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Difference in Reported Symptoms by Type of Medical Nutrition Therapy Provided in Adults with Irritable Bowel Syndrome

Justina S. Kim
Byrdine F. Lewis College of Nursing and Health Professions

Abby Johnson

Molly Paulson
Byrdine F. Lewis College of Nursing and Health Professions

Anita M. Nucci
Byrdine F. Lewis College of Nursing and Health Professions

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ACCEPTANCE

This thesis, DIFFERENCE IN REPORTED SYMPTOMS BY TYPE OF MEDICAL NUTRITION THERAPY PROVIDED IN ADULTS WITH IRRITABLE BOWEL SYNDROME, by Justina Kim was prepared under the direction of the Master's Thesis Advisory Committee. It is accepted by the committee members in partial fulfillment of the requirements for the degree Master of Science in the Byrdine F. Lewis College of Nursing and Health Professions, Georgia State University. The Master's Thesis Advisory Committee, as representatives of the faculty, certify that this thesis has met all standards of excellence and scholarship as determined by the faculty.

Anita M. Nucci, PhD, RD, LD
Committee Chair

Molly Paulson, MS, RD, LD
Committee Member

Abby Johnson, MS, RD, LD
Committee Member

6/24/24
Date

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Justina Kim
6436 Shadow Ct
Douglasville, GA 30134

The director of this thesis is:

Anita M. Nucci, PhD, RD, LD
Professor
Department of Nutrition
Byrdine F. Lewis College of Nursing and Health Professions
Georgia State University
Atlanta, Georgia 30302

VITA

Justina Kim

ADDRESS: Atlanta, GA, 30329

EDUCATION: M.S. 2024 Georgia State University
Health Sciences, Concentration: Nutrition

B.S. 2022 Georgia State University
Nutrition Science

PROFESSIONAL EXPERIENCE:

- Graduate Teaching Assistant, NUTR 2100 — 2022-Present
  Georgia State University, Atlanta, GA
- Wound Care Tech — 2019-2023
  Piedmont Atlanta Hospital, Atlanta, GA
- Culinary Medicine Lab Assistant — 2021-2022
  Georgia State University, Atlanta, GA
- Undergraduate Research Assistant — 2020-2021
  Georgia State University, Atlanta, GA

PROFESSIONAL SOCIETIES AND ORGANIZATIONS:

- Greater Atlanta Dietetic Association — 2022-present
- Academy of Nutrition and Dietetics — 2022-present
- American Society of Nutrition — 2021-present
- Lewis College Services Committee Member — 2021-2022
- Nutrition Student Network (President) — 2021-2022

AWARDS AND PUBLICATIONS:

- Lettie Pate Whitehead Foundation Scholarship Recipient — 2024
  Georgia State University
- Outstanding Undergraduate Nutrition Researcher Award — 2022
  Georgia State University
- Undergraduate Nutrition Student of the Month — 2022
  Georgia State University
- American Society of Nutrition, Vol 5, Supplement 2; — 2021
  Raspberry Consumption Decreases the Expression Of Interleukin-6 in the Liver of Angiotensin II-infused rats

ABSTRACT

DIFFERENCE IN REPORTED SYMPTOMS BY TYPE OF MEDICAL NUTRITION THERAPY PROVIDED IN ADULTS WITH IRRITABLE BOWEL SYNDROME

By

Justina Kim

Background: Irritable bowel syndrome (IBS) is a common gastrointestinal disorder, affecting 9-23% of the population and characterized by abdominal pain related to bowel habits. Previous studies show that a low-FODMAP diet can reduce IBS symptoms. Emerging research is focusing on personalized dietary treatments like the Lifestyle Eating and Performance (LEAP) program, which uses the Leukocyte Activation Assay-Mediator Release Test (LAA-MRT) to identify foods causing inflammation. The effectiveness of MRT in improving IBS symptoms and quality of life remains uncertain. The aim of this study is to retrospectively analyze symptom reduction in adults with IBS who received either LEAP/MRT or low-FODMAP diet therapy.

Methods: This study involves a retrospective (observational) electronic medical record review of a convenience sample of adults aged 18 to 65 with IBS. Inclusion criteria include patients referred by a primary provider or gastroenterologist with an IBS diagnosis or symptoms consistent with IBS. Additionally, patients must have completed an initial symptom survey during their first visit and a follow-up survey within four weeks.

Results: Twenty-one adults diagnosed with IBS or with IBS symptoms were included in the study. Of these, 16 received LEAP/MRT therapy, while 5 were counseled on the low-FODMAP diet regimen. Participants in the LEAP/MRT group experienced a significant reduction in weight and BMI between the initial and 1-month follow-up visits (75.5 $\pm$ 21.8

vs. 74.0 ± 21.6 and 27.3 ± 6.6 vs. 26.8 ± 6.3, respectively; P<0.05). Statistically significant differences were observed within the LEAP/MRT group in multiple individual categories (constitutional, emotional, neurological, skin, nasal/sinus, mouth/throat, lung, eyes, ears, digestive, weight management) and in the total symptom score (86.5 [IQR: 59, 110] vs. 41 [IQR: 22, 60], respectively; P<0.001). Although the reported individual system symptoms were reduced at the follow-up visit for those in the Low-FODMAP group, the change in median scores over time was not statistically significant. However, the total median symptom score was significantly reduced at the follow-up visit (79 [IQR: 35, 132] vs. 22 [IQR: 10, 101.5], respectively; P=0.043).

Conclusion: We identified statistically significant reduction in the symptom summary scores between the initial and follow-up visits in multiple individual categories within the LEAP/MRT group. The LEAP/MRT approach may provide a personalized treatment option for individuals with IBS by addressing specific dietary sensitivities and enhancing patient outcomes. Additional research is needed to confirm these findings through larger, randomized, controlled trials and further solidify the clinical significance and long-term advantages of the LEAP/MRT intervention.

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By
Justina Kim

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Department of Nutrition

Georgia State University

Atlanta, GA
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TABLE OF CONTENTS

LIST OF TABLES

ABBREVIATIONS

BMI	Body Mass Index
CBC	Complete Blood Count
CD	Celiac Disease
EHR	Electronic Health Record
ESR	Erythrocyte Sedimentation Rate
FDA	Food and Drug Administration
FGID	Functional Gastrointestinal Disorder
FODMAP	Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols
GI	Gastrointestinal
GSRA	Gastrointestinal Symptom Rating Scale
HDL	High-Density Lipoprotein
IBD	Inflammatory Bowel Disease
IBS	Irritable Bowel Syndrome
IBS C	Irritable Bowel Syndrome Constipation
IBS D	Irritable Bowel Syndrome Diarrhea
IBS M	Irritable Bowel Syndrome Mixed
IBS-SSS	IBS Symptom Severity Score
IBS U	Irritable Bowel Syndrome Unclassified
ID	Identification
IL-8	Interleukin-8
IRB	Institutional Review Board

LAA-MRT	Leukocyte Activation Assay-Mediator Release Test
LDL	Low-Density Lipoprotein
LEAP	Lifestyle Eating and Performance
MCHC	Mean Corpuscular Hemoglobin Concentration
MCH	Mean Corpuscular Hemoglobin
MCV	Mean Corpuscular Volume
mNICE	modified National Institute for Health and Clinical Excellence
MNT	Medical Nutrition Therapy
MRT	Mediator Release Test
NCP	Nutrition Care Process
NFPE	Nutrition Focused Physical Exam
NSAIDS	Non-Steroidal Anti-Inflammatory Drugs
QOL	Quality of Life
RDN	Registered Dietitian Nutritionist
SBI	Serum-derived bovine immunoglobulin
SES	Socioeconomic Status
SIBO	Small Intestinal Bacterial Overgrowth
SI	Isomaltase
SPSS	Statistical Program of Social Sciences
TDA	Traditional Dietary Advice
TIBC	Total Iron-Binding Capacity
TNF- α	Tumor Necrosis Factor Alpha

TRP	Tryptophan
VAS	Visual Analog Scale
WBC	White Blood Count

CHAPTER 1

Introduction

Irritable bowel syndrome (IBS) is a persistent functional gastrointestinal disorder (FGID) marked by abdominal pain linked to defecation or alterations in bowel habits.[1] Irritable bowel syndrome is a prevalent condition that afflicts 9-23% of the overall population, predominately affecting females (80%). This condition exerts a significant influence on both the quality of life and healthcare expenses.[2] Functional gastrointestinal disorders (FGID) encompass a collection of conditions marked by persistent gastrointestinal (GI) symptoms, such as abdominal pain, dysphagia, dyspepsia, diarrhea, constipation, and bloating, without evident pathology detected through conventional testing.[3] Irritable bowel syndrome is one type of FGID. Chang et al conducted a trial where adults with IBS were randomized to a dietary intervention involving either a low or moderate amount of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) foods. The study results indicated that a low-FODMAP diet resulted in a reduction of gastrointestinal symptoms and changes in bowel habits.[4]

