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EFFECT OF HIGH- AND LOW-FODMAP DIET INSTRUCTION ON FODMAP INTAKE AND DIETARY QUALITY IN HEALTHY YOUNG ADULTS

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EFFECT OF HIGH- AND LOW-FODMAP DIET INSTRUCTION ON FODMAP

INTAKE AND DIETARY QUALITY IN HEALTHY YOUNG ADULTS

BY

JAMES O'TOOLE

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2014

MASTER OF SCIENCE THESIS

OF

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UNIVERSITY OF RHODE ISLAND
2014

ABSTRACT

Objective: Irritable Bowel Syndrome (IBS) is the most commonly diagnosed Gastrointestinal (GI) condition in the United States affecting 30 million (10%) people. Symptoms include abdominal pain, bloating, distension, excessive wind and altered bowel habits when anatomical abnormalities and inflammation have been excluded. A low-FODMAP diet is now considered as an effective strategy for managing symptoms of IBS in Australia, with interest expanding across the world. Several limitations of a low-FODMAP diet pertaining to dietary quality and health benefits have been suggested. Malabsorbed FODMAPs provide multiple benefits which include a natural laxative effect due to their osmotic effects, a prebiotic effect with beneficial fermentation by-products and production of a low glycemic response compared to other carbohydrates. Additionally, Dietary adherence is crucial to the success of a low-FODMAP diet, however most people do not find the diet easy to incorporate into their life. Not one study has looked exclusively at healthy adults or looked at changes in FODMAP intake and diet quality as compared to established guidelines. A study is needed looking at dietary quality of low- vs. high-FODMAP diets and should consider how adherence and other factors that may influence efficacy of the diet.

Design: This study used a single-blinded crossover design. Subjects (n=16) were instructed about following a low-FODMAP and a high-FODMAP diet for three days each, presented in a random order and separated by an 11-day wash out period. The study was entitled "The Carb Study" and diets labeled "diet 1" and "diet 2" without reference to FODMAP. No food was provided. Dietary instruction was provided for each diet along

with a dietary booklet. Dietary assessment consisted of four 24-hour recalls using NDS-R. Recalls assessed the day prior to each intervention period (2 baselines) and assessed day 3 of each intervention period (2 interventions). FODMAP intake was estimated based on the sum of fructose, lactose and polyol intake and dietary quality was calculated based on the Healthy Eating Index 2010 (HEI-2010).

Setting: Free living subjects recruited from a northeastern university.

Subjects: Participants were healthy adults without gastrointestinal disorders (n=16, 63% female, 20.47±1.77 years).

Results: There was no effect of diet order. There was a non-significant trend for a between treatment difference in FODMAP intake ($F_{(1,14df)}$=4.27, p=.058) and a significant difference between groups in HEI-2010 total score ($F_{(1,14df)}$=10.45, p=.001). Within the low-FODMAP treatment, FODMAP intake decreased from 36.30±22.62 grams to 19.29±15.79 grams (-t=2.84, p=.01) and HEI-2010 scores increased from 53.60±17.16 to 63.09±17.23 (t=2.20, p=.04); Energy intake also significantly decreased from 2259±1325 kcals to 1510±795 kcals (-t=2.68, p=.017). Within the high-FODMAP treatment, there was no change in FODMAP intake (t=.35, p=.731) but HEI-2010 scores decreased from 60.83±12.76 to 52.04±11.27 (-t=2.45, p=.027); There was no difference in energy intake (1993±962 to 2251± 864, -t=1.57, p=.14)

Conclusions: This study suggests that reducing FODMAP is feasible in healthy, free-living young adults and that this reduction is associated with an increase in dietary quality. However, the high-FODMAP intervention in this study was not effective in increasing FODMAP intake. Future research with larger samples is needed to develop interventions for increasing healthy FODMAP intake in young adults. In addition, future

research is needed to assess long-term effects of these dietary modifications in healthy individuals.

ACKNOWLEDGEMENTS

I would like to first thank my parents. This would not have gotten done if it wasn't for your support. I would like to dedicate this thesis to you. I would like to thank Kathleen Melanson for all her help and guidance these past few years. I would also like to thank Linda, Dr. Greene, Dr. Redding, Dr. Nash and all of my friends for their help and support.

PREFACE

This thesis was written to comply with the University of Rhode Island Graduate School Manuscript Thesis Format. This thesis contains one manuscript entitled "Effect of High- and low-FODMAP Diet Instruction on FODMAP Intake and Dietary Quality in Healthy Young Adults". This manuscript has been written in a form suitable for publication in *The Journal of the Academy of Nutrition and Dietetics*.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

MANUSCRIPT INTRODUCTION PAGE

MANUSCRIPT- 1

To be submitted to The Journal of Nutrition and Dietetics

Effect of High- and Low-FODMAP Diet Instruction on FODMAP Intake and Dietary Quality in Healthy Young Adults

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Effect of High- and Low-FODMAP Diet Instruction on FODMAP Intake and Dietary Quality in Healthy Young Adults

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ABSTRACT

Objective: The purpose of this study was to investigate the effects of dietary instruction for low- and high-FODMAP diets on FODMAP intake and dietary quality in healthy young adults.

Design: This study had a single-blinded crossover design. Subjects (n=16) were instructed about following a low-FODMAP and a high-FODMAP diet for three days each, presented in a random order and separated by an 11-day wash out period. The study was entitled "The Carb Study" and diets were labeled "diet 1" and "diet 2" without reference to FODMAP. No food was provided. Dietary instruction was provided for each diet along with a dietary booklet. Dietary assessment consisted of four 24-hour recalls reflecting the day prior to each intervention period (2 baselines) and assessed day 3 of each intervention period (2 interventions). FODMAP intake was estimated based on the sum of fructose, lactose and polyol intake and dietary quality was calculated based on the Healthy Eating Index-2010 (HEI-2010).

Setting: Free living subjects were recruited from a northeastern university.

Subjects: Participants were healthy young adults without gastrointestinal disorders (n=16, 63% female, 20.47±1.77 years).

Results: There was no effect of diet order. There was a non-significant trend for a between treatment difference in FODMAP intake ($F_{(1,15df)}$=4.27, p=.06), but a significant difference between treatment groups in HEI-2010 total score ($F_{(1,14df)}$=10.45, p=.001). Within the low-FODMAP treatment, FODMAP intake decreased from 36.30±22.62 grams to 19.29±15.79 grams (-t=2.84, p=.01) and HEI-2010 scores increased from 53.60±17.16 to 63.09±17.23 (t=2.20, p=.04); Energy intake also significantly decreased from 2259±1325 kcals to 1510±795 kcals (-t=2.68, p=.017). Within the high-FODMAP treatment, there was no change in FODMAP intake (t=.35, p=.73) but HEI-2010 scores decreased from 60.83±12.76 to 52.04±11.27 (-t=2.45, p=.027); There was no difference in energy intake (1993±962 to 2251± 864, -t=1.57, p=.14)

Conclusions: This study suggests that reducing FODMAP is feasible in healthy, free-living young adults and that this reduction is associated with an increase in dietary quality. Long term studies are needed to confirm these results. The high-FODMAP intervention used in this study was not effective in increasing FODMAP intake. Future research with larger, more diverse samples is needed to develop interventions for increasing healthful FODMAP intake in young adults. In addition, future research is needed to assess long-term effects of these dietary modifications in healthy individuals.

1. <u>INTRODUCTION</u>

In 2005 at Monach University in Australia, the term FODMAP (fermentable oligo-, di-, mono-saccharides and polyols) was coined to identify a group of poorly absorbed short-chain carbohydrates (CHO) that when ingested in excess, or when consumed by individuals with bowel disorders, can induce the gastrointestinal (GI) symptoms of abdominal pain, bloating, distension, flatulence and diarrhea [12]. These CHO are widespread in the diet [1] and include the oligosaccharides fructooliogosaccharides (fructans or FOS) and galactooligosaccharides (GOS), the disaccharide lactose, the monosaccharide fructose and all sugar alcohols (polyols) [2]. FODMAPs have three common functional properties. They are 1) poorly absorbed in the proximal small intestine, allowing substrate to reach the distal small intestine and proximal colon 2) small and osmotically-active, increasing the liquidity of luminal content due to osmosis and 3) rapidly fermented by gut microbiota, increasing the amount of gas in the colon [1]. These characteristics combine to increase luminal distension, the physiological basis for the genesis of many GI symptoms [1].

It is hypothesized that GI symptoms are created primarily by luminal distention[3] creased by fermentation and osmosis [4]. Studies have concluded that high-FODMAP diets induce GI symptoms [5,6], and low-FODMAP diets relieve GI symptoms associated with functional GI disorders [7-10] with GI symptoms returning when FODMAPs are reintroduced into the diet [11]. Overall GI symptoms have been seen in up to 86% of Irritable Bowel Syndrome (IBS) patients [7]. Accordingly, a low-FODMAP diet has been recommended for managing GI symptoms for IBS patients[12]. Applications are expanding

to enteral feeding formulas [13], a low-FODMAP diet for patients with non-celiac gluten sensitivity[14] and the treatment of infantile colic [15].

