers listed below. Also note how many servings are in the entire container to help estimate what one serving size looks like.
- 3. Calories:** The average adult needs about 2,000 calories a day from food and beverages. Use this number to help determine if this product fits into your daily eating plan or not. Too many calories each day can lead to weight gain.
- 4. Fat:** Not all fat is created equal. There are 4 types of fat in our foods: saturated fat, trans fat, monounsaturated fat and polyunsaturated fat. The FDA only requires that food manufacturers list saturated fat and trans fat on their Nutrition Facts labels, but sometimes you might find all 4 types listed.

| Nutrition Facts | |
|--------------------------|----------------|
| 6 servings per container | |
| Serving size | 1 cup (140g) |
| Amount per serving | |
| Calories | 170 |
| | % Daily Value* |
| Total Fat 8g | 10% |
| Saturated Fat 3g | 15% |
| Trans Fat 0g | |
| Cholesterol 0mg | 0% |
| Sodium 5mg | 0% |
| Total Carbohydrate 22g | 8% |
| Dietary Fiber 2g | 7% |
| Total Sugars 16g | |
| Includes 8g Added Sugars | 16% |
| Protein 2g | |
| Vitamin D 0mcg | 0% |
| Calcium 20mg | 2% |
| Iron 1mg | 6% |
| Potassium 240mg | 6% |

*The % Daily Value tells you how much a nutrient in a serving of food contributes to a daily diet 2000 calories a day is used for general nutrition advice.

Source: Adapted from U.S. Food and Drug Administration



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Too much saturated fat or trans fat in the diet can lead to health problems, such as heart disease or cancer. An average adult following a 2000 calorie diet should aim to limit total fat to 45 to 75 grams per day (20-35% total calories), saturated fat to 11 to 13 grams per day (5-6% total calories) and trans fat should be avoided as much as possible. Check the list below to see how much you should have if you eat a different amount of calories per day.

| <u>If your daily calorie total is:</u> | <u>Your total fat limit fat per day is:</u> | <u>Your saturated fat limit per day is:</u> |
|--|--|--|
| 2000 calories | 45 to 75 grams | 11 to 13 grams |
| 1800 calories | 40 to 70 grams | 10 to 12 grams |
| 1500 calories | 35 to 60 grams | 8 to 10 grams |
| 1200 calories | 25 to 45 grams | 6 to 8 grams |

Note: Although the food label may say the food item has 0 grams of trans fat, it may contain up to 0.5 gram per serving. The best way to check for trans fats is to look at the ingredient list and look for “partially hydrogenated oils.” If you see these words, try to find an alternative product made with different ingredients.

5. **Cholesterol:** Cholesterol is found in animal products, such as cheese, egg yolks, milk and butter. Eating too many of these foods can increase your risk for heart disease. Try to limit total cholesterol intake to 300 mg per day. If you are at risk for heart disease or have Type 2 Diabetes, 200 mg per day is the maximum recommended amount. Plant-based foods do not contain any cholesterol.
6. **Sodium:** Many processed foods contain sodium, which acts as a preservative and adds flavor. Most Americans are eating too much sodium. Keeping your sodium intake low may decrease high blood pressure and lower your risk for stroke, heart disease and kidney disease. The 2015 Dietary Guidelines for Americans suggests limiting sodium intake to no more than 2,300 mg per day although some older individuals or those with high blood pressure may want to limit this intake even more.
Guideline: Look for foods that have less than 300 mg of sodium per serving. Watch the number of servings of any food you eat.
7. **Total Carbohydrates:** Carbohydrates are in foods like bread, pasta, potatoes, fruits and vegetables. Some individuals, like those with diabetes, may want to control the amount of carbohydrate that they have with their meals and snacks.
8. **Dietary Fiber:** Fiber is the bulk part of grains, beans, peas, fruits and vegetables. Fiber helps the body’s digestive system work well and may help lower the risk of some cancers and heart disease. If you want to increase your fiber intake, look for foods with at least 3 grams of fiber per serving.
9. **Added Sugar:** Some sugars are naturally occurring, like those in fruit, and others are added during the processing or packaging of foods. Too many of these “added sugars” can increase your risk for developing diabetes, heart disease, obesity and other health conditions. Aim to limit added sugar intake to 10% of total calories, or about 30 to 55 grams per day for most people. Make sure to check beverages for added sugar content.
10. **Protein:** Protein can help to build muscle, regulate hormones and is involved in immune function. Most individuals should aim for about 60 to 100 grams of protein per day.

11. Vitamins and Minerals: Most Americans are not meeting the recommended amount of these nutrients each day. Look for food products that are a good source of these nutrients. Your goal is to reach 100% of each for the day.