In addition to the low-FODMAP diet, there are various treatment options for managing IBS. One avenue involves further diet modifications, which extend beyond the restrictions of the low-FODMAP diet. These modifications encompass incorporating dietary fiber and probiotics and adopting a generally healthy diet.[5] Increasing dietary fiber is a common approach in IBS management. Fiber can be found in fruits, vegetables, and whole grains. With regular consumption, it can aid in regulating bowel movements and promoting a healthy digestive system.[6] Probiotics promote a healthy gut microbiota, which

has been shown to alleviate and reduce IBS symptoms. Probiotics include beneficial bacteria that can restore a balanced gut flora and improve gastrointestinal function. Various fermented foods such as yogurt, kefir, and sauerkraut contain probiotics.[6] Maintaining a generally healthy diet plays a key role in managing IBS symptoms, and incorporating specific dietary adjustments further enhances its effectiveness. Emphasizing whole foods, lean proteins, and a diverse range of fruits and vegetables is particularly beneficial.[6]

Irritable bowel syndrome is categorized into four different subtypes: 1) IBS with diarrhea (IBS-D), 2) IBS with constipation (IBS-C), 3) IBS with mixed bowel patterns (IBS-M), and 4) IBS unclassified (IBS-U).[2] Currently, there is no universally accepted nutritional protocol for patients with IBS-D. However, it is increasingly evident that comprehending the influence of different dietary approaches on the composition of intestinal microbiota is crucial. This understanding is essential for defining an effective strategy to manage this functional disorder.[1] A burgeoning area of research focuses on tailoring dietary modifications for personalized IBS treatment. The Lifestyle Eating and Performance (LEAP) program represents one such intervention, employing the Leukocyte Activation Assay-Mediator Release Test (LAA-MRT). This approach utilizes inflammatory markers to identify foods and food chemicals that provoke inflammation, as determined by the mediator release test (MRT).[7] The efficacy of the MRT in improving outcomes such as reducing IBS symptoms is and quality of life in patients with IBS is unknown. This retrospective observational study will examine the degree of symptom reduction in adults with IBS who were referred for nutrition counseling to a private practice in an urban environment. Reported symptoms will be compared between those who received LEAP/MRT and the low-FODMAP diet. The goal is to assess the change in

symptoms between the initial visit and within one month after the initial visit as well as the difference in symptoms by treatment type.

Research Hypothesis: Within one month of therapy, participants in the LEAP/MRT group will have greater reduction in IBS symptom score than those in the low-FODMAP group.

Null Hypothesis: No difference in the IBS symptom score will be observed within one month of therapy between the LEAP/MRT and low-FODMAP diet groups

CHAPTER II

Literature Review

Epidemiology of Irritable Bowel Syndrome

On a global scale, IBS affects 1 in 10 people, where prevalence of the disease varies by country.[1] Irritable bowel syndrome is the most common gastrointestinal complaint from the United States and Canada, where 12% of the population in North America are affected. The lowest prevalence is in South Asia (7%) and highest in South America (21%). Although IBS research studies have been predominately conducted in North America and Europe, global prevalence of the disease has been reported, affecting patient livelihood and quality of life (QOL).[1,2] Irritable bowel syndrome has resulted in 1.6 million healthcare visits and 5 million prescriptions, placing a burden not only on the patient but also the healthcare team. Doshi et al. evaluated the annual total healthcare costs that were related to GI-related and IBS-related cause in patients from the United States. From their results, they found the average yearly healthcare expenses for individuals with IBS-C amounted to $11,182, with more than half (53.7%) of these costs associated with outpatient services. This includes expenses for visits to physician offices and other outpatient services, accounting for 13.1% and 40.6% of the total costs, respectively.[8] Another study showed that the annual cost of IBS in the USA ranges from $1,562 to $7,547. Health-care costs for IBS in the UK ranges from £45.6–200 million and US $2 billion in China, per year.[1]

While the condition is non-life threatening, it's effect on day-to-day activities, especially in working adults, can be drastically affected. Ballou et al. found employed adults in the US reported 8.0 days out of the month were affected by their IBS condition

and missed 1.5 days of work or school per month.[9] Other studies from European countries and Canada have reported 5% and 50% of individuals taking time off of work. Surveys conducted in European countries have also shown that individuals with IBS took double the number of days off from work compared to those who do not have IBS.[1] Due to the complexity and many uncertainties of IBS, a diagnosis can take up to an average of 4 years, as patients often feel their symptoms are not taken seriously and access to effective treatment(s) can be challenging. Irritable bowel syndrome has been seen to develop before the age of 50 and affects more woman than men by 80%. [2,10] A higher number of diagnoses has been reported in women, as the female-to-male ratio of who seeks medical care is 2-2.5:1.

Although women present with higher prevalence of IBS, the relationship between gender and seeking medical care remains unclear, as seeking medical care behaviors are comprised of various factors (e.g., accessibility, disease severity, stress, and socio-cultural circumstances). Diagnosis of IBS in women typically occurs during puberty through early adulthood and decline as age increases. Whereas for men, prevalence of IBS presents around the age of 70 and above. Sex hormones may play a potential role in the prevalence of IBS, as it affects the clinical manifestation and symptoms, as well as treatment options. Clinical symptoms can differ by gender as women are likely to experience IBS-constipation (IBS-C) and men are likely to experience IBS-diarrhea (IBS-D). Initial symptoms of IBS in women present as abdominal pain whereas men present with diarrhea like symptoms.[11]

Irritable bowel syndrome can occur in any age group. However, 50% of patients have reportedly been diagnosed before the age of 35 years. A lower prevalence of IBS has been observed in patients over the age of 50 years, indicating that IBS susceptibly may

decline with age. Since the prevalence of IBS decreases with age, this may suggest that IBS is not a chronic condition. If IBS were a chronic condition, it would remain or increase in prevalence with age. Socioeconomic status (SES) is another factor that has been studied and considered as a risk factor for IBS. Studies initially suggested IBS was associated with lower SES, as it has been indicative of reduced access to healthcare and poor health outcomes. However, it has been reported that stress may be a factor for the increased risk and susceptibility for IBS, as findings present those working in manual labor have higher prevalence. This may explain the higher prevalence in countries such as South America, as manual labor makes up most of their workforce.[6] Genetics may also play a role. Those who have biological relatives with IBS, are twice as likely to develop IBS. However, twin studies demonstrated when either a mother or father have IBS, it is considered an independent risk factor for the development of IBS. The greater influence for IBS development was rather learned behaviors and environment.[12]

The natural history of IBS diagnosis and prognosis have been followed by misdiagnosis, symptom patterns, and co-existing functional conditions. Studies found when patients were initially diagnosed with IBS, their colonoscopy results did not yield organic lesions at the rate of healthy control subjects (10% to 40%). However, those diagnosed with IBS at the time of their endoscopy results, displayed a rise in the diagnosis of inflammatory bowel disease (IBD) at 9 to 16 times higher when compared to the general population.[6]

Patients with IBS will experience an ebb and flow of symptoms, as some symptoms will resolve but new symptoms may arise. From the patients who do experience resolution, 45% of those will develop other gastrointestinal symptoms and complications, such as

dyspepsia.[6] Other functional conditions that co-exist or have been associated with IBS are chronic pain, fibromyalgia, chronic fatigue syndrome, and temporomandibular joint dysfunction. These associated functional conditions occur twice as much in people with IBS. The etiologies of these conditions are not fully understood, as there are multifactorial in their development. However, most consider IBS, and these functional conditions could be placed under a single umbrella for 'functional somatic syndromes'. Mental illnesses such as depression or anxiety has been reported in more than half of IBS patients. These patients are considered to experience more severe somatic symptoms.[6]