A first consideration for FODMAP diets is the overall quality and adequacy of the diet, as well as associated health benefits. FODMAPs are CHO or related polyols found in fruits, vegetables, legumes, wheat and other grain products as well as milk and dairy products. A FODMAP restricted diet limits the available options in these nutrient-dense food groups. Additionally, in all populations FODMAPs are malabsorbed [16-20]. Malabsorbed CHO can provide a prebiotic effect due to fermentation by-products [12] and CHO products high in FODMAPs tend to generate a lower glycemic response compared to CHO products lower in FODMAPs [21]. A low-FODMAP diet may adversely affect gut microflora and compromise fiber intake [12] and dietitians instructing patients on low-FODMAP diet should provide options for high-fiber alternative fruits, vegetables and grains as well as adequate sources of calcium and vitamin D [4,16,22]. There is limited evidence comparing the effect of low- vs. high-FODMAP diets on fiber or any other nutrient intake [12]. One retrospective study found limited differences in macronutrient intake comparing current diets of free-living subjects who had received low-FODMAP dietary advice two years previously to healthy controls [23].

Another consideration for FODMAP diets is dietary adherence. Adherence appears to be crucial to the success of a low-FODMAP diet with correlations between adherence and symptom improvement reported [8]. Most people do not find the diet easy to incorporate into their life [8,10], although controlled studies with IBS patients have shown high adherence rates both when all foods are provided [11] and when provided with dietary advice [8]. Potential barriers to adherence include buying the appropriate food[10],

implementing the diet[8,10], following the diet[8] and taste [8,10]. There is limited research available about following a high-FODMAP diet, but individuals are likely to face barriers given the presence of adverse GI symptoms[5,6].

The primary aim of this study was to investigate the effect of dietary instruction on implementing low- and high-FODMAP diets on FODMAP intake as well as on dietary quality in healthy, free living, young adults. Secondary aims were to investigate changes in mood, GI symptoms and subjects' opinions regarding the diet, as potential variables that may impact dietary adherence.

2. METHODS

2.1 Subjects

Twenty healthy, young adults, free from GI disorders were enrolled in this study. Four subjects withdrew from this study, one for medical conditions unrelated to the study and three failed to compete any assessments beyond baseline. Thus 16 subjects completed the study and were considered the study sample. Exclusionary GI disorders included celiac disease, IBS, lactose or gluten intolerance, diverticular disease, colitis such as Crohn's disease or ulcerative colitis and stomach ulcers. Additional exclusion criteria included currently following a weight loss diet, food allergies, smoking, pregnancy or lactation, diabetes, adrenal disease, kidney or bladder problems, a thyroid disease or currently taking any appetite suppressant medication. All subjects were recruited via classroom announcements at the University of Rhode Island or emails sent to adults who were candidates/participants in previous, nutrition-related studies. Subjects received a $80 stipend for completing the study. The study was approved by the

Institutional Review Board of the University of Rhode Island and subjects provided written informed consent prior to participating.

2.2 Study Design

The study was a randomized, single-blinded, cross-over study that compared two diet-interventions in a free-living setting; instruction on low- vs. high-FODMAP diet. In order to ensure that the diets were single-blinded, the study was entitled "The Carb Study" and the two interventions were labeled "Diet 1" and "Diet 2" representing the low-FODMAP diet and high-FODMAP diet respectively. No food was provided. Each intervention had a corresponding diet instruction booklet that was developed specifically for this project with foods identified as either high- or low in FODMAPs at the time of the study[1,5,7,23-25]. Subjects were provided with 15-minute instructions about each dietary treatment and asked to follow this booklet to the best of their ability for each three day intervention period.

An initial screening was conducted to verify potential participants met inclusion criteria. Body fat percentage was assessed using the BOD POD Body Composition System (Life Measurement Instruments, Concord, Calif., USA). Subjects where then randomized to start with either the low-FODMAP diet (order 1) or the high-FODMAP diet (order 2). Each dietary period was followed by an eleven day wash out period where subjects consumed their normal diet. Following the wash out period, subjects completed the remaining dietary intervention. Each intervention lasted three days: Tuesday, Wednesday, and Thursday.

Four 24 hour recalls were conducted with each subject. At the start of each dietary intervention period on Tuesday, each 24-hour recall measured dietary intake on Monday

(baseline). After completion of each intervention period on Friday, each recall measured intake on Thursday (intervention). FODMAP intake, Healthy Eating Index-2010 (HEI-2010) scores, and intake of other selected nutrients were obtained from these 24 hour recalls. Subjects also completed questionnaires on Fridays of each intervention period assessing mood and GI symptoms. An additional "opinion regarding the diet" questionnaire was filled out by a convenience sample of subjects at the end of each intervention period.

2.3 Dietary Instructions and Diet Booklet

At the baseline visit for each diet, subjects met with a trained research assistant who provided each subject with a 16 page diet instruction booklet. The booklets contained a detailed list of recommended and restricted foods corresponding to either the low-FODMAP diet or the high-FODMAP diet. A brief, 15 minute diet instruction session was provided, which included identifying encouraged and discouraged foods, tips, and emphasized the importance of adhering to the diet for research purposes.

2.4 NDSR 24 Hour Food Recall

As described above, four in-person 24 hour recalls were conducted by trained research assistants. Recalls were conducted using the Nutrition Data System for Research (NDS-R) software version 12 developed by the Nutrition Coordinating Center (NCC), University of Minnesota, Minneapolis. NDS-R utilizes a multiple pass method described in full elsewhere [26]. Briefly, pass one included obtaining a quick list of foods consumed in the past 24 hours. In pass two, participants were asked to produce details regarding foods on their quick list including portion sizes and amounts eaten. In pass three the list was recited and participants are asked if any information was forgotten. Food amount

booklets distributed by the NCC as well as food models were available during food recalls in order to assure accurate portion sizes.

Foods that were not in the NDS-R database were listed as "missing foods" and resolved after the interview was completed. Resolution of a missing food required finding an NDS-R substitute (similar food or a generic version of a food) in the database and matching that substitute for CHO, protein, fat and kcal. Matching was defined as within 1-3 grams for each macronutrient and within 10 kcals for energy. For some foods, the potential FODMAP content was considered too variable for application of the normal missing food substitution protocol (for example ice cream brands and artificially sweetened beverages). These foods were sent to the NCC, who provided an accurate nutrient breakdown for those items.

2.5 FODMAP intake

NDS-R output files were used to sum total intake (g) of fructose, lactose and the polyols (erythritol, inositol, isomalt, lactitol, maltitol, mannitol, pinitol, sorbitol and xylitol). These items were used to estimate FODMAP intake. Because NCC does not calculate consumption of galacto-oligosaccharides or fructo-oligosaccharides (GOS or FOS), estimated FODMAP intake underestimates total FODMAP intake and FODMAP in this study was defined based on the available FODMAP items. Although oligosaccharide intake is difficult to estimate, intake of FOS may vary from 3-13 g/day in western countries [27].

2.6 Dietary Quality: Healthy Eating Index 2010

From NDS-R output files, The Healthy Eating Index 2010 (HEI-2010) [28] was calculated. The Healthy Eating Index is a measure of dietary quality assessing how well

an individual's diet compares with Dietary Guidelines for Americans 2010 (DGA) [29]. The total HEI score ranges from 0 (low) to 100 (high). The total score is based on eight "adequacy" components: total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins as well as four "moderation" components: fatty acids, refined grains, sodium, and empty calories [29]. Intake is in energy adjusted per 1,000 kcal.

Calculation of the HEI-2010 for this study was based on a protocol developed by the NCC based on methods described in a previous study [30]. The calculations were made using Microsoft Excel, 2007 and performed twice to check accuracy.

2.7 Assessment of mood state and gastrointestinal symptoms

All subjects completed two questionnaires regarding their mood state and GI symptoms prior to bed on the final day of each intervention. The mood questionnaire used 10-cm VAS response scale anchored at each end "0=Very Little" and "10=Very Much" that had been used in a previous study [31].The 10 items included: how alert do you feel, how sad do you feel, how tense do you feel, how much of an effort is it to do anything, how happy do you feel, how weary do you feel, how calm do you feel, and how sleepy do you feel. The symptoms questionnaire was a 3-item scale with a similar VAS response scale based on scales used with IBS patients. Items included: how severe is your abdominal pain, how severe is your abdominal distention/tightness, and how satisfied are you with your bowel movements.

2.8 Opinion regarding the diet

Following each intervention 24 hour recall, a convenience sample completed a 4-item evaluation of the diet using with a 10-cm VAS response scale from previous

FODMAP-related studies [8,10,11]. Items included: how easy/difficult had it been to implement the diet, how easy/difficult had it been to adhere to the diet, how easy/difficult was it to obtain the appropriate food, how would you rank the overall taste.

2.9 Statistics

Statistical analyses were performed using SPSS, version 22.0 (IBM Corporation, Summers, NY, USA). All variables met criteria for normality. Baseline comparisons between subjects assigned to the two orders were conducted using t-tests and χ^2 tests. Primary outcomes (grams of FODMAP and HEI-2010 scores) were assessed using separate 2 (treatment) x 2 (time) x 2 (order) mixed factorial ANOVA followed by within-treatment paired t-tests (baseline and intervention). The η^2 was calculated to estimate effect size using Cohen's categories of small (.10), medium (.25) and large (.40) [32]. Energy intake (kcal/day) was assessed using similar analyses. All other inferential analyses of dietary components were performed using a 2 x2 repeated measures ANOVA where the independent variables were treatment (low- vs. high-FODMAP) and time (baseline vs. intervention). Paired t-tests compared mood, symptoms and compliance factors between treatments and Pearsons bivariate correlations explored relationships between variables. Median scores were reported for diet opinion. $P < .05$ was considered statistically significant.

3. RESULTS

There were no differences in demographic variables between subjects assigned to the two orders. Mean age of the 16 subjects was 20.6 years (range 18-23) and 10 were female. Further information is presented in Table 1.