12. % Daily Value: Daily values are the percentage of nutrients the product provides based on a diet of 2,000 calories per day. Your nutrient needs may be less or more than the Daily Value depending on your individual health concerns. For certain nutrients, like sodium and added sugar, aim for lower percentages. For other nutrients, like fiber, vitamins and minerals, aim for 100% a day.

The Ingredient List

In addition to the Nutrition Facts Label, look at a product's ingredient list to help you make better food selections. The ingredient list tells you what is in the food. Manufacturers list ingredients by weight in order of greatest amount to least amount in the food. It is a valuable resource for people with food allergies. Use the table to help you identify ingredients that are high in a nutrient.

| Nutrient | Common Ingredients | |
|--------------------------|--|--|
| Sodium | <ul style="list-style-type: none"> Baking powder Baking soda Monosodium glutamate | <ul style="list-style-type: none"> Salt (regular or sea salt) Sodium |
| Cholesterol | <ul style="list-style-type: none"> Any animal fats Lard | <ul style="list-style-type: none"> High fat products, such as whole milk and cheese |
| Saturated and Trans Fats | <ul style="list-style-type: none"> Any animal fats except fish Coconut butter Coconut oil | <ul style="list-style-type: none"> Palm oil Partially hydrogenated oils |
| Sugar | <ul style="list-style-type: none"> Brown sugar Carob powder Corn syrup/solids Dextrin Dextrose Fructose Glucose | <ul style="list-style-type: none"> High fructose corn syrup Honey Invert sugar Lactose Mannose Molasses Sucrose |

Talk to your doctor or health care team if you have any questions about your care.

For more health information, go to patienteducation.osumc.edu or contact the Library for Health Information at 614-293-3707 or health-info@osu.edu.

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High Fiber Diet

About dietary fiber

Dietary fiber, also known as roughage or bulk, is found only in plant products. These products include fruits, vegetables, beans, whole grains, and cereals. Fiber in the diet is important to the body in many ways. It helps the digestive system work properly, promotes regularity, prevents / treats constipation, and may even decrease the risk of colon and rectal cancer. It also may help to decrease blood cholesterol, improve glucose control in diabetes, and control weight.

The recommendation for fiber is 25 to 35 grams daily from a variety of food sources. It is important to raise your level of fiber slowly to reduce possible abdominal discomfort. For example, replace 1 refined food with a high fiber food every few days. It also is important to drink extra water as you add fiber to your diet. Try to drink at least 8 cups of water per day.

High fiber foods

Bread, Pasta and Grains

| Examples | Serving Size | Fiber in Grams (g) | Calories |
|--|--------------|--------------------|----------|
| Bran muffin | 1 each | 2.6 | 154 |
| 100% whole grain bread (varies, check label) | 1 slice | 3-4 | 70 |
| Spaghetti, 100% whole wheat | 1 cup | 6.3 | 174 |
| Brown rice | ½ cup | 1.7 | 108 |
| Pumpernickel bread | 1 slice | 2.1 | 80 |

Legumes

| Examples | Serving Size | Fiber in Grams (g) | Calories |
|----------------------------|--------------|--------------------|----------|
| Kidney beans, canned | ½ cup | 4.5 | 104 |
| Lima beans, baby, frozen | ½ cup | 5.4 | 95 |
| Navy beans, canned | ½ cup | 6.7 | 148 |
| Baked beans, vegetarian | ½ cup | 6.4 | 118 |
| Lentils, cooked | ½ cup | 4 | 115 |
| Black beans, boiled | ½ cup | 7.5 | 115 |
| Soybeans (edamame), boiled | ½ cup | 5.1 | 149 |
| Pinto beans, canned | ½ cup | 5.5 | 103 |



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Fruit

| Examples | Serving Size | Fiber in Grams (g) | Calories |
|------------------------|--------------|--------------------|----------|
| Apple with skin | 1 medium | 3.7 | 80 |
| Apricot, canned | 3 halves | 1.4 | 54 |
| Banana | 1 medium | 2.7 | 105 |
| Blueberries, raw | ½ cup | 2 | 40 |
| Cantaloupe | ¼ melon | 1 | 30 |
| Cherries, sweet | 10 | 1.6 | 50 |
| Dates, dried | 3 | 1.8 | 70 |
| Orange, fresh | 1 medium | 3.1 | 60 |
| Peach, fresh with skin | 1 medium | 1.7 | 35 |
| Prunes, dried | 3 | 1.8 | 60 |
| Raisins | ¼ cup | 1.3 | 110 |
| Strawberries | 1 cup | 3.4 | 45 |
| Pear | 1 medium | 4 | 98 |