Unnecessary surgery and surgical procedures have been the consequence for people with IBS who have been misdiagnosed. Irritable bowel syndrome symptoms can overlap with other functional gastrointestinal and pelvic diseases. Common surgical interventions for IBS patients are cholecystectomy, appendectomies, or hysterectomies. Although the unnecessary surgical procedures can affect patient's QOL, it has not been associated with increased mortality.[6] Chang et al. observed the mortality rate in 4,000 patients with functional gastrointestinal disorders (FGID) in the US. From this study, mortality rates were not associated with FGID, when compared to the general population (hazard rate 1.06 [95% CI 0.86-1.32)].[4] A study performed in China by Tang et al. found similar results in the Chinese population (N = 263), where morality was not associated in patients with FGID. However, elderly patients with IBS-C had an increased incidence for colorectal cancer.[5]

Subtypes of Irritable Bowel Syndrome

Irritable bowel syndrome is categorized into four different subtypes: 1) IBS with diarrhea (IBS-D), 2) IBS with constipation (IBS-C), 3) IBS with mixed bowel patterns (IBS-M), and 4) IBS unclassified (IBS-U).[2] These classifications were based on the Rome IV criteria, stool patterns, and the Bristol Stool Scale. The subtypes are described using the percentage of hard and loose stools. IBS-C is identified when there are more than 25% hard stools and less than 25% loose stools. IBS-D is when there are more than 25% loose stools and less than 25% hard stools. IBS-M is when there are more than 25% loose stools and more than 25% hard stools. IBS-U is when there are less than 25% loose stools and less than 25% hard stools. From these different subtypes, it has been reported IBS-D is the most common subtype, affecting 40% of the patient population.[13] From a survey of 1102 individuals, patients with IBS-D significantly experienced greater health impairments, when compared with a control group (n = 65,389; $p < 0.001$). Those with IBS-D also experienced more work absenteeism, as symptoms affected their inability to work compared to controls (5.1% vs 2.9%, respectively; $p = 0.004$).[7]

Clinical manifestations of IBS present predominately as abdominal pain, flatulence, and changes in gas or bowel movements. Gas is produced due to the accumulation of indigested food products, that become fermented, producing intestinal bacteria.[2] The subtypes of IBS have been distinguished along with these symptoms, as well as the Rome IV criteria, which further defines the type related to the symptoms associated with stool types and frequencies (Table 1).

Table 1: Irritable Bowel Syndrome Subtypes

	IBS-D	IBS-C	IBS-M	IBS-U
>25% Hard Stools		X	X	
<25% Hard Stools	X			X
>25% Loose Stools	X		X	
<25% Loose Stools		X		X

Etiology of Irritable Bowel Syndrome

Given that IBS is considered as a "functional disorder", it is typically diagnosed after ruling out all other causes, from the patient's symptoms. Diagnosis is typically from patient history, symptoms, and using Rome IV criteria.[2] Previously from Rome IV criteria, other diagnostic measures and criteria such as the Kruis score, Manning and Rome I-III criteria were used. In 1978, the Manning criteria was the first to be used globally for IBS diagnostic criteria, as IBS symptoms were identified and distinguished from GI diseases.

The Manning criteria consisted of population questionnaire studies, asking patients about their abdominal pain and bowel movement frequencies. In 1978, the Manning criteria were introduced, identifying symptoms believed to be more common in individuals with IBS than in those with organic diseases. A sample size of 32 patients with IBS and 33 patients with an organic disorder were evaluated by Manning and colleagues, where four main symptoms were associated with IBS: stools becoming looser at the onset of pain, heightened frequency of bowel movements following the onset of pain, alleviation of abdominal pain after a bowel movement, and abdominal distension.[14] Using 2 out of the 4 main symptoms yielded a sensitivity of 91% and a specificity of 70%. When employing 2

out of the 6 symptoms, the sensitivity ranged from 84% to 94%, with a specificity of 55%. Lastly, employing 3 or more out of the 6 symptoms resulted in a sensitivity ranging from 63% to 90% and a specificity ranging from 70% to 93%. Although the Manning criteria helped to differentiate the symptoms between IBS and organic diseases, it is no longer favorable as it is unable to differentiate between IBS-D and IBS-C.[14]

By 1984, the Kruis score was used to determine IBS diagnosis, as it utilized a patient's detailed history and basic laboratory test (complete blood count (CBC) and erythrocyte sedimentation rate (ESR)) to confirm a positive diagnosis for IBS.[14] The Rome I-III criteria was developed in 1988, that further specified IBS related symptoms. Rome I was studied and evaluated with 339 IBS patients. From this study, it was reported with an 85% sensitivity and 71% specificity. Rome I was revised to Rome II, as the criteria incorporated the term "discomfort" in the diagnostic. It was not until Rome III where IBS was categorized into different subtypes. The subtypes were determined by stool consistency rather than stool frequency. As research progressed, further understanding and investigation of IBS pathogenesis and etiologies allowed for the development of the most recent criteria used, Rome IV, was developed in 2016.[14]

The Rome IV criteria is an IBS diagnostic criterion that is defined as, "recurrent abdominal pain on average at least 1 day/week in the last 3 months, associated with two or more of the following criteria: (1) related to defecation, (2) associated with a change in the frequency of stool, (3) associated with a change in the form (appearance) of stool". Patients should fulfill these criteria for at least three months along with symptom onset at least six months prior to diagnosis.[14] The exact cause of IBS is unknown but potential etiological factors that contribute to the symptoms of IBS have been identified. The factors

contributing to IBS are multifactorial as it includes genetics, food sensitivities, altered microbial environment, elevated inflammatory response, small intestinal bacterial overgrowth (SIBO), enteric nervous system's sensitivity increased, and the abnormal release, transport, or recognition of serotonin. These factors can be categorized into three components: communication between body systems, GI tract function and environment, and GI symptoms.

Gastrointestinal tract function and environment includes altered motility, abnormal visceral reflexes, mucosal immune activation, and altered gut flora/abnormal colonic fermentation. Gastrointestinal symptoms, which are used to monitor IBS diagnosis, includes food sensitivity/food intolerance, excessive gas/GI gas accumulation, abnormal gas handling, or constipation/hard stools. Under the communication between body systems, factors are sex hormones, dysregulation of the central-enteric nervous system, or by the increased or abnormal communication between the GI tract and muscle. These potential etiological factors contribute to the symptoms of IBS, abdominal distention, and bloating. Celiac disease (CD) is an autoimmune disease, where the intake of gluten can cause damage to the intestinal walls. Irritable bowel syndrome has been associated with CD and should be screened alongside with lactose maldigestion.[2]

In patients with IBS-D symptoms, hypomorphic sucrase – isomaltase (SI) gene variation has been evaluated. The brush border of the small intestine utilizes the enzyme, sucrase – isomaltase, to metabolize sucrose. However, those with IBS-D have been found to be deficient of this enzyme, causing the inability of the small intestine to digest disaccharides from starch and sucrose. The indigestion of disaccharides accumulates, producing fermenting gas, causing diarrhea, abdominal pain, and discomfort.[13] Overall,

IBS pathophysiology is complex due to the various contributing factors. However, the major contributing factor is the abnormal motility experienced among IBS patients as it impacts symptoms such as abdominal pain and altered bowel habits.[2]

Pharmacologic Interventions for Irritable Bowel Syndrome

Common medical treatments for IBS consist of antidiarrheals, laxatives, antispasmodics, antidepressants, and peppermint oil. Patients diagnosed with IBS-D may be prescribed antidiarrheals, to reduce bowel motility and to improve stool form. Common antidiarrheal medications prescribed to patients are diphenoxylate atropine and loperamide. Loperamide has been the most studied and effective for the management of IBS-D. Loperamide has been approved by the Food and Drug Administration (FDA) to treat IBS. The mechanism of action of loperamide is through the opioid receptors, where peristalsis is inhibited on the circular and longitudinal muscles. Eluxadoline, another approved medication for IBS-D, has shown to effectively treat symptoms, when loperamide was not effective. Lacy et al. found 61.8% of IBS-D patients had inadequate symptom management with loperamide. Their study demonstrated the efficacy of eluxadoline (75 or 100 mg) treatment for IBS-D management for twelve weeks (P=0.001). However, adverse reactions include nausea and abdominal pain.[15] Peppermint oil can be taken to relieve abdominal pain and cramping. Another medication prescribed for IBS-D is alosetron, a 5-HT_3 receptor agonist. However, this medication is strictly prescribed in the United States. Antispasmodics, such as hyoscamine and dicyclo-mine are used to decrease GI motility and relieve muscle spasms. Pharmacologic interventions may be ideal for the treatment and management of IBS, however, medications may result in adverse side effects, such as

anhidrosis, blurred vision, confusion, urinary retention, and drowsiness. Most medications for IBS are also in trial phases, where further development and testing are needed. With increased interest for IBS management and treatment, non-pharmacologic interventions have become popular. These treatment options include cognitive-behavioral therapy, probiotics, and nutrition therapy. [2,16]