Values for FODMAP intake and all dietary data including both the total and subscales of the HEI-2010 did not differ at baseline between the two orders.

There were non-significant trends for grams of FODMAP per day for time ($F_{(1,14df)}$=4.38, p=.06, η^2=.24) and time*treatment($F_{(1,14df)}$= 4.27, p=.06 η^2=.23), but no main effect of order ($F_{(1,14df)}$=.17, p=.68, = η^2.01) or time*treatment*order interaction ($F_{(1,14df)}$=.33, p=.57, = η^2.02). Within treatments, FODMAP intake decreased in the low-FODMAP treatment (36.30±22.62 grams to 19.29±15.79 grams, t=2.84, p=.01) but there was no change in the high-FODMAP treatment (35.93±18.08 grams to 34.04±13.72 grams, t=.35, p=.73) (Figure 1).

HEI-2010 scores are listed in Table 2. For total HEI-2010, there was no main effect of order ($F_{(1,14df)}$=.16, p=.70, = η^2.01), and no treatment*time*order interaction $F_{(1,14df)}$=.32, p=.58, η^2=.02. There was no main effect for time ($F_{(1,14df)}$=.02, p=.90, η^2=.00), there was a treatment*time interaction ($F_{(1,14df)}$=10.45, p=.006, η^2=.43) with a large effect size[32]. Within treatments, total HEI-2010 scores increased during the low-FODMAP treatment and decreased during the high-FODMAP treatment. When comparing values during the treatment periods, there was a higher total HEI-2010 score in the low-FODMAP treatment compared to the high-FODMAP treatment (63.09±17.23 vs. 52.04±11.27; t=2.40, p=.03).

HEI-2010 component scores are presented in Table 2. No time*treatment interactions were found for any component scores. There was a main effect of time for the total protein score, ($F_{(1,15df)}$=4.66, p=.048, η^2=.24) and sodium score ($F_{(1,15df)}$= 4.92, p=.042, η^2=.25).Within treatments, there was an increase in protein score during the low-FODMAP treatment but no change in the high-FODMAP treatment and a decrease in

sodium score indicating an increase in sodium intake in the high-FODMAP treatment with no change in the low-FODMAP treatment. Because HEI-2010 component scores are energy adjusted and there was a change in energy intake (see next paragraph), non-energy adjusted component scores were calculated. There were time*treatment interactions for total refined grains ($F_{(1, 15df)}$= 10.56, p=.005, η^2=.41) and total empty calories $(F_{(1,15df)}$= 8.02, p=.013, = η^2=.35).Within treatment analyses found a decrease in refined grains during the low-FODMAP treatment (6.47±4.65 oz to 2.79±3.46 oz, t=3.63, p=.002) and no change during the high-FODMAP treatment (5.59±4.62 to 7.20± t=4.63, p=.13) and a decrease in empty calories in the low-FODMAP treatment (620.02±455.62 kcal to 342.08±283.96 kcal, t=2.64, p=.02) with no change in the high-FODMAP treatment (552.56±445.97 to 610.49±411.47, t=-.77, p=.46)

Macro- and micronutrient information is presented in Table 3. The primary analysis was a time*treatment*order ANOVA for energy intake. There was no main effect of order ($F_{(1,14df)}$=0.66, p=.43, η^2=.05), and no treatment*time*order interaction ($F_{(1,14df)}$=0.03, p=.87, η^2=.00). There was no main effect of time ($F_{(1,14df)}$=2.24, p=.16, η^2=.14). There was a significant treatment*time interaction for energy intake ($F_{(1,14df)}$=8.62, p=.01, η^2=.40) with a large effect size. Within treatments, energy intake decreased in the low-FODMAP condition but did not change in the high-FODMAP condition. Looking at specific macronutrients, the most variability came in the carbohydrate variables. There was a significant treatment*time interaction for total carbohydrate intake in grams, ($F_{(1,14df)}$=6.28, p=.02), lactose intake in grams, ($F_{(1,15df)}$=5.20, p=.04), calcium intake in mg, ($F_{(1,15df)}$=4.65, p=.048) and sodium intake in mg, ($F_{(1,15)}$=9.98, p=.006). Within treatments there was a decrease in total carbohydrates

in the low-FODMAP treatment but no change in the high-FODMAP treatment. Lactose intake decreased during the low-FODMAP treatment and did not change in the high-FODMAP treatment. Sodium intake did not change in the low-FODMAP treatment and increased in the high-FODMAP treatment. Calcium intake did not change in either treatment, but there was a significant time*treatment interaction, $F_{(1, 15df)}= 4.64$, $p=.048$, $\eta^2=.24$.

There were no differences in mood score between conditions except "how weary do you feel" was significantly higher in the low-FODMAP treatment than the high-FODMAP treatment (5.86 vs. 3.88, $t=2.89$, $p=.01$).There were no differences in symptoms, however, both abdominal pain and distention had extremely low mean scores (less than 1) for both treatments and satisfaction with bowel movements did not differ between treatments (6.29±1.56 vs. 6.36±2.44, $t=.13$, $p=.90$).

At the end of each intervention period, a convenience sample of subjects (low-FODMAP n=9, high-FODMAP n=7) were asked about their diets. For the low-FODMAP diet, more subjects found it difficult to implement the diet (6.4±2.1 vs. 4.8±2.8) and adhere to the diet (5.7±1.9 vs. 4.6±2.4) and ranked the taste poorly (4.6±2.4 vs. 7.0±1.5) compared to the high-FODMAP diet.

4. DISCUSSION

4.1 Summary

The purpose of this study was to investigate the effects of dietary instruction for low- and high-FODMAP diets on dietary quality and FODMAP intake in healthy young adults. We found that the low-FODMAP diet resulted in an increase in dietary quality

14

with a reduction in FODMAP intake. The high-FODMAP diet had no effect on FODMAP intake while dietary quality decreased. This was the first FODMAP study to the researchers' knowledge that looked at changes in dietary quality when implementing FODMAP diets and indicated that a low-FODMAP diet may have a positive impact on diet quality. Future studies should also consider this diet's effect on weight change given the substantial energy decrease observed here.

Another strength of this study was the use of the HEI-2010. The HEI-2010 is a valid and reliable measure of dietary quality [33] in conformance with the 2010 Dietary Guidelines for Americans (DGA) [28]. (The HEI utilizes set energy density standard (per 1000 kcals) [28], important since a large difference in energy intake was found). The mean HEI-2010 scores in this study were higher than for the average U.S. adult, 20-30 years of age (45.4±1.1) [33] but similar to past studies at the University of Rhode Island [34].

The high-FODMAP intervention did not affect FODMAP intake. During the high-FODMAP intervention, no food was completely prohibited like foods were during the low-FODMAP intervention. Instead, low-FODMAP foods were "discouraged" and high-FODMAP foods were "encouraged". Future studies should test other types of high-FODMAP dietary instructions. A more effective possible future strategy could be to prescribe a set number of servings of foods on the high-FODMAP diet per meal. Future research is needed to develop interventions for increasing healthful FODMAP intake in young adults.

4.2 Subjects

Healthy young adults free of any GI disorders were included in this study. To the researchers' knowledge, this is the only FODMAP study that has looked exclusively

at healthy adults. Previous FODMAP focused on populations with IBS [5-10]. In one of the few FODMAP studies that included healthy adults, Ong et al.[5] compared healthy adults (n=15) to IBS patients (n=15) and compared high-FODMAP conditions (50g/day) to low-FODMAP conditions (9 g/day) during a two day intervention. The study was a single-blinded crossover intervention comparing low- vs. high-FODMAP conditions in which all foods were provided for two days. The study found that a high-FODMAP diet had no effect on symptoms except for increased flatulence in healthy adults. Similarly, our study found that both abdominal pain and distention were not factors in this population however we did not assess flatulence.

4.3 The effect of a low-FOMAP diet on Dietary Quality

Due to the restriction of fruits, vegetables, dairy and legumes, dietary quality was hypothesized to decrease on the low-FODMAP diet, whereas the opposite occurred. Looking at the change in dietary quality, the low-FODMAP intervention was most effective at restricting refined products and "empty calories" including solid fat, added sugar and sodium-rich foods. This restriction contributed to the large decrease in energy and carbohydrate intake. These results indicate that a low-FODMAP diet has potential to have a positive influence on dietary quality in college students but future studies are needed with adults showing more dietary diversity. The implications of the decrease in energy intake should be examined in future research.

To the researchers' knowledge this was the first FODMAP study that examined dietary quality in healthy adults. Ostgaard et al. [23] examined diet composition of IBS patients who received low-FODMAP education (guided n=43) two years prior. This study showed no difference between the guided and control group for calories, CHO,

protein, fat, sugars or fiber intake and did not measure dietary quality. This study used food frequency questionnaires (FFQ) to measure nutrient intakes as opposed to our study which used 24 hour food recalls.

4.4 The effect of a low-FODMAP diet on other health benefits

Fibers provide plant structure and are thus found in plant-derived vegetables, fruits, whole grains and legumes [35]. A low-FODMAP diet restricts these food groups, suggesting fiber intake might be of concern. In our study however fiber intake did not change in either intervention. Total, soluble and insoluble fiber intake were considerably lower than the recommendations[36], indicating attention should be paid to ensuring assuring adequate fiber in FODMAP modified diets in this population [12].