Vegetables

| Examples | Serving Size | Fiber in Grams (g) | Calories |
|-------------------------------|--------------|--------------------|----------|
| Bell peppers (red) | 1 cup | 1 | 12 |
| Broccoli, frozen | ½ cup | 2.8 | 25 |
| Brussels sprouts, frozen | ½ cup | 3.2 | 33 |
| Carrot, raw | 1 medium | 2.2 | 31 |
| Cauliflower, frozen | ½ cup | 2.4 | 17 |
| Corn, frozen | ½ cup | 2 | 65 |
| Green beans, frozen | ½ cup | 2.2 | 25 |
| Green peas, frozen | ½ cup | 4.4 | 65 |
| Spinach, frozen | ½ cup | 2.8 | 27 |
| Tomato, raw | ½ cup | 1.4 | 26 |
| Potato, baked with skin | 1 each | 4.8 | 220 |
| Sugar snap peas | 1 cup | 2.5 | 41 |
| Summer squash | 1 whole | 2 | 33 |
| Sweet potato, baked with skin | 1 each | 3.4 | 117 |

High fiber sample menu - 1,674 calories, 37.4 grams of fiber

Breakfast - 266 calories, 5.2 grams of fiber

- 1 scrambled egg
- 1 slice of whole grain toast
- 1 tablespoon peanut butter
- ½ cup blueberries

Snack - 170 calories, 2 grams of fiber

- ¼ cup trail mix

Lunch - 540 calories, 13 grams of fiber

- Turkey and cheese sandwich on wheat bread
- 1 cup baby carrots
- 1 medium apple

Snack - 107 calories, 1.7 grams of fiber

- 1 string cheese
- ½ cup blue berries

Dinner - 591 calories, 15.5 grams of fiber

- Black bean burrito bowl:
 - 1 cup brown rice
 - ½ cup black beans
 - 1 cup grilled onions and peppers
 - ¼ cup guacamole
 - ¼ cup salsa
 - ¼ cup shredded cheese

| | | | |
|----------------------|--|-----------------|--|
| Prepared For: | | Date: | |
| Prepared By: | | Contact: | |

1,500-Calorie 5-Day Menus

The menus in this handout provide about 1,500 calories per day. Each daily menu has:

- **7 servings of protein (P)**
 - Proteins can include: lean meat, fish, poultry, beans, reduced-fat cheese or egg.
 - Weight for meat is after cooking.
 - A 3-ounce (oz) portion would count as 3 servings.
- **12 servings of carbohydrate (C)**
 - Carbohydrates can include: fat-free or 1% milk or "light" yogurt with less than 100 Calories, fruit, bread, grains, starchy vegetables or other carbohydrates.
 - Measure cooked hot cereals and pasta.
 - Substitute 2 slices reduced calorie (40 Calories/slice) bread for 1 slice regular bread.
- **3 or more servings non-starchy vegetables (V)**
 - Non-starchy vegetables can include: lettuce, broccoli, cabbage, carrots, cauliflower, green beans, tomatoes, etc.
- **4 servings of fat (F)**
 - Fats can include: margarine, salad dressing, mayonnaise, nuts, olives, etc.
 - Substitute 1 tablespoon reduced-fat margarine for 1 teaspoon regular.
- **"Free" foods (*)**
 - Free foods are foods with very few calories and little fat or carbohydrate.

Day 1

| Meal | Menu | Pattern |
|---------------------|--|-------------------------------|
| Breakfast | 1 slice toast (C) with 1 tablespoon peanut butter (P, F) 6 oz "light" fruit yogurt (C) Orange (C) | 1 P 3 C 1 F |
| Lunch | Ham sandwich: 1 oz ham (P), 1 slice low-fat cheese (P), 2 slices bread (2C), lettuce and tomato (V), 1 teaspoon mayonnaise (F), mustard (*) Raw broccoli (V) Small pear (C) 15 fat-free or baked snack chips (C) | 2 P 4 C 2 V 1 F * |
| Evening Meal | 4 oz boneless, skinless chicken breast (4P), 2/3 cup cooked pasta (2C) with mushrooms, zucchini, pepper (V), 1 teaspoon olive oil (F) Green salad (V) with 2 tablespoons reduced-fat salad dressing (F) 17 small grapes (C) | 4 P 3 C 2 V 2 F |
| Snack | 3 (2 ½ inch) graham crackers (C) and 1 cup fat-free milk (C) | 2 C |