Medical Nutrition Therapy for Irritable Bowel Syndrome

Modifications in dietary habits and behavior has been considered as a first-line approach for symptom management. The foods and beverages that have been closely linked to IBS symptoms are the fermentable oligo-, di-, and monosaccharides and polyols (FODMAP). Registered dietitian nutritionists (RDN) assist patients with IBS with nutrition therapy, emphasizing regular meals, fiber, and fluid intake and to reduce the intake of fatty and spicy foods, alcohol, and caffeine. Nutrition therapy for IBS consists of a nutrition assessment, diagnosis, and intervention.[2,13]

Nutrition assessment for IBS evaluates the patient's eating habits, as symptoms of IBS may impact oral intake and food avoidances. Limiting food intakes can decrease not only nutrient intake but increase the risk for malnutrition. Nutrition assessment for people with IBS consists of client history, food-/nutrition related history, anthropometric measurements, nutrition-focused physical exam (NFPE), and biochemical data. The assessment of the client history and food-/nutrition related history allows for the RDN to understand their patient with IBS from a holistic view. The client history covers all their medical history/diagnoses, socioeconomic status (SES), medications, support systems, and their education. Obtaining a medication list from people with IBS-D is important, as certain

medications may cause diarrhea. Medications that have been associated with diarrhea symptoms are laxatives, stimulant laxatives, erythromycin, cisapride, antimicrobials, antineoplastics, NSAIDS, α-glucosidase inhibitors, lipase inhibitors, antineoplastic agents, acid- reducing agents, beta-blockers, prokinetic agents, glucose lowering agents, and sorbitol-containing medications. Mechanisms of diarrhea from these medications vary from osmotic diarrhea, secretory diarrhea, motility and microbial changes, and maldigestion/malabsorption of carbohydrates.[2]

The food related history covers GI related symptoms (e.g., problem swallowing, nausea, vomiting, diarrhea, and constipation), food preferences, allergies, use of alcohol, supplements, and minerals, previous nutrition education, and eating patterns. The anthropometric measurements consist of weight, height, weight history or recent changes, and BMI. The NFPE focuses on fat and muscle changes, as well as vital signs. With unintentional weight loss and gain, muscle and fat changes can be displayed drastically. The skin, neck, head/neck, and hair can also display changes, as nutrient deficiencies affect these areas. Biochemical data and medical tests will analyze lab values from visceral protein assessment, inflammation assessment, hematological assessment, and lipid assessment.[2]

Assessment of visceral protein status can be done by reviewing laboratory values of albumin, prealbumin, transferrin, and retinol-binding protein. Inflammation assessment includes inflammatory markers such as C-reactive protein, erythrocyte sedimentation rate, white blood cell (WBC) count, tumor necrosis factor alpha (TNF- α), interleukin 8 (IL-8), calprotectin, lactoferrin, polymorphonuclear neutrophil elastase. Hematological assessment includes hemoglobin, hematocrit, mean corpuscular volume (MCV), mean

corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), total iron-binding capacity (TIBC), and ferritin. Lipid assessments includes total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides. Other lab values that are utilized for lower GI-specific biochemical data, medical tests and procedures are vitamin B_{12}, vitamin C, vitamin D, vitamin K, vitamin A, vitamin E, biotin, niacin, riboflavin, vitamin B_6, and thiamin. These assessment data provide the guidance for the appropriate nutrition are for the IBS subtype.[2]

The nutrition diagnosis for a patient is determined by the RDN, based off the nutrition assessment. From the nutrition assessment, the RDN identifies the proper nutrition diagnosis by addressing the problem, etiology, signs, and symptoms. These factors are taken into consideration, which can then guide the RDN and the patient through the nutrition care process (NCP). Common IBS diagnoses are altered GI function, inadequate oral intake, food- and nutrition -related knowledge deficit, and disordered eating patterns.[2]

Although the RDN cannot officially diagnose a patient with IBS, the nutrition diagnosis allows for the proper nutrition intervention to be implemented. The nutrition intervention for IBS may present differently among patients. However, common interventions include nutrition education, eliminating or incorporating foods, symptom management, and optimizing nutrition intake to decrease gas production and abnormal bowel motility. Elimination diets are used to treat IBS, as its approach is to identify which foods may trigger the associated symptoms. Patients on an elimination diet will eliminate all possible food items in their diet that may be related to their symptoms, for at least 14 days. Once all possible food items that could cause IBS symptoms to have been eliminated,

they are then slowly incorporated back into the diet. If the patient can tolerate the food that was initially eliminated, it can then be added back into their regular diet. If symptoms occur from the eliminated food item, it will be considered as a trigger and is excluded from the diet. Patients who attempt elimination diets have a response rate of 15% to 71%, with those with IBS-D having the highest response rate.[2,17]

A non-pharmacologic treatment for IBS has been with the supplementation with probiotics. Probiotics are live microorganisms that can be consumed in the regular diet (e.g., fermented foods, yogurt, kefir) or as a supplement to maintain and improve the gut microbiota.[18] Supplements that are available for consumers contain lactobacillus GG and Bifidobacterium. The live organisms in probiotics may alleviate the bloating and gas production, especially in those with IBS.[2] Shekhar and Pradhan performed a randomized clinical trial (RCT) in 72 cases of IBS (diarrhea n = 31, constipation n = 23, and mixed n = 18). Participants were either given a probiotic supplement that contained live organisms including lactobacillus, Bifidobacterium, and streptococcus species or a placebo capsule. Their results indicated 29 out of 36 patients showed improvement, while 18 of the patients had significant relief. Among the different IBS cases, the IBS-D group was the predominant group to display relief and maximum benefit with the probiotic supplementation.[18]

The low-FODMAP diet has been a significant nutrition focused approach to improving IBS symptoms. Foods high in FODMAPs do not digest well, producing gas from the fermentation. Patients are guided through a three-step treatment process of a low-FODMAP diet by an RDN. Similarly, to the elimination diet, the first step would be to eliminate all foods in the patient's diet that contain FODMAP foods. On a low FODMAP diet, certain fruits, vegetables, and grains are eliminated. Meats and proteins are generally

considered low FODMAP. Incorporating an low FODMAP diet has shown to globally reduce IBS symptoms.[2,7]

Although several research studies have stated the efficacy of low-FODMAP diets for IBS patients[2], Paduano et al. investigated the effects of three different diets to assess the symptoms of IBS patients and their QOL.[19] The study proposed low-FODMAP, gluten-free, and balanced diets for all 42 enrolled patients to follow each for four weeks. The low-FODMAP diet had a reduction of all FODMAP containing foods, gluten free diet was strictly gluten free, and the balanced diet consisted of a Mediterranean based diet. At the end of the study period, the results from each diet demonstrated a reduction of IBS symptom severity ($p < 0.01$), bloating ($p < 0.01$) and abdominal pain ($p < 0.01$). Patients from the study also expressed the diets improved their QOL ($p < 0.05$). Following the FODMAP diet may have contributed to the reduction in symptom severity; however, patients from the study preferred the balanced diet (86%), compared to the FODMAP diet (3%) ($p < 0.01$). Patients preferred the balanced diet as they found the FODMAP diet to be restrictive and was still able to find relief in their symptoms through a balanced diet.[19] Cuff et al. demonstrated how larger doses of fructose should be re-introduced into the diet in those with non-constipated IBS.[20] With the FODMAP diet, patients do have difficulty assessing their tolerance to fructose. Patients who had non-constipated IBS ($n = 39$), completed a four-week trial, where they were randomized into three solution groups (100% fructose, 56% fructose/44% glucose, or 100% glucose) with four different doses (2.5, 5, 10, or 15 g) for three days. Patient tolerance to the solutions was reported to be severe if the score was >20 mm from the visual analog scale (VAS). From the study, the authors concluded that IBS patients without constipation can be reintroduced to fructose in higher

doses than 15 g, as tolerance should be monitored.[20] Algera et al. found the low FODMAP diet to reduce GI symptoms in adults with IBS.[21] IBS patients (n = 29) diagnosed using the Rome IV criteria followed the diet for two 7-day periods; one with either low (4g/day) or moderate (23 g/day) FODMAPs. A wash-out period (≥14 days) was used to separate the two periods. Results from the study indicated those with lower FODMAPs in their diet presented with reduced GI symptoms (i.e., symptom severity, abdominal pain intensity and frequency, bowel habits dissatisfaction, and daily life interference was $p < 0.05$).[22]