FODMAPs are low glycemic index nutrients [37,38] producing a lower glycemic response compared to other CHO [21]. Low glycemic index foods may provide benefits in the treatment and prevention of metabolic syndrome, diabetes and CVD [39-42], due to their ability to maintain better regulation on blood glucose, decreases oxidative stress and lowering inflammation [42]. No other study has considered how implementing a low-FODMAP diet effects overall glycemic load or glycemic index. In our study, glycemic load (glucose reference) significantly decreased on the low-FODMAP diet, however, glycemic index (glucose reference) did not change (62.33 ± 5.27 to 60.98 ± 7.41, $t=.597$, $p=.56$). This change may very well be due to the decrease in overall CHO intake. Future studies should consider how FODMAP intake affects blood glucose regulation.

4.5 The effect of overall FODMAP intake for the low-FODMAP diet

The low-FODMAP intervention was successful at reducing overall FODMAP intake and lactose intake; although it is important to keep in mind that oligosaccharides

17

were not calculated (see section 4.5, strengths and limitations). Overall FODMAP intake was almost cut in half on the low-FODMAP diet and 81% of subjects decreased FODMAP intake.

The low-FODMAP diet strategy does not recommend a FODMAP elimination diet for long term use and stresses the importance of reducing any unnecessary restrictions that may compromise nutritional status [1,12]; The use of a strict low-FODMAP diet is warranted for 6-8 weeks [1] and subsequently discontinued if symptoms are not controlled [4,43]. The cutoff point used to define low-FODMAP is based on the individual's tolerance and typical eating pattern [1], therefore to the researcher's knowledge there is no formal definition of "low-FODMAP". A previous study where all foods were provided defined low-FODMAP intake as <9 g/day[5], which is lower than the 19.29 g consumed during our intervention. However comparisons to a standardized definition for low- or high-FODMAP cannot be made.

The low-FODMAP diet reduced lactose intake to under 3 grams and there was a nonsignificant trend towards calcium reduction. The "dairy" HEI-component, and vitamin D intake did not significantly decrease. The scores also rated poorly compared to desirable standards. The dairy score was lower than the average score for U.S. adults ages 20-30 (5.6±0.2) despite the total HEI score greatly exceeding the population average (45.4±1.1) [33]. Calcium intake at baseline exceeded the RDA of 1,000 mg/d [44] but dropped below the EAR of 800 mg/d [45] during the low-FODMAP diet. Vitamin D intake did not meet the EAR [45] at any point of the study. Calcium and vitamin D status in any nutrition intervention that greatly restricts lactose and/or dairy products should be considered [22].

4.6 Strengths and Limitations

There were several limitations. FOS and GOS were not included because they are not analyzed by NDS-R. Future studies could use Barrett and Gibson's food frequency questionnaire[46]. A second limitation was that only a single 24 hour food recall was used per intervention period which provides an unstable estimate of usual intake[26,47]. A third limitation was that the high-FODMAP intervention was not effective at reducing FODMAP intake. Other limitations to this study include a small sample size, a short duration and reduced generalizability due to the homogeneity of college-aged subjects. Strengths of the study included the use of the HEI-2010, a well controlled, randomized single-blinded crossover experimental design, and use of healthy adults.

5. <u>CONCLUSION</u>

Dietary instruction for implementing a low-FODMAP diet may be effective in helping young healthy individuals reduce FODMAP intake without compromising overall dietary quality. Although calcium intake was low, this study found that the low-FODMAP diet was associated with a reduction in overall energy and carbohydrate intake as well as glycemic load. Long term studies are needed to confirm these results. Future research is also needed to assess the effects of increasing FODMAP intake in young adults.

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Table 1: Demographics, n=16

Variable	
Female, n (%)	10 (62.5)
Male, n (%)	6 (37.5%)
Age (yr), M±SD	20.47±1.77
Body Weight (kg), M±SD	63.85±11.65
Body Mass Index (kg/m^2), M±SD	22.21±2.45
Waist Circumference (cm), M±SD	78.98±7.57
Body Fat Percent (%)*, M±SD	18.80±10.37

*body fat percent obtained via BOD POD Body Composition
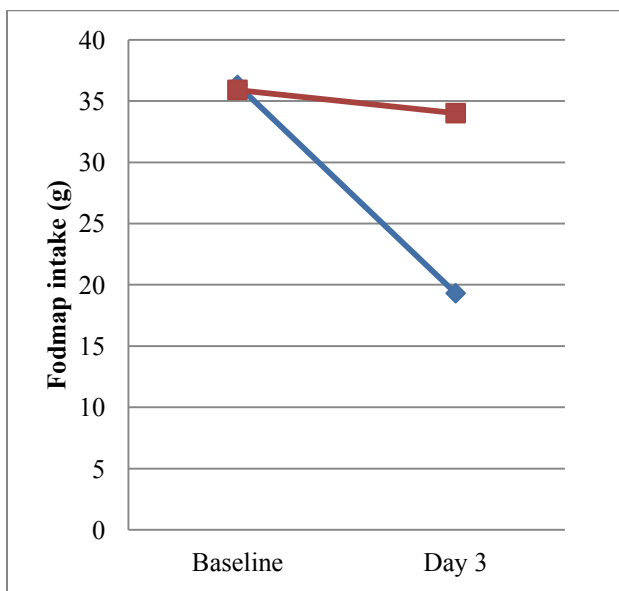System (Life Measurement Instruments, Concord, Calif., USA)

Figure 1: Comparison of FODMAP intake for low- vs. high-FODMAP diets.

Table 2: Diet quality as measured by the Healthy Eating Indix-2010

HEI Component	Low-FODMAP diet			High-FODMAP diet			ANOVA[a]	
	Baseline	Day 3	Δ	Baseline	Day 3	Δ	F (1,15)	η[2]
Total Fruit Score	1.93±1.99	2.83±2.19	0.9	2.35±2.21	2.29±1.69	-0.06	1.19	-
Whole Fruit Score	2.46±2.41	3.01±2.30	0.55	2.52±2.19	2.37±2.04	-0.15	1.23	-
Total Vegetable Score	3.38±2.02	3.62±1.94	0.24	4.32±1.19	3.22±1.88	-1.1	2.38	-
Greens & Beans	0.71±1.91	2.39±2.51	1.68	2.18±2.24	1.89±2.28	-0.29	4.39	-
Whole Grain Score	3.59±3.89	4.28±4.74	0.68	4.36±4.24	4.24±3.96	-0.11	0.28	-
Diary Score	6.73±3.34	4.64±3.73	-2.09	7.17±3.07	6.80±3.63	-0.37	2.64	-
Total Protein Score	2.99±1.75	4.40±1.30	**1.41***	3.55±1.89	3.94±1.38	0.38	4.20	-
Seafood & Plant Score	1.53±2.03	2.18±2.56	0.65	2.50±2.58	1.22±2.02	-1.28	1.75	-
Fatty Acid Score	4.39±3.97	6.78±3.79	2.39	4.10±3.86	3.01±2.75	-1.09	3.53	-
Refined Grain Score	5.28±4.28	7.69±3.69	2.4	6.41±4.06	5.03±3.82	-1.38	4.32	-
Sodium Score	5.77±3.72	4.96±4.49	-0.81	6.13±3.50	2.99±3.35	**-3.14****	1.78	-
Empty Calorie Score	14.83±5.23	16.31±5.74	1.48	15.25±4.37	15.04±5.37	-0.21	0.97	-
HEI-2010[b]	53.60±17.16	63.09±17.23	**9.49***	60.83±12.76	52.04±11.27	**-8.79***	**10.452****	**0.43**

*= p<.01, **=p<.001

A 2 (Order) X 2 (Treatment) X 2 (time) mixed factorial ANOVA with post hoc ttest was used for total HEI-2010
and a 2 (treatment) X 2 (Time) repeated measured ANOVA with post hoc ttest was used for individual components

[a]= Time*treatment interaction F statistic reported

[b]= A measure of dietary quality reflecting federal guidelines. Scores range from 0-100 with higher scores reflecting better diet quality. The value is expressed as a per 1,000 kcal standard.