Day 2

| Meal | Menu | Pattern |
|------|------|---------|
|------|------|---------|

| | | |
|---------------------|--|-------------------------------|
| Breakfast | 1 slice low-fat cheese or 1 egg or ¼ cup egg substitute (P) 4-inch waffle (C, F) with 2 tablespoons sugar-free syrup (*) 1 cup fresh or frozen (sugar-free) berries (C) 1 cup fat-free or 1% milk (C) | 1 P 3 C 1 F * |
| Lunch | Bean salad with ¼ cup grated low-fat cheese (P), ½ cup beans (P, C), tomato, onion, carrots, lettuce, cucumbers (V), 2 tablespoons reduced-fat ranch dressing (F) and salsa (*) 15 fat-free or baked snack chips (C) Large banana (2C) | 2 P 4 C 1 V 1 F * |
| Evening Meal | 4 oz roast beef (4P) ½ cup potatoes (C) 1 oz roll (C) with 1 teaspoon margarine (F) Steamed carrots and cauliflower (V) Tossed salad (V) with 2 tablespoons reduced-fat salad dressing (F) 1 cup melon cubes (C) | 4 P 3 C 2 V 2 F |
| Snack | 6 saltine crackers (C) Small apple (C) | 2 C |

Day 3

| Meal | Menu | Pattern |
|---------------------|--|-------------------------------|
| Breakfast | 1 egg or ¼ cup egg substitute (P) ½ cup oatmeal (C) with 1 teaspoon margarine (F) and sugar substitute (*) 1 cup fat-free or 1% milk (C) ½ grapefruit (C) | 1 P 3 C 1 F * |
| Lunch | Grilled chicken Caesar salad: romaine lettuce (V), 2 oz boneless skinless chicken breast (2P), mushrooms, peppers (V), 1 tablespoon Caesar dressing (F), ½ cup croutons (C), 1 tablespoon grated parmesan cheese (*) 1 cup chicken noodle soup (C) with 6 saltine or 24 oyster crackers (C) Small pear (C) | 2 P 4 C 2 V 1 F * |
| Evening Meal | Cheeseburger: 3 oz lean ground beef (3P), 1 slice low-fat cheese (P), 1 hamburger bun (2C), onion, lettuce, tomato (V), 1 teaspoon mayonnaise (F), mustard (*) Green beans (V) with 1 teaspoon margarine (F) Large kiwi fruit (C) | 4 P 3 C 2 V 2 F * |
| Snack | ¾ cup wheat flakes cereal (C) and 1 cup fat-free or 1% milk (C) | 2 C |

Day 4

| Meal | Menu | Pattern |
|------------------|--|------------------------|
| Breakfast | 1 slice low-fat cheese (P) 1 English muffin (2C) with 1 teaspoon margarine (F) and sugar-free jam (*) ½ cup unsweetened applesauce (C) | 1 P 3 C 1 F * |

| | | |
|---------------------|--|-------------------------------|
| Lunch | Roast beef sandwich: 2 oz roast beef (2P), 2 slices bread (2C), lettuce and tomato (V), 1 teaspoon mayonnaise (F) Raw celery (V) Small banana (C) and sugar-free gelatin dessert (*) 8 animal crackers (C) | 2 P 4 C 2 V 1 F * |
| Evening Meal | 4 oz broiled fish (4P) 8 inch corn on cob or 1 cup whole kernel corn (2C) Steamed broccoli (V) 1 teaspoon margarine (F) for seasoning vegetables Tossed salad (V) with 2 tablespoons reduced-fat salad dressing (F) Nectarine (C) | 4 P 3 C 2 V 2 F |
| Snack | 2 rice cakes (C) and 1 cup fat-free or 1% milk (C) | 2 C |

Day 5

| Meal | Menu | Pattern |
|---------------------|--|-------------------------------|
| Breakfast | Vegetable omelet: 1 egg or ¼ cup egg substitute (1P), onion, mushroom, pepper (V), nonfat cooking spray (*) 1 slice toast (C) with 1 teaspoon margarine (F) 1 cup fat-free or 1% milk (C) Orange (C) | 1 P 3 C 1 F * |
| Lunch | Tuna salad: 2 oz water pack tuna, drained (2P), celery, onions (V), dill pickle (*), 1 teaspoon mayonnaise or (F) Baby carrots and romaine lettuce (V) 12 saltine crackers or 2 slices bread (2C) Small apple (C) ½ cup sugar-free, fat-free pudding (C) | 2 P 4 C 2 V 1 F * |
| Evening Meal | Chicken fajitas: 4 oz boneless, skinless chicken breast (4P), six-inch low fat tortilla (C), grilled onions, peppers and tomatoes (V), 2 tablespoons sour cream (F), salsa (*) 2/3 cup rice (2C) Green salad (V) with 2 tablespoons reduced-fat salad dressing (F) | 4 P 3 C 2 V 2 F * |
| Snack | 8 animal crackers (C) and 1 cup fat-free or 1% milk (C) | 2 C |