Although the FODMAP diet has been reported as a reputable nutrition intervention, other studies have found that patients do not adhere well to the low-FODMAP diet, as it decreases their diet quality and QOL. Staudacher et al. found the low-FODMAP diet to be rather restrictive for IBS patients. The study included 130 patients with IBS and evaluates their habitual nutrient intake, diet quality, and diversity on a 4-week low FODMAP diet. Participants were randomly assigned to either a low FODMAP diet (n=63) or a control diet (sham n=48, habitual diet n=19). An RDN was assigned to counsel participants on either a low-FODMAP diet or control diet. The main outcome measures were the habitual dietary intake at baseline (n=130) and after a 4-week intervention period. The outcomes were measured by using 7-day food records. From the results, fiber intake was low when habitual intake was examined in those with IBS. Target fiber intake was only achieved by 5% (n=6) from the individuals with IBS. There was no difference in nutrient intake from those on the low-FODMAP diet, when compared with controls. Those on the low-FODMAP diet displayed lower intake of starch (109 g/day) versus habitual control diet (128 g/day; P=0.030); but higher intake of vitamin B12 (6.1 ug/day), when compared to the habitual control diet (3.9 ug/day) and sham control diets (4.7 ug/day; P<0.01). However, those

counseled on a low-FODMAP diet had lower diet quality compared to the habitual control diet ($P<0.01$). Overall, the low FODMAP diet was not ideal with regard to increasing diet diversity and quality for IBS patients.[23] Patients have also found the low-FODMAP diet to be burdensome, as it impacts not only themselves, but as well as the people around them (friends and family). Implementing a low-FODMAP can be time consuming and costly, as patients would need to prepare their meals on their own.[7] Whigham et al. found the cost per patient on a low FODMAP diet was US $115, whereas the professional nutrition and dietary consultation sessions were US $238, per group pathway. Cost analysis was assessed per patient and group session, with six-week follow-ups in-between sessions.[24]

MNT for IBS-D Effectiveness

The low FODMAP diet has been shown to be a reasonable dietary approach for symptom management for people with IBS-D.[10] Nutrition intervention for diarrhea depends on the volume of gastrointestinal losses. Initial concerns for diarrhea are dehydration and electrolyte losses, as large-volume losses are associated with acid-base imbalances, leading to the risk for hyponatremia and hypokalemia. Metabolic acidosis can also occur with large volume loss from diarrhea, as excessive bicarbonate ions are loss through rapid stool output. Nutrition intervention for diarrhea typically focuses on restoring normal fluid and electrolyte balance. With diarrhea, foods that should be avoided to reduce motility are high-sugar beverages, simple carbohydrates (lactose, sucrose, or fructose), sugar alcohols (sorbitol, xylitol, mannitol, caffeine, and alcoholic beverages. For IBS-D, management with MNT is similar to the nutrition intervention for diarrhea, as it aligns with the low-FODMAP diet. A common clinical issue that has developed is chronic diarrhea, as

it affects 5% of the population every year. Those who present with chronic diarrhea are seen to have structural problems related to the GI and are diagnosed with inflammatory bowel disease (IBD) or celiac disease. However, majority of the patients do not fall under these disease states, as they do not fall under the diagnostic criteria. Patients who are not diagnosed with celiac disease are diagnosed with IBS-D.[25] The most recommended treatment for IBS-D is a low-FODMAP diet. The low-FODMAP diet for IBS-D patients have displayed improvement in symptoms. Chojnacki *et al.* found patients with IBS-D may find the treatment of a low-FODMAP diet along with lowering their tryptophan (TRP) intake to be helpful in symptom management.[26] Tryptophan is found in low-FODMAP diets, such as hard cheeses, dark meats, and some dairy products. The rational in reducing TRP in the low-FODMAP diet is to reduce serotonin synthesis and possible neurotoxic kyurenines to improve symptoms in IBS-D patients. In their study, IBS-D patients were divided between two groups of a low-FODMAP diet (group IIA) and a low-FODMAP with limited TRP (group IIB) intake for eight-weeks. Abdominal complaints were assessed using the Gastrointestinal Symptom Rating Scale (GSRA-IBS). Group IIB displayed significant improvements from the GSRA-IBS, compared to group IIA (GSRS score: 38.1% vs 49.8%). People with IBS-D may implement a low-FODMAP diet with reduced TRP intake for symptom management.[26] Goyal *et al.* compared a short and long-term low FODMAP diet in those with IBS-D to evaluate symptom improvements and QOL. Patients were randomized to either a strict 4-week low-FODMAP group or to a traditional diet group. After the initial 4-week period, the low-FODMAP group were then switched over to a “modified” FODMAP group, by reintroducing FODMAPs back into their diet. Patients from the strict to modified FODMAP group found significant improvements in their

symptoms and QOL.[27] Eswaran *et al.* compared the FODMAP diet to the modified National Institute for Health and Clinical Excellence (mNICE) dietary intervention for IBS-D patients to evaluate nutrient deficiencies with the FODMAP diet. The nutrition intervention included either a low-FODMAP or the mNICE diets for the participants to follow for four weeks at a time. Those following a mNICE diet were to consume smaller frequent meals, along with avoiding excess alcohol, caffeine, and trigger foods. The study found both diets limited caloric and carbohydrate intake, which may have affected the significant decrease in micronutrients. The low FODMAP group did not meet the Dietary Reference Intakes for thiamin and iron. The decreases in these micronutrients from the low-FODMAP diet disappeared, after adjusting for the patient's energy intake.[28]

Rej *et al.* has recommended a traditional dietary advice over the low FODMAP diet for IBS patients without constipation. A randomized controlled trial of three dietary groups were followed by patients for four weeks. The following groups patients were randomized into were a traditional dietary advice (TDA), low FODMAP diet, and gluten-free diet. The study evaluated the IBS symptom severity score (IBS-SSS) as their primary end point, as it was considered the clinical response. The secondary end point assessed the patient's QOL, stool quality, and baseline factors associated with clinical response. Among the diets, patients found the TDA a cost-effective diet and easier to follow and adhere to compared to the low FODMAP and gluten-free diet ($P < .01$). Patients found the TDA easier to incorporate into their day to day life, than the low FODMAP ($P = .02$) The authors concluded that the TDA should be recommended as a dietary therapy, as it is cost-efficient and convenient for patients.[29]

Martoni *et al.* found an improvement of symptoms and severity with probiotics for those with IBS-D. A randomized, double-blind, placebo-controlled study investigated the clinical efficacy of lactiplantibacillus plantarum (*L*. plantarum) for those with IBS-D. Participants received the supplementation for 8 weeks and were evaluated for the primary outcome for IBS severity and a secondary outcome for abdominal pain, QOL, stool and microbial profile, and perceived stress. Compared to the placebo, the intervention group found improvement in their IBS symptoms ($P < 0.001$). *L*. plantarum has demonstrated not only improvements in symptom severity in IBS-D patients but it is also well tolerated.[30]

Treatment with probiotics and a low-FODMAP has been examined in patients with IBS. Ankersen *et al.* aimed to determine if a low-FODMAP could reduce IBS symptoms as much as an intervention with probiotics. In a randomized cross over trial, patients either received probiotics or followed a low-FODMAP diet for four weeks. There were no significant differences observed between the low-FODMAP diet and probiotic supplementation. Further research is warranted to understand these outcomes.[31]

Serum-derived bovine immunoglobulin (SBI) is a nutritional supplementation that was evaluated in IBS-D patients for symptom management. In a randomized, double-blind, placebo-controlled study, thirty patients either received 5g/day of SBI ($n = 15$) or 10 g/day ($n = 15$). Symptoms were significantly improved in the treatment group compared to the placebo group from week 2 to week 6, ($p = 0.01$ and $p < 0.01$, respectively.[32] Olivia *et al.* found that supplementation of SBI improved IBS-D symptoms of flatulence ($p = 0.04$) and incomplete evacuation ($p < 0.05$) seen at week 6 for the group receiving SBI 5 g/day. Those who received 10 g/day of SBI found significant improvement from baseline, with multiple symptoms such as abdominal pain ($p < 0.01$), bloating ($p < 0.05$), flatulence ($p < 0.01$),

loose stools (p = 0.01), and urgency (p = 0.05).[33] SBI treatment and intervention has produced significant improvement in IBS-D patients, but is unfortunately not a widely used treatment as further investigation is needed.