Table 3: Intake of selected nutrients in Low- vs. High-FODMAP diets

Item	Low-FODMAP diet			High-FODMAP diet			ANOVA[a]	
	Pre-Intervention	Day 3	Δ	Pre-Intervention	Day 3	Δ	F(1,14)	η²
Calories (kcals)	2255.83±1325.14	1510.11±794.96	**-745.71***	1993.24±962.44	2251.92±864.46	258.68	**8.62***	**0.38**
Total:								
Fat (g)	83.76±65.77	55.24±33.28	-28.52	70.11±42.01	78.54±34.77	8.43	3.68	-
Protein (g)	75.69±53.08	74.12±56.78	-1.57	74.92±34.14	91.53±36.51	16.61	1.30	-
Carbohydrate (g)	291.72±186.21	182.86±116.27	**-108.85***	277.60±144.01	288.01±131.68	10.41	**6.28***	**0.30**
Starch(g)	126.09±86.00	72.22±59.00	**-53.87***	107.51±61.14	130.80±79.10	23.29	**5.78***	**0.28**
% Calories from:								
Fat	30.76±10.88	32.92±13.26	2.16	29.59±7.23	30.79±8.56	1.2	0.06	-
Protein	13.45±5.15	19.21±9.02	**5.76****	15.79±5.24	17.41±6.09	1.62	2.74	-
Carbohydrate	51.97±13.32	46.96±16.66	-5.01	54.28±8.02	49.47±8.78	-4.81	0.15	-
Sugars & Fibers								
Total Fiber (g)	21.22±14.15	16.13±8.27	-5.09	24.37±15.74	19.46±9.00	-4.91	0.00	-
Soluble (g)	6.83±4.66	4.47±3.08	-2.36	7.01±4.29	6.42±3.60	-0.58	0.79	-
Insoluble (g)	14.17±9.82	11.59±5.75	-2.58	17.26±12.35	12.89±5.90	-4.37	0.17	-
Glucose (g)	21.87±14.73	18.52±16.07	-3.36	19.22±10.95	21.07±13.24	1.85	0.70	-
Fructose (g)	20.52±15.03	16.10±15.03	-4.42	19.05±9.64	20.96±10.80	1.90	0.99	-
Lactose (g)	14.35±14.08	2.89±5.79	**-11.46****	15.96±16.40	11.29±12.11	-4.68	**5.21***	**0.26**
Sucrose (g)	64.13±73.51	38.59±32.68	-25.54	69.04±65.49	60.64±70.53	-8.40	0.62	-
Total Sugars (g)	124.14±101.37	76.99±53.22	-47.15	126.96±83.41	118.47±80.88	-8.49	2.22	-
Added Sugar (g) by total sugar	74.49±80.17	44.41±53.58	-30.09	77.07±80.23	75.03±73.62	-2.03	1.74	-
Vitamins & Minerals:								
Vitamin D (mcg)	5.57±6.93	3.89±5.29	-1.68	4.75±3.54	3.86±2.55	-0.89	0.23	-
Calcium (mg)	1085.97±794.13	689.12±451.61	-396.85	996.46±475.41	912.64±316.42	-83.83	**4.65***	**0.24**
Phosphorus (mg)	1278.96±803.39	998.83±578.54	-280.13	1314.86±583.87	1270.30±413.24	-44.56	1.51	-
Sodium (mg)	3210±1760	2540±1810	-670	2730±1100	4260±1910	**1530****	**9.98****	**0.40**
Potassium (mg)	2770.93±1429.83	2182.15±1171.89	-588.78	2549.06±752.78	2280.55±758.72	-268.52	0.51	-
Glycemic load	170.46±117.52	105.15±77.33	**-65.31***	151.88±84.39	162.29±84.52	11	**6.77***	**0.31**

*p<.05, **p<=.01

[a]= Time x treatment interaction F statistic reported

A 2 (Order) X 2 (Treatment) X 2 (time) mixed ANOVA used for total calories intake and a 2 x 2 repeated measures ANOVA with post hoc ttests were used for all components

27

APPENDICES

Appendix A: Review of Literature

1.   Irritable Bowel Syndrome

Irritable Bowel Syndrome (IBS) is the most commonly diagnosed

Gastrointestinal (GI) condition in the United States [48]. In 2012, it was estimated that 10%

of Americans meet the diagnosable criteria for IBS, translating to 30 million people [48]. It

is considered a functional disorder with no known identifiable underlying

pathophysiology [49] with diagnosis based on exclusion of other conditions rather than a

biological marker and may involve lengthy, and intrusive procedures such as

sigmoidoscopies and barium enemas [50]. Historically, medical management has focused

on individualized symptomatic treatment[48]. IBS is an umbrella term that incorporates a

spectrum of chronic or recurrent symptoms including abdominal pain, bloating,

distension, excessive wind and altered bowel habits when anatomical abnormalities and

inflammation have been excluded [12]. Symptoms are experienced to varying degrees, often

with a single symptom manifesting predominately. Some symptoms can be perceived to a

lesser degree by the healthy population, indicating that some treatment strategies may be

beneficial to the general population[5].

1.2 IBS'S Burden on Healthcare and Affect on People's HRQoL

It is well documented that IBS is associated with a decrease in people's sense of

well-being, or Health Related Quality of Life (HRQoL) in relation to the general

population [51-54]. In 2009, Spiegel et al. [51] found that patients with IBS visit the doctor more frequently, use more diagnostic tests, consume more medications, miss more workdays, have lower work productivity, are hospitalized more frequently, and consume more overall direct costs than those without IBS. Recent studies have compared HRQoL of IBS patients to patients with other gastrointestinal conditions. A 2000 study looked at 877 ambulatory adults from 1994-1998 and compared HRQoL of IBS patients with the general population and with patients with GERD, Diabetes Mellitus (DM), depression and End Stage Renal Disease (ESRD) on dialysis [55]. The study found that patients with IBS had significantly worse reported HRQoL than the general population and patients with GERD. Additionally, patients with IBS scored significantly lower on selected aspects of HRQoL than patients with DM and ESRD. The study concluded that IBS patients experience significant impairments in HRQoL and these impairments are most pronounced in energy/fatigue, role limitation caused by physical health problems, bodily pain and general health perception [53].

IBS's impact on the healthcare system has also been heavily researched. The overall associated cost is 1.6 billion in direct and 19.2 billion in indirect annual costs [56]. The mean annual direct health care cost per patient is $5,049 and the annual out-of-pocket expenses (for example non-prescription medication and alternative treatment like special diets and therapy per patient) is $406 [57]. The individual cost has been found to increase based on disease severity and recent exacerbation of bowel symptoms [57]. Regarding burden for healthcare practitioners, IBS accounts for 12% of the patients seen in the primary care practice and is the largest diagnostic group seen in GI practice [58] with inpatient care accounting for 17.5% of total costs [57].

1.3 Treatment of IBS Focusing on the Role of Diet

Current treatments for IBS include pharmaceuticals such as antispasmodics and stool softeners [12], psychological therapy, fiber, probiotics and lifestyle and diet modification [8]. The American Gastrointestinal Association (AGA) suggests that treatment of IBS should be based in part on the correlation of IBS symptoms with food intake and defecation [58]. Food's role in symptom management is further reinforced by an Academy of Nutrition and Dietetics (AND) study that concluded symptoms in one quarter of IBS patients may be caused or exacerbated by one or more dietary components [59] as well as multiple studies finding people with IBS believe food plays a significant role in exacerbation of their symptoms [60-64].

Multiple foods or food components have been examined regarding their role in IBS symptom exacerbation. Dietary fat, caffeine and alcohol have been sought after as potential triggers with physiological mechanisms suggesting that these may play a role, but inconsistencies in symptom improvement have been seen when these items are restricted [12]. In 2009, the AND [59] released a position paper comparing the current practical treatment strategies for IBS. The position paper states that the traditional dietary strategy of increased fiber is only marginally beneficial. In addition, a subgroup of fiber, insoluble fiber, may actually worsen symptoms, making the traditional dietary advice confusing and potentially counterproductive. Indeed, randomized controlled clinical trials have shown conflicting results [65,66]. The AND also examined new treatment strategies, specifically supplemental prebiotics and probiotics and dietary fermentable oligo-, di-monosaccharides and polyols (FODMAPs) restriction. FODMAP is a term used to

identify a collection of poorly digested, highly osmotic and rapidly fermented short chain carbohydrates (CHO). At the time of that paper, the AND stated that prebiotics have not been adequately tested, the usefulness of probiotics was not yet established and the restriction of dietary FODMAPs may be beneficial in reducing IBS symptoms, but confirmatory studies were needed[59].

2.   FODMAP: Definition & General Properties

In 2005 the term FODMAP was coined to identify a collection of poorly digested, highly osmotic and rapidly fermented short chain carbohydrates (CHO). FODMAP stands for fermentable oligosaccharides, disaccharides, monosaccharides and polyols. They are widespread in the diet [1] and include the oligosaccharides, fructooliogosaccharides (fructans or FOS), found in wheat, rye, onions and garlic, and galactooligosaccharides (GOS) found in legumes and some nuts; the disaccharide lactose found in milk products; the monosaccharide fructose in apples, pears, watermelons, mango and asparagus and the sugar polyols used as artificial sweeteners and naturally occurring as sorbitol in stone fruits and mannitol in mushrooms and cauliflower [12]. Both dietary fibers and resistant starches are also poorly digested in the small intestine and reach the colon, however they are not fermented as fast and are less osmotically active making them less likely to induce gastrointestinal symptoms [12] and thus not considered as part of this IBS-focused dietary strategy. Indeed, studies have shown the benefits of low-FODMAP diets in alleviating IBS symptoms even when adequate resistant starches and fibers are included [5,7].

FODMAPs have three common functional properties. They are 1) poorly absorbed in the proximal small intestine, allowing substrate to reach the distal small intestine and proximal colon 2) small and osmotically-active, which increases the liquidity of luminal content due to osmosis and 3) rapidly fermented by gut microbiota, increasing the amount of gas present in the colon. These three characteristics combined to increase luminal distension [1], the basis for the genesis of many functional gut syndrome[1]. A low-FODMAP diet is now considered an effective strategy for managing symptoms of IBS in Australia, with interest expanding across the world [12]. Studies have also shown that a low-FODMAP diet can relieve gastrointestinal symptoms in up to 70% of patients with Crohn's disease and Ulcerative Colitis[10], two conditions that historically exhibit functional gastrointestinal symptoms similar to IBS. Additionally, FODMAPs in enternal nutrition (EN) feeding formulas have been suggested as a contributing factor to high frequency of diarrhea in patients receiving EN support [67].The predominant symptoms of IBS are diarrhea, bloating, abdominal pain and flatus [48]. It is important to note that low-FODMAP diets do not treat IBS; rather they provide a therapeutic strategy for managing symptoms. The osmotic nature of FODMAPs contributes to diarrhea and the fermentation gaseous by-products contribute to abdominal pain and flatus [12]. The improvement to constipation-predominate IBS seen by the FODMAP approach needs further exploration [12]. Lastly, the threshold of visceral pain, or visceral sensitivity may help determine the severity of symptoms, in particular abdominal pain [3].

2.2 FODMAP Studies: Studies Confirming the Success of Low-FODMAP in Treating Gastrointestinal Symptoms

Since the AND's 2009 position paper, multiple studies have concluded that high-FODMAP diets induce gastrointestinal symptoms [5,6] and that a low FODMAP diet relieves gastrointestinal symptoms associated with functional gastrointestinal disorders [7-10]. Overall symptom improvement has been seen in up to 86% of IBS patients[7] and, although the majority of FODMAP studies focus in on IBS patients, limited studies on patients with Inflammatory Bowel Disease (IBD) displaying IBS-like symptoms show up to 70% symptom improvement [8]. The first and only prospective study confirming that low-FODMAP diet improve IBS symptoms was conducted in 2013 [8]. The study examined 90 patients with a mean follow up of 15.7 months. With the exception of 'burping' ($p=.275$), 'feeling full even long after stopping eating' ($p=.051$) and 'the passage of mucus'($p=.890$), (all of which are symptoms not traditionally associated with IBS), there was a significant improvement in all of the 20 questions pertaining to bowel habits. This included significant improvements in abdominal pain, bloating, flatulence and diarrhea ($p<.0001$ for all) [8], the predominant symptoms of IBS [48].

Shepherd et al. [11] conducted the first and only randomized placebo-controlled study showing evidence that restriction of FODMAPs causes symptomatic improvement in IBS patients. The study was a 25 subject, double-blinded, randomized, quadruple arm placebo-controlled rechallenge trial. The aim of the study was to determine if improvement in symptoms in IBS patient following fructose restriction was due to fructose specifically or FODMAPs in general. The 25 patients were provided all foods for the study duration. The subjects first completed an initial 4 week period where foods that contained FODMAP were restricted, followed by a 26 day period where subjects consumed specially formulated test drinks containing fructose, fructans, a combination of

33

fructose and fructans or glucose (the control) in different dosages. Symptoms were measured using daily diaries and questionnaires. For each arm, participants started with the low dose (50mL/week) for the first 3 days, followed by the medium dose (100 mL/day) for 3 days and finally the high dose (170 ml/d) for the remaining 2 weeks of each arm. Dose stages were increased as tolerated with no significant difference in patients' ability to reach the high dose in any of the drinks. Each 500 ml bottle contained 19 g fructans, 50 g fructose, a combination of the fructose and fructans representing a FODMAP containing drink, or 20 g glucose representing the control. The test drinks were initially tested on seven healthy adults without IBS. None of the healthy adults reported their symptoms were not adequately controlled; However four healthy subjects reported mild symptoms, three reported bloating (VAS scores of 27,35,43 mm) and four reported increased wind (VAS scores 27,28,33, and 44 mm). Following the initial arm, subjects could not begin the subsequent arm of the study until baseline symptoms were obtained for at least seven days. The overall adherence was >95%. The median wash out period was 14 days. The study resulted in 70% of patients receiving fructose, 77% receiving fructans and 79% receiving a high FODMAP drink reported uncontrolled symptoms compared to only 14% of subjects receiving glucose ($p \leq .002$). Every IBS symptom evaluated was significantly greater with ingestion of the high FODMAP drink than the control. In addition, intensity of overall symptoms increased as the doses of fructose, fructans and fructose-fructan mix increased ($p < .01$ for all dose comparison) but the severity of overall symptoms did not change for increasing doses of glucose ($p > .2$).

2.3 Comparing low-FOMDAP diets to standard dietary advice

In 2011 Staudacher et al.[7] compared symptom responses in IBS patients after advice to follow a diet low in FODMAPs verses following the standard dietary advice by on the UK National Institute for Health and Clinical Excellence (NICE) guidelines. The study took place in the United Kingdom and all dietary advice was given by experienced dietitians. The NICE guidelines consist of general dietary advice including regular meal patterns (adjusting fiber intake and reducing alcohol and caffeine) as well as symptom specific guidelines [7]. The study looked at 82 consecutive IBS patients (standard n=39, low-FODMAP n=43) who attended a follow-up dietetic outpatient appointment after following dietary advice for management of IBS for at least 6 months. The validated IBS Global Improvement Scale was used to compare symptom changes between the two groups. The study found that the low-FODMAP diet produced greater satisfaction in symptom responses (76%) compared to the standard advice (54% $p<.038$) and better overall symptom responses (86%) compared to the standard group (49% $p<.001$). Improved symptoms included reduced bloating, abdominal pain and flatulence.

2.4 FODMAP malabsorption

Although all FODMAPs are poorly absorbed, the anatomical reasoning underlying the incomplete or complete lack of absorption differs among FODMAPs. Fructose is a hexose sugar being increasingly consumed in its monosaccharide form as an added sweetener and in its more natural forms such as fruit juice [68].There is no clearly established fructose malabsorption mechanism [68] and most of the understanding of fructose transport has been based on animal studies [69]. In the conventional model of fructose transport, fructose is transported across the apical membrane of intestinal

epithelial cells by the facilitative transporter GLUT5 [68], a facilitative transporter specific to fructose. Transport of fructose across the basolateral membrane of gastrointestinal epithelial cells takes place by means of the facilitative transorter GLUT2, which has the ability to transport both hexose monosacchrides, fructose and glucose [68]. A study conducted in GLUT5 knockout mice identified GLUT5 as the primary protein responsible for fructose absorption and malabsorption [70]. These GLUT5 knockout mice displayed decreased fructose absorption by 75% and decreased serum fructose by 90% when compared to wild-type mice. Furthurmore, GLUT5 knockout mice fed a high fructose diet experienced more distended colons and significantly more fecal contents including fluid and gas compared to mice on a normal or high glucose diet. Fructose absorption in humans appears to be limited at high concentrations of fructose consistent with the absorption capacity of a facilitative transport system, and appears to occur as a result of a reduced absorption threshold [68]. This means that among both healthy and symptomatic people, there is a range of fructose absorptive capacity that is balanced against dietary fructose consumption [68].

Lactose malabsorption is a common condition characterized by a deficiency of lactase, an intestinal cell produced enzyme occurring in the brush border membrane of the intestinal mucosa that hydrolyzes lactose to its components, galactose and glucose [71]. Secodary hypolactasia can be the result of any condition that damages the small intestinal mucosa brush border or significantly increases the gastrointestinal transit time [71]. Both of these conditions result in malabsorbed lactose reaching the colon. Only when the malabsorbed lactose is associated with clinical manifestation of bloating, flatulence, abdominal pain and diarrhea is it referred to as "lactose intolerance"[71].

FOS or Fructans are oligo- and polysaccharides of fructose with a glucose terminal end [16,72]. They are classified according to their bonds as inulins (β1-2 bonds) or levans (β2-6 bonds) with most dietary sources coming from inulins [16]. When an inulin has <10 degrees of polymerization (DP) it is referred to as a fructo-oligosaccharide, whereas >10 DP is referred to as an inulin [16]. The β-bonds that hold fructose molecules together are unable to be hydrolyzed by human digestive enzymes, thus theoretically FOS travel unabsorbed in all humans, resulting in more than 90% of fructans reaching the colon [16]. That being said, FOS absorption in the human gastrointestinal tracts has not been assessed, studies come exclusively from rat models [73].

GOS are nondigestible CHO usually composed of 2-10 molecules of galactose and 1 molecule of glucose [74]. The two most common dietary sources are raffinose, comprised of one fructose, one glucose and one galatose molecule and stachyose, which is a raffinose with one an additional galactose [16]. Humans lack α-galactosidase, the enzyme that hydrolyses the galactosidic linkages of stachyose and raffinose to their simple sugar constituents, resulting in minimal absorption in humans [16].

Polyols are sugar alcohols that include sorbitol, lycasin, malitol and mannitol, [75,76]. Sorbitol and mannitol are six-carbon polyols isomers that are only partly absorbed via passive diffusion across the small intestine epithelium [76], with a total of 80% ingested reaching the colon [16].

2.5 Intestinal gas production and the hydrogen breath test

Once CHO are malabsorbed in the small intestine they become substrate for bacteria fermentation, which in turn releases gaseous byproduct into the lumen. More

than 99% of intestinal gas is hydrogen (H_2), oxygen (O_2), methane (CH_4), carbon dioxide (CO_2) and nitrogen (N_2) while less than 1% is composed of various odoriferous gases [77]. CO_2, H_2 and CH_4 represent the predominant, intraluminal gases [77]. H_2 and CH_4 are generated solely by bacterial metabolic processes, demonstrated by studies conducted with both germ free rats and newborns, which show that these gases are not produced during the first 12 hours of life [78,79]. Colonic gases will be used by bacteria, excreted in stool or absorbed into the blood stream [80]. Absorbed H_2 is almost completely cleared in a single passage through the lungs [80], thus the measurement of breath H_2 concentration may be considered an expression of intestinal H_2 production [81]. The human colon contains around 10^15 bacteria [82], predominantly anaerobes that produce large quantities of hydrogen gas [83]. Anaerobic bacteria prefer to metabolize sugar molecules, which get broken down into short-chain fatty acids (SCFA), CO_2 and H_2 [83]. Like H_2, SCFA generate an osmotic gradient, attracting water into the colon, which can lead to diarrhea [83]. There are two main pathways for colonic H_2 disposal, including conversion to methane by methanogens and hydrogen sulfide production from reduction of sulfate by sulfate reducing bacteria [77]. Of the general population, 30% have microbia containing enough methanogens to allow for consumption of large quantities of hydrogen, while producing small amounts of H_2 [84] made possible since four moles of H_2 can be reduced to a single mole of CH_4 [77].