Studies have found bile acid malabsorption occurs in 28.1% in IBS-D patients. A treatment with bile acid sequestrant therapy, cholestyramine, has been investigated as a therapeutic approach for IBS-D. A surrogate marker for bile acid malabsorption, serum 7 α-hydroxy-4-cholesten-3-one (7C4) levels, was shown to be elevated in IBS-D patient than those with IBS-C.[34,35] Camilleri *et al.* found those supplemented with colesevelam achieved improvement in stool consistency from baseline (using the Bristol stool chart, 4.8 to 4.4; p = 0.04). Bile acid sequestrant may be an option for IBS-D patients who have undergone a cholecystectomy, as those patients typically have concomitant bile acid malabsorption.[7]

Mediator Release Test

Pharmacological, non-pharmacological, and nutrition interventions have been studied for the treatment and management of IBS and IBS-D. However, study results vary, as each treatment can have side effects or reduce the patient's QOL, as the intervention may be restrictive. The intake of food and chemical food additives may impact the clinical manifestations of IBS. Patients have reported and expressed how certain foods may trigger their symptoms, but a standardized dietary approach does not account for personal customization of care.[36] An approach for personalized dietary modification for IBS treatment has been an emerging research field. The Lifestyle Eating and Performance (LEAP) program is a Leukocyte Activation Assay-MRT (LAA-MRT) based intervention

that utilizes inflammatory markers to produce inflammatory provoking foods and food chemicals from the mediator release test (MRT).[37] The clinical characteristics in food and food-chemical sensitivities are difficult to target, which makes it challenging to identify the exact trigger that could cause IBS in patients. Mediator Release Testing addresses this issue by identifying various food and food chemicals that could promote the inflammatory response from the body via a blood sample.

Mark Pasula from Oxford Biomedical Technologies invented and patented MRT. The methods behind MRT uses advanced flow cytometry and the ribbon impedance method. Inflammatory responses are measured from food and chemical reactions. MRT collects patient blood samples that are dispensed into individual test vials. Blood samples are then incubated and then reacted with test substances. The mechanism behind this process is the immune cells from the blood will react and release "mediators". Mediators that are typically released from this process are histamine, prostaglandins, serotonin, and cytokines. With food intolerance, these mediators are released, contributing to the symptoms of IBS. The test covers 123 most common foods and 27 most common additives/chemicals for adults. The blood test components comprise of the blood cells and plasma. The test follows the principle V1 + V2 = V3, where V3 is the total volume of blood, V1 is the total volume of cells and V2 is the total volume of plasma. If the blood test produces a reaction to a food or chemical additive, mediators are released. A reactive test will have the cells (V1) become smaller and the plasma (V2) will become bigger, but the total volume stays the same (V3). Different reactive levels are used to categorize the substances tested. If the blood test displays as reactive, it will be red, moderately reactive will be yellow, and non-reactive will be green. MRT allows to reduce trial and error from

other dietary approaches, as it measures and addresses the reactive food category individually for each patient. MRT studies have demonstrated symptom reductions with MRT, as patients are able to directly identify their trigger foods without a restrictive or a lengthy exclusion diet. The goal of MRT is to produce maximum outcomes in the shortest period of time. This method can expediate patient care and treatment, and potentially reducing financial burden.[38]

Zarini *et al*. investigated the clinical effectiveness of MRT with IBS patients. The majority of the participants were female (87.0%) and were followed by an RD throughout the study for 10.1 ± 6.4 weeks. The study used the Global Gastrointestinal Symptom Survey Score to assess the patient's symptoms post-intervention. A reduction in the survey score ($P < 0.001$) and an improvement in patient's QOL ($P < 0.001$) was shown. The authors concluded that MRT is an alternative treatment for IBS, as this personalized approach allows for better understanding of the relationship between IBS and food intake.[36]

Williams conducted a study with ten IBS-D patients with the LEAP MRT elimination diet. Patients were offered to attempt the LEAP MRT testing, if they did not have any improvement with standard therapies, such as increasing fiber intake and anti-spasmodic medications. Blood was collected to test for non-IgE mediated reactivity with an in vitro assay. From the test, 150 foods and food additives were tested for and were utilized to design the patient's personalized diet. Patient improvements were followed by using a Symptom Survey, which graded multiple GI and systemic symptoms. Highest possible point on the survey was 236. The GI section included 36 points. An average score of 56.9 was for the entire survey, while 19.1 points were from the GI portion. Overall,

patients saw improvement in not only their IBS-D symptoms, but as well as an increase in their QOL.[37]

Mediator Release Testing conducted by Oxford Biomedical Technologies currently tests for 176 foods and food chemicals that could potentially be releasing mediators from the body. Unlike the low-FODMAP diet, MRT presents patients with foods they can and cannot have from their test. Once food items are identified, this can help patients and their provider to build an eating plan, to reduce and manage their IBS symptoms.[38]

CHAPTER III

Methods

Study Design

This investigation entails a retrospective (observational) analysis of medical records, employing a design known for its cost-effectiveness, efficiency, and capacity to explore diverse outcomes within the designated population. The chosen study design aimed to assess the extent of symptom reduction and management in adults with IBS who received medical nutrition therapy. Specifically, either LEAP, FODMAP, or FODMAP then LEAP. Consequently, it is important to note that this study did not have the capability to establish causation and may not identify latent diseases that might have been present during data collection. Submission for approval of this study was made to the Institutional Review Board (IRB) at Georgia State University.

Setting

The research team avoided direct interaction with the patients. Information was extracted from the patients' electronic health records (EHR), and they were de-identified before they were entered into a dedicated Microsoft Excel spreadsheet. To enhance patient identity and privacy protection, each patient was assigned a unique identification number (ID). No physical source documents were preserved for this study, and both recruitment and follow-up periods were absent.

Participants

The target population for this study included a convenience sample of adults with IBS between the ages of 18 to 65 years old, who received nutrition care at Harmony Nutrition & Harmony Wellness Partners in Alpharetta, Georgia. Inclusion criteria included patients who were referred by a primary provider or gastroenterologist to Harmony Nutrition & Harmony Wellness Partners with a diagnosis of IBS or symptoms consistent with a diagnosis of IBS. In addition, patients must have completed an initial symptom survey at the time of the first visit at Harmony Nutrition and a follow-up symptom survey within four weeks from the initial visit. The Founder of Harmony Nutrition queried the EHR for adults who met the study inclusion criteria. The student-PI entered the patient's name on the study key and assigned a unique identification number. Subsequently, the Student-PI extracted de-identified variable data from the EHR. The student-PI entered the study data into a separate, de-identified data collection spreadsheet. All data abstraction was conducted by the Student PI. Only the Student PI had access to the study key and data spreadsheet during the data extraction process. Participants were stratified into two distinct groups: LEAP/MRT and low-FODMAP diet with a minimum of 20 participants total. Exclusion criteria included patients who fell outside the age range of 18 to 65, who were not referred by their primary provider or gastroenterologist for IBS or IBS symptoms or who have not completed a symptom survey at the initial visit and follow-up symptom survey within one month of the initial visit.

Variables

The outcome of this study examined symptom resolution with LEAP testing alone, FODMAP alone and FODMAP then LEAP. Existing data in the EHR for patients initially seen between the January 1, 2019 and December 31, 2023 were reviewed. The extracted de-identified data was entered onto a data collection spreadsheet. Extracted data included: demographic characteristics (sex, age and IBS subtype) anthropometrics (weight, height, body mass index), nutrition characteristics (food allergies/intolerances), and Initial Symptom Survey data (Appendix A). Each participant was assigned a unique identification number which appeared on the data collection spreadsheet. A separate, password protected study key contained a list of participant names and unique identification numbers. This was maintained by the Student-PI and stored on a secure Google drive at Harmony Nutrition. The study key was accessible only to the Student-PI. The initial and follow-up *Symptom Survey* form asks patients to rate the intensity and frequency of the symptoms they experience on a weekly basis. The symptom categories listed included constitutional, emotional/mental, neurological, skin, genitourinary, nasal/sinus, mouth/throat, lungs, eyes, ears, musculoskeletal, digestive, and weight management. Patients were to score the symptoms they experienced from 0 through 4, where 0 = *No Symptoms*, 1 = *Was MILD and OCCASIONAL (1 time per week or less)*, *2 = Was MILD and FREQUENT (2 or more times per week)*, 3 = *Was SEVERE and OCCASIONAL* (*1 time per week or less)*, 4 = *Was SEVERE and FREQUENT (2 or more times per week)*. Scores were independently computed for each specified category, followed by the calculation of an overall grand total of symptom points. Within the survey, patients provided information on their height, weight, additional symptoms, and the number of work or school days missed in the past seven days.