The hydrogen-breath test is a simple, non-invasive tool currently used in gastroenterology to diagnose certain clinical conditions, thus avoiding more invasive test [85]. Additionally, it represents the most effective test for CHO malabsorption [86] and is used extensively in both individual and collective FODMAP studies. It relies on the fact that

humans do not normally produce H_2 and thus its presence indicates breakdown of CHO in the intestines, primarily the colon, by anaerobic bacteria [87]. FODMAPs have been called fast food for bacteria [16] and breath hydrogen testing studies have shown that CHO molecules with DP<10, such as FODMAPs, are broken down twice as fast those with DP>10 [88]. In 2000, a breath hydrogen detection machine entitled the Quintron Microlyzer Breath H_2 Analyzer was validated for diagnosis of CHO malabsorption [87].

2.6 FODMAP malabsorption in healthy adults

The predominant way that diet alters luminal distention is via intraluminal gas production [5]. Even in healthy individuals, FODMAPs are malabsorbed [12], shown using breath hydrogen testing to compare the prevalence of CHO malabsorption between functional GI disorder (FGID) patients and healthy subjects. Barrett et al. [17] found that 34% of healthy people (n=71) malabsorb fructose compared with 45% of those with FGID (n=201) when given 35 g of fructose prior to breath hydrogen testing (malabsorption was defined as >10 ppm). In that same study [17] it was demonstrated that lactose malabsorption occurred in 16% of healthy adults compared to 23% with FGID after ingesting 50 g of lactose. Two years later, Yao et al [18] conducted a randomized, double-blinded, placebo-controlled cross over study comparing polyol malabsorption between IBS patients (n=20) and healthy adults (n=21) after ingestion of 10 g of polyols. The study found that IBS patients had less malabsorption than healthy adults (sorbitol 1629 ± 210 ppm. 4 hour vs. control 2766 ± 591; mannitol 601 ± 228 vs 2062 ± 468, p= 0.02; t-test) and the prevalence of malabsorption among healthy adults was 60%. As far

as the oligosaccharide FODMAPs, as stated previously, malabsorption occurs in everyone [19,20].

Intestinal gas produced after ingestion of total FODMAP in both healthy individuals and individuals with IBS has also been considered. In 2010, Ong et al.[5] examined both healthy individuals (n=15) and patients with IBS (n=15) and compared high-FODMAP diets (50g/day) to low-FODMAP diets (9 g/day) during a two day intervention. The design was a single-blinded crossover intervention where all food was provided. Breath hydrogen samples were collected hourly over 14h on day two of each diet. The study found higher levels of breath hydrogen produced over the day with the high-FODMAP diet for healthy subjects (181± 77 ppm vs. 62±23 ppm; mean $p<.0001$) and patients with IBS (242±79 vs. 62±23; $p<.0001$) [5].

2.7 Importance of visceral sensitivity in symptom production

With CHO malabsorption present in both healthy population and FGID patients, and fermentation patterns similar in both populations, a low threshold for visceral pain appears to be the key mediator for gastrointestinal symptoms manifestation, particularly abdominal pain[3]. This was demonstrated by Richie et al. [3] who studied the effect of inflating a balloon into the distal colon and compared pain responses between IBS patients (n=67) and healthy adults (n=16). The study found that inflation to 60 mL caused pain in 6% of the control at a mean diameter of 3.8 cm and in 55% of patients with IBS at a mean diameter of 3.4, despite that gut wall tension at that volume appeared to be normal in both groups and gut wall diameter could be further increased. Additionally, in 6% of the controls and 52% of patients with IBS, pain occurred at balloon diameters that

could still be increased by 10% or more with further inflation, pointing to a low threshold for visceral pain in patients with IBS compared to healthy adults [3].

2.8 Poorly digestible and Osmotic effect of FODMAP

The proposition that dietary FODMAPs increase the liquidity of luminal content due to osmotic properties was explored in a 'proof-of-concept study' in 2007 [9] and further explored in a similar study in 2010[6]. The Australian study examined the change in frequency and consistency of effluent of patients without a colon when reducing consumption of dietary FODMAPs. The use of colonoscopy patients controlled for the reabsorptive capacities of the large bowel to help better understand how much liquid diffuses into the intraluminal space in the small intestine. In the small, 15 subject study that incorporated both retrospective and prospective data, patients who recently received a colectomy and ileal pouch formation (n=13) or a ileorectal anastomosis (n=2) had the frequency and consistency of effluent output per day measured prior to and during a low-FODMAP intervention. All participants had breath hydrogen testing done prior to participating in the study. Regarding breath hydrogen testing, 50% of the participants did not produce hydrogen. This is understandable given the absence of colonic fermentation in patients without a colon. In the retrospective arm of the study, five of the seven patients had significant improvement in stool frequency (8-4 stools; p=0.02) and consistency as shown by patient self reporting [9]. In addition, patients uniformly reported that reintroduction of prohibited foods worsened symptoms [9]. In the prospective arm of the study, (n=5), no significant change in stool frequency (median 6 to 5 per day; p=ns) occurred. The lack of significance was attributed to acute or chronic pouchitis

experienced by three subjects [9]. However the reasoning for the lack of response in patients with inflammation was unclear [9].

Similarly, a 2010, randomized, single-blinded cross over study where subjects without a colon were given high-FODMAP diets found that effluent liquid output closely related to FODMAP output, clearly demonstrating FODMAPs osmotic properties [6]. This was found by measuring FODMAP output in the stool of subjects. The study consisted of twelve illeostomy patients who for four days consumed diets differing only in FODMAP content. Effluent was collected for 14 hours during the final day of each intervention. Effluent recovered from the high-FODMAP diet contained 32% (range 6-73) of ingested sorbitol and fructans [6]. Furthermore, stool weight increased by 22% (95% CI, 5-39), water content by 20% (2-38%) and dry weight by 24% (4-43%) [6].

3.   Studies Examining Adherence to low-FODMAP diets

Dietary adherence is crucial to the success of a low-FODMAP diet, however most people do not find the diet easy to incorporate into their life [8,10]. That being said, studies have shown high adherence rates among functional gastrointestinal disorder (FGID) subjects both when all foods are provided in the form of test drinks (>95%) [11] and when asked to follow dietary advice (75.6%)[8]. Adherence among the healthy population who do not experience comparable symptoms has yet to be studied.

Croagh et al. [9] considered change in FODMAP intake, which was used to define adherence in a study examining administration of a low-FODMAP diet. The study was a small, combination retrospective/prospective study, with a total of 15 subjects. In the prospective group, adherence was measured on five subjects using seven-day food

records reflecting the intake on the final week of the six week intervention. Adherence was based on total number of "problematic serves" per day, defined as any food that contained >.5 g of free fructose or fructans, >4 g lactose or any sorbitol, which was based on guidelines from a previous study[25]. Each of the five participants reduced the number of problematic serves per day by at least 6.5 serves (P1=8-1.5, P2=12-2, P3=11-0, P4=9-0, P5=12-5) by the end of the intervention. According to Croagh et al.[9], those with a high baseline intake of dietary FODMAPs and good adherence to the diet responded, while those with a low baseline intake and partial adherence did not [9].

In another study, de Roest et al.[8] measured correlations between adherence and symptoms among IBS patients, finding a positive correlation between adherence to a low-FODMAP diet and symptom improvement. Follow up questionnaires were used to measure both adherence and symptoms at a mean follow up time of 15.7 months. All symptom improvement, including abdominal pain, bloating, flatulence and diarrhea was significantly associated with adherence ($r>0.27$, $p<0.011$). In this 90 subject study, 75.6% (n=68) of IBS patients adhered to the diet regimen. Breaking down adherence into subcategories, 45.6% (n=32) followed the diet as taught at all times except on some occasions; 12.2% (n=11) followed the diet at all times; 13.3% (n=12) patients followed the diet all the time except eating away from home; 14.4% (n=13) considered themselves adherent at least 50% of the time; 24.4% (n=22) followed the diet up to 3 months, but not anymore; 5.6% (n=5) followed the diet as taught immediately, but less than 50% of the time at the end of the follow-up questionnaire; 4.4% (=4) never followed the diet [8].

3.2 Factors that may contribute to adherence

Gearry et al. [10] conducted a pilot study that explored factors that may contribute to non-adherence to a low-FODMAP diet in patients with Inflammatory Bowel Disease (IBD) based on findings from a previous FODMAP study[11]. Dietary advice consisted of a single one-on-one or group counseling session with a dietitian as well as FODMAP literature and food lists. Adherence was measured using questionnaires via structured telephone interviews regarding FODMAPs consumption as well as specific questions concerning FODMAP-containing foods in order to validate the patient's responses. According to Gearry et al.[10] 70% of IBD patients who suffered from FGID were adherent to advice to follow a low-FODMAP diet. Upon completion of the study, the 72 participants were asked to rate their opinion of the diet on a scale of 0-10 (0=easy, 10=impossible) and obtained median score. Low scores were obtained for the questions 1] how easy was it to implement the diet (median response 3; SD 2.9, range 0-10, interquartile range 0-5), 2] and how easy was it to buy the appropriate foods (median responds 3; SD 2.9, range 0-10, interquartile range 1-4) and 3] how would you rank the overall taste of the diet (median responds 2; SD 2.2, range 0-10 interquartile range 1-4)[10]. In addition, 44/72 (61%) said that the foods were not available at their usual shops, the higher cost of the diet was thought to be problematic for 46/72 (64%) and the median estimated increase in the cost of food while on the diet was 10% (SD 19, range -10-110%, interquartile range 1-25%).