Data Management Plan and Statistical Analysis

All data utilized in this study was derived or computed from information present in the participants' EHR. Each participant received a unique study ID, visible on the Microsoft Excel data collection spreadsheet. The student principal investigator (PI) maintained a separate, password-protected list containing participant names and their corresponding study IDs, securely stored on the private server at Harmony Nutrition. Access to the study key was restricted solely to the Student PI. Accessing the study key or EHR data remotely was not possible, requiring all data extraction to take place on-site. After assigning a study ID, the Student PI manually extracted relevant data from the participant's EHR, entering it into a distinct, password-protected Microsoft Excel spreadsheet. The Student PI assumed responsibility for the selection, coding, and extraction of participant data. Following the conclusion of the study, both the study key and all extracted data will be permanently deleted.

Frequency analysis will be conducted to describe the characteristics of the IBS population by treatment category. Normality statistics will be conducted to determine if the continuous demographic, anthropometric and survey data are normally distributed or skewed. The T-test for normally distributed data or the Mann-Whitney U test for skewed data will be used to assess differences in reported symptoms by type of nutrition therapy (LEAP/MRT, low-FODMAP diet) groups at each time point. The paired t-test for normally distributed data or the Wilcoxon test for skewed data will be used to assess differences in reported symptoms over time within each nutrition treatment group. The statistical analysis was conducted using Statistical Program of Social Sciences (SPSS) version 27.0 database

(SPSS, Inc., an IBM Company, Chicago, IL.). A p-value of <0.05 was considered statistically significant.

CHAPTER IV

Results

Twenty-one adults diagnosed with IBS or with IBS symptoms were included in the study. Of these, 16 received LEAP/MRT therapy, while 5 were counseled on the low-FODMAP diet regimen. A description of the demographic characteristics of the study population is shown in Table 1. The majority of the population was female. There was no significant difference in the mean age of the participants by treatment group. Participants in the LEAP/MRT group experienced a significant reduction in weight and BMI between the initial and 1-month follow-up visits (75.5 ± 21.8 vs. 74.0 ± 21.6 and 27.3 ± 6.6 vs. 26.8 ± 6.3, respectively; $P < 0.05$). No changes in anthropometric values over time were observed in the Low-FODMAP group.

Table 2. Demographic Characteristics of the Irritable Bowel Syndrome Population by Treatment Status

Variable	**LEAP/MRT n=16**		**Low-FODMAP n=5**	
Sex				
Male	2 (12.5)		1 (20)	
Female	14 (87.5)		4 (80)	
Age at Initial Visit (years)*	42.8 ± 12.2		41.2 ± 10.5	
	Initial Visit	Follow-Up Visit	Initial Visit	Follow-Up Visit
Weight (kg)*	75.5 ± 21.8	74.0 ± 21.6**	85.1 ± 18.6	86.6 ± 19.9
Height (cm)*	165.3 ± 8.7	165.3 ± 8.7	169.0 ± 6.7	169.0 ± 6.7
BMI (kg/m^2)*	27.3 ± 6.6	26.8 ± 6.3**	29.7 ± 5.7	30.2 ± 6.1

Kg – kilograms, cm – centimeters, m – meters, BMI – body mass index

*mean ± standard deviation, **Significant difference from the initial visit ($P<0.05$)

Individual system and total symptom summary scores (median (Interquartile Range [IQR]) at the initial and follow-up visits by intervention type are shown in Tables 2 and 3. No statistically significant differences in median scores between treatment type were reported at the initial or follow-up visit.

Table 3. Symptom Summary Scores by Treatment Type at the Initial Visit

Symptom Category	LEAP/MRT (n=16)	Low-FODMAP (n=5)	P-Value
Constitutional	9.5 (7, 12)	10 (3.5, 15.5)	0.842
Emotional	11 (6.5, 14.8)	7 (3.5, 20.5)	0.842
Neurological	3 (2, 6.8)	0 (0, 0)	0.603
Skin	6.5 (2, 9.8)	6 (1, 6.5)	0.398
Genitourinary	1(0, 2)	2 (0, 2.5)	0.905
Nasal/Sinus	5 (2.3, 8)	3 (1.5, 12)	0.968
Mouth/Throat	2 (1, 4.8)	2 (0.5, 7)	0.905
Lungs	2 (0, 2.8)	0 (0,1)	0.208
Eyes	6(2.5, 8)	2.5 (2.5, 9.5)	0.719
Ears	1 (0, 3.5)	0 (0, 7.5)	0.905
Musculoskeletal	3 (1, 11)	8 (0, 13.5)	1.000
Cardiovascular	0 (0, 2)	0 (0, 4)	0.548
Digestive	14.5 (11, 23)	19 (3, 25.5)	0.842
Weight Management	5.5 (3.3, 6.8)	4 (2, 6)	0.398
TOTAL	86.5 (59, 110)	79 (35, 132)	1.000

Scores reported as Median (Interquartile Range, 25%, 75%)

0 = *No Symptoms*, 1 = *Was MILD and OCCASIONAL (1 time per week or less)*, *2 = Was MILD and FREQUENT (2 or more times per week)*, 3 = *Was SEVERE and OCCASIONAL* (*1 time per week or less)*, 4 = *Was SEVERE and FREQUENT (2 or more times per week)*

Table 4. Symptom Summary Scores by Treatment Type at the Follow-Up Visit

Symptom Category	LEAP/MRT (n=16)	Low-FODMAP (n=5)	P-Value
Constitutional	5.5 (2.5, 8.3)	4 (1.5, 13)	0.905
Emotional	7 (3.3, 11)	2 (0, 15)	0.445
Neurological	1.5 (1, 2)	3 (1, 6)	0.179
Skin	2 (1, 4)	2 (1, 4.5)	0.719
Genitourinary	0.5 (0, 2)	0 (0, 2)	0.495
Nasal/Sinus	3 (0.3, 6)	1 (0, 9.5)	0.905
Mouth/Throat	1.1 (0, 1.8)	2 (0.5, 3)	0.313
Lungs	0 (0, 1)	0 (0, 1)	0.354
Eyes	2 (0.3, 4)	2 (0, 11)	0.905
Ears	0 (0, 0)	0 (0, 4)	0.548
Musculoskeletal	3 (0, 8.5)	3 (0, 11.5)	1.000
Cardiovascular	0.5 (0, 0)	0 (0, 4)	0.905
Digestive	5.5 (2.5, 9.5)	6 (1, 11.5)	0.905
Weight Management	1.5 (0, 2.8)	3 (1, 7)	0.275
TOTAL	41 (21.8, 59.8)	22 (10, 102)	0.968

Scores reported as Median (Interquartile Range, 25%, 75%)

0 = *No Symptoms*, 1 = *Was MILD and OCCASIONAL (1 time per week or less)*, *2 = Was MILD and FREQUENT (2 or more times per week)*, 3 = *Was SEVERE and OCCASIONAL* (*1 time per week or less)*, 4 = *Was SEVERE and FREQUENT (2 or more times per week)*

Individual system and total symptom summary scores between the initial and follow-up visits by treatment type are shown in Tables 4 and 5. Statistically significant

differences were observed within the LEAP/MRT group in multiple individual categories (constitutional, emotional, neurological, skin, nasal/sinus, mouth/throat, lung, eyes, ears, digestive, weight management) and in the total symptom score (86.5 [IQR: 59, 110] vs. 41 [IQR: 22, 60], respectively; $P < 0.001$). Although the reported individual system symptoms were reduced at the follow-up visit for those in the Low-FODMAP group, the change in median scores over time was not statistically significant. However, the total median symptom score was significantly reduced at the follow-up visit (79 [IQR: 35, 132] vs. 22 [IQR: 10, 101.5], respectively; $P = 0.043$).

Table 5. Symptom Summary Scores at the Initial and Follow-Up Visits:

LEAP/MRT Group (n=16)

Symptom Category	Initial Visit	Follow-Up Visit	P-Value
Constitutional	9.5 (7, 12)	5.5 (2.5, 8.3)	**0.001**
Emotional	11 (6.5, 14.8)	2 (1, 2.8)	**0.002**
Neurological	3 (2, 6.8)	1.5 (1, 2)	**0.008**
Skin	6.5 (2, 9.8)	2 (1, 4)	**0.002**
Genitourinary	1 (1,2)	0 (0, 2)	0.359
Nasal/Sinus	5 (2.3, 8)	3 (0.25, 6)	**0.039**
Mouth/Throat	2 (1, 4.8)	1 (0, 1.8)	**0.01**
Lungs	2 (0, 3.8)	0 (0, 1.8)	**0.018**
Eyes	6 (2.5, 8)	2 (0.25, 4)	**0.007**
Ears	1 (0, 3.5)	0.5 (0, 2)	**0.036**
Musculoskeletal	3.5 (1, 11)	3 (0, 8.5)	0.113
Cardiovascular	0 (0, 2)	0 (0, 0)	0.055
Digestive	14.5 (11, 23)	5.5 (2.5, 9.5)	**<0.001**
Weight Management	5.5 (3.3, 6.8)	1.5 (0, 2.8)	**0.001**
TOTAL	86.5 (59, 110)	41 (22, 60)	**<0.001**

Scores reported as Median (Interquartile Range, 25%, 75%)

0 = *No Symptoms*, 1 = *Was MILD and OCCASIONAL (1 time per week or less)*, *2 = Was MILD and FREQUENT (2 or more times per week)*, 3 = *Was SEVERE and OCCASIONAL* (*1 time per week or less)*, 4 = *Was SEVERE and FREQUENT (2 or more times per week)*

Table 6. Symptom Summary Scores at the Initial and Follow-Up Visits: Low-FODMAP Group (n=5)

Symptom Category	Initial Visit	Follow-Up Visit	P-Value
Constitutional	10 (3.5, 15.5)	4 (1.5, 13)	0.066
Emotional	7 (3.5, 20.5)	2 (0, 15)	0.066
Neurological	5 (2, 9)	3 (1, 6)	0.141
Skin	6 (1, 6.5)	2 (1, 4.5)	0.109
Genitourinary	2 (0, 2.5)	0 (0,2)	0.276
Nasal/Sinus	3 (1.5, 12)	1 (0, 9.5)	0.144
Mouth/Throat	2 (0.5, 7)	2 (0.5, 3)	0.180
Lungs	0 (0, 1)	0 (0, 0.5)	0.317
Eyes	5 (2.5, 9.5)	2 (0, 11)	0.5
Ears	0 (0, 7.5)	0 (0, 4)	0.18
Musculoskeletal	8 (0, 13.5)	3 (0, 11.5)	0.18
Cardiovascular	0 (0, 4)	0 (0, 4)	1.000
Digestive	19 (3, 25.5)	6 (1, 11.5)	0.078
Weight Management	4 (2, 6)	3 (1, 7)	0.713
TOTAL	79 (35, 132)	22 (10, 101.5)	**0.043**

Scores reported as Median (Interquartile Range, 25%, 75%)

0 = *No Symptoms*, 1 = *Was MILD and OCCASIONAL (1 time per week or less)*, *2 = Was MILD and FREQUENT (2 or more times per week)*, 3 = *Was SEVERE and OCCASIONAL* (*1 time per week or less)*, 4 = *Was SEVERE and FREQUENT (2 or more times per week)*

CHAPTER V

Discussion and Conclusion

This retrospective study aimed to gain insights into the comparative effectiveness of the LEAP/MRT, given its status as a relatively novel intervention for IBS treatment, vs. the traditional low-FODMAP diet. The analysis focused on evaluating the efficacy of these interventions in reduction IBS symptoms, which should ultimately improve the participants' quality of life. We identified statistically significant reduction in the symptom summary scores between the initial and follow-up visits in multiple individual categories within the LEAP/MRT group. No significant differences in symptom severity were observed between treatment types at the initial or follow-up visit times. Although the symptom summary scores at the initial and follow-up visits for the low-FODMAP group did not show significant reduction within individual categories, the total symptom score was significantly reduced at follow-up. Additionally, participants in the LEAP/MRT group experienced a reduction in weight and BMI within the month between visits.

The low-FODMAP diet has been shown to be effective in significantly reducing GI symptoms, including abdominal pain, bloating, and stool frequency.[22] The differences between the results from this study and those from other studies could be attributed to diet compliance. Studies that enroll participants on the low-FODMAP diet provide protocol guidelines. In contrast, participants in this study were not required to adhere to a strict protocol, which may have contributed to the non-significant findings in the individual symptom categories. Paduano et al. reported significant reduction in GI symptoms.

However, the authors stated that compliance was not verified.[19] Chojnacki et al. found significant responses to the low-FODMAP diet when it involved reducing foods high in tryptophan, such as hard cheeses, dark meats, and certain dairy products. Since food recalls and diaries were not assessed in this study, it cannot be verified whether the patients following the low-FODMAP diet also reduced these specific food items. This omission might have influenced the severity and frequency of their symptoms.[26] Staudacher et al. reported that a 4-week low-FODMAP intervention did not impact nutrient intake or diet diversity, but diet quality was decreased in the low-FODMAP group compared to controls ($P<0.01$). Those on the low-FODMAP diet consumed lower intake of starch (109 g/day) compared to the control group (129 g/day). The authors stated that meeting dietary guidelines is difficult even with guidance from a specialist Dietitian. Despite this, participants adhered to the dietary intervention. In this study, the Dietitians closely monitored the participants' dietary intake and provided detailed instructions on how to record their diet recalls.[23] Overall adherence and compliance to a dietary intervention can be significantly improved with detailed instructions and frequent follow-ups, as these measures provide continuous guidance and support throughout treatment.

The results from the LEAP/MRT group in our population align with the existing literature, which has demonstrated a reduction in symptoms. This observation underscores the potential efficacy of the LEAP/MRT intervention in alleviating symptoms associated with IBS. Particularly noteworthy is the consistent reduction in symptoms across most categories, indicating the intervention's robust and widespread impact. The removal of the dietary triggers identified by the LEAP/MRT interventions from previous studies have shown symptom survey score reductions. Zarini et al. reported a significant symptom

survey score reduction ($P < 0.001$) after 10.1 ± 6.4 weeks.[36] Williams conducted a study with patients who had IBS-D and reported notable improvement in IBS-D related symptoms, fewer symptomatic symptoms, and an overall boost in their sense of well-being.[37] These results support use of LEAP/MRT and suggests its potential applicability in routine clinical practice.

Despite the valuable insights gained from this research, there are several limitations that should be noted. The retrospective nature of the analysis may have introduced selection bias, as the data were collected from past records rather than through a controlled, prospective study. The sample size was relatively small, particularly in the low-FODMAP group. This may have limited the generalizability of the findings to a broader population. The study relied on self-reported measures, which can be subjected to inaccuracies or biases such as recall bias. The study did not account for potential confounding variables such as dietary habits, lifestyle factors, or other concurrent treatments that the participants might have been using. The confounding variables could have influenced the overall outcomes.

While the LEAP/MRT intervention is relatively new and promising, the long-term effects and sustainability of its benefits remain uncertain due to the short duration of follow-up. The limited follow-up period in our study and previous studies makes it challenging to ascertain whether the improvements observed are enduring or if they diminished over time. The novelty of the intervention means that there is limited existing research to corroborate our findings. Future research with larger, more diverse populations is essential to enhance the generalizability of the results. Prospective designs that track participants over extended periods will provide more robust data on the long-term efficacy

and potential side effects of the LEAP/MRT intervention. Assessing the impact of potential confounding factors, including lifestyle changes, dietary habits, and concurrent treatments, will provide a more comprehensive understanding of how these variables influence the intervention's effectiveness. Overall, addressing these limitations through rigorous and expansive future research will be crucial in confirming the preliminary findings of this study. Established LEAP/MRT interventions can provide a reliable and effective treatment option for IBS.

The LEAP/MRT approach could offer a personalized treatment option for people with IBS. The intervention addresses individual dietary sensitivities, while improving patient outcomes. The encouraging results from this study pave the way for future research to validate these findings through more extensive, randomized, controlled trials. By exploring the mechanisms underlying symptom improvement and identifying patient populations that may benefit the most, subsequent studies can further establish the clinical relevance and long-term benefits of the LEAP/MRT intervention.

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