The de Roest et al. [8] study (described above) examined similar factors contributing to non-adherence in a study consisting of 90 IBS patients. Using questionnaires, the study found that that fifty-one (60%) patients stated the diet was easy to follow, 56 (65.1%) could easily find suitable products and 37 (54.7%) were able to

incorporate the diet easily into their lives; the overall taste was liked by 47 (54.7%) patients, 21 (24.4%) of patients thought the diet was too expensive[8]. Last, regarding dietary advice, sixteen (44.6%) patients believed that simply being given a list of foods to avoid would have been as effective as seeing a dietitian while 37 (44.6%) of patients would have liked to have seen the dietitian for a further follow-up appointment [8]. Additionally, patients were asked to rank order 5 variables reflecting how they contributed to efficacy/adherence to the diet. Written information (mean rank 1.73 (±0.76)) and dietitian consultation (1.89 (±1.09)) were ranked highest while the support of family and friends (3.33 (±1.15)), low FODMAP cookbooks (3.89(±1.00) and online information (4.11 (±1.00)) were ranked as less important. Factors contributing to non-adherence have been investigated in both IBS and IBD populations, but not in healthy adults.

4.   *Potential Limitations of a low-FODMAP diet*

Several limitations of a low-FODMAP diet pertaining to dietary quality and health benefits have been suggested. Malabsorbed FODMAPs provide multiple benefits including a natural laxative effect due to their osmotic effects[6], a prebiotic effect with beneficial fermentation by-products [12] and production of a low glycemic response compared to other CHO [21]. Some beneficial by-products of fermentation include short chain fatty acids (SCFA), which may protect against colon cancer as well as promote satiety [89], and synthesis of B vitamins and vitamin K [90].

4.2 FODMAPs: Low-glycemic index nutrients

45

FODMAPs are nutrients with lower glycemic indexes [37,38]. Low glycemic index foods are proven beneficial in the treatment and prevention of metabolic syndrome, diabetes and CVD [39-42]. Although the mechanisms underlying the effects of these foods are not completely understood it is hypothesized that low-GI diets maintain better regulation of blood glucose, which decreases oxidative stress and lowers inflammation [42]. In addition to immediate response, consumption of low glycemic foods reduces glycemic response at subsequent meals up to 4 hours later [21].

Nilsson et al.[42] conducted a study examining the effect of evening consumption of indigestible and low glycemic-index foods (50 grams) on a subsequent breakfast. The study included healthy subjects exclusively and used breath hydrogen testing to reflect colonic fermentation. Testing was done prior to and after a subsequent standardized breakfast as well as three hours postprandial. Results were healthy subjects improved glucose tolerance, lowered inflammatory markers and increased satiety (which contributes to weight control and obesity prevention) suggesting multiple benefits of including indigestible and low-GI foods. Upon further investigation, glucose response was inversely correlated with colonic fermentation (r=-0.25; $p<0.05$) and breath hydrogen was positively correlated to satiety (r=0.27; $p<0.01$). Nilsson et al. concluded that the effects could be attributed to mechanisms involving the prebiotic effect of poorly digested CHO.

4.3 FODMAPs: Prebiotic Actions

Prebiotics are any nondigestible substances that encourage the growth and activity of favorable intestinal bacteria, known as probiotics, therefore improving the host

health [91] and include the FODMAPs FOS, GOS and inulins [92]. Studies have shown that supplementing with FOS, GOS and inulin encourages growth of the beneficial bacteria *bifidobacteria,* at the expense of less desirable groups of bacteria [93,94]. Beneficial probiotics also include the bacteria *lactobacilli*; However *bifidobacteria* are the usual target since these bacteria are more readily altered and more prevalent in the human colon [95]. *Bifiobacteria* also exhibit a preference for oligosaccharides [95]. Prebiotics may promote satiety, weight loss and prevent obesity, lower some risk factors for cardiovascular disease, enhance the bioavailability and uptake of minerals including calcium, magnesium and possibly iron, exert protective effects that may prevent colon cancer, reduce inflammation and symptoms of inflammatory bowel disease and reduce the prevalence and duration of infectious and antibiotic-associated diarrhea[95]. Recent studies have shown that prebiotics can have positive effects on insulin and immune response and decrease total cholesterol and total glucose concentration after just six weeks of use [94] and increase the amount of *bifidobacteria* after just four weeks [96], however no longer term studies have been reported.

Not all dietary fibers are prebiotics, but all prebiotics such as oligosaccrides are dietary fibers [97]. Benefits of consuming adequate fiber include weight management, lowering of blood cholesterol, colon cancer risk reduction, prevention and control of diabetes and enhancement of colonic health [35]. Fiber provides the structure of plants and are thus found in plant-derived foods including vegetables, fruits, whole grains and legumes[35]. A low-FODMAP diet restricts these foods suggesting that dietary fiber intake might be reduced. No study has measured change in fiber intake in diets that vary in FODMAP content.

4.4 Dietary quality of Low-FODMAP diets

Only one retrospective study has calculated the diet of free-living subjects who received low-FODMAP dietary advice. Not one study has looked exclusively at healthy adults, changes in intake or looked at overall diet quality as compared to established guidelines. Ostgaard et al.[23] examined the breakdown of IBS patients diets who received low-FODMAP dietary education (guided n=43) two years prior. The study compared those results to IBS patients who did not get FODMAP education (unguided n=36) and to a group of healthy individuals (control n=35). Food frequency questionnaires (FFQ) were used to assess dietary intake. Dietary advice consisted of two sessions with a trained nurse for one hour each. The FFQ found there was no statistical difference in the intake of calories, CHO, protein, fat or sugar between the guided, unguided and control and a significantly lower consumption of alcohol (beer and wine) in both the guided and unguided IBS patients when compared to the control. (Beer and wine: control;45.0±10.9 and 34.2±.9 ml, guided; 21.0±6.5 and 16±2.9 ml, unguided; 13.9±5.9 and 14.5 ±4.3 ml respectively) [23]. Fiber however was not assessed as significantly different among the three groups and overall dietary quality was not measured.

5.   CHO malabsorption 's effect on mood

Multiple studies have been conducted linking specific CHO malabsorption to changes in mood or increases in undesirable mood states. Ledochowski et al. conducted a series of studies in otherwise healthy adults linking fructose malabsorption [98] and lactose malabsorption [99] to early signs of depression and mood disturbances, and fructose and

sorbitol reduced diets [100] to increases in mood among malabsorbers. Mood was defined by the participants' score on the Beck's Depression Inventory-Questionnaire (BDI) [101].

When examining the connection between malabsorption and mood scores, Ledochowski et al. considered plasma tryptophan [98]. This particular study enrolled fifty adults with gastrointestinal discomfort but without any clinical diagnosis. Subjects were tested for fructose malabsorption using breath hydrogen testing. Baseline testing was done followed by administration of 50 grams of fructose. Breath hydrogen testing was then repeated every 30 minutes for the next two hours. Fructose malabsorption was defined as an increase of more than 20 ppm over basal fasting value. Patients (n=35) (70%) were classified as fructose malabsorpers. Fructose malabsorbers and non-malabsorbers then had their plasma trophophan measured and completed the BDI. A non-significant trend to higher BDI scores was seen comparing fructose malabsorbers to non-malabsorbers (9.47±7.35 vs. 7.07 ± 4.62, p=NS). However once divided based on gender, BDI was higher for female fructose malabsorbers (12.30±7.16) than female non-malabsorbers (6.66 ±5.50, p=.002). No difference was seen in males. Mean plasma typtophan was significantly lower in fructose malabsorbers than non-malabsorbers (p=.02) and once again, divided by gender, lower tryptophan concentrations were only seen in females (fructose malabsorbers: 61.3±14.0µM, normal:74.7±16.5 µM, p=.03). Upon further statistical analysis, individuals with tryptophan concentrations lower than the median (=67.0µM) more often presented with a BDI score above the median (p=.036; Fisher exact test) and when analyses was restricted to fructose malabsorbers, a significant inverse relationship between tryptophan concentration and BDI scores were found both

overall (n=35; r=-0.348, *p*=.043) and when restricted to females (n=24; rs=-0.503, *p*=.014).

5.2 Tryptophan levels and Mood

Although serotonin (5-HT) is often thought of as a neurotransmitter exclusive to the central nervous system (CNS) due to its well-defined role in expression of depression, arousal, pain and other characteristics commonly attributed to CNS functioning, the major source of bioavailability is located in the bowel [102]. Low levels of brain 5-HT can contribute to decreases in mood [103] and are therefore the target of several antidepressants. The precursor of 5-HT is tryptophan, which is considered an essential amino acid, indicating it cannot be produced internally and must be obtained externally via the diet. Lowering tryptophan levels through dietary modifications is associated with a postprandial mood-lowering effect [104].

Ledochowski et al.[98] demonstrated that malabsorption of an individual FODMAP has been associated with decreases in tryptophan levels. According to this study, high intestinal fructose concentrations, as is the case with fructose malabsoprtion, seem to interfere with L-tryptophan metabolism and thus reduce the bioavailability of 5-HT. It was then hypothesized that this could be due in part to a combination of increased transit time and the phenomenon known as the Maillard reaction. The Maillard reaction, which is primarily associated with food science, is a heat-driven process where an amino acid becomes bound to a simple sugar. Ledochowski et al. theorized that malabsorbed fructose results in a fructose-L-tryptophan complex, which is then lost in excretion. Based on this theory, a diet high in multiple, poorly absorbed CHOs such as a high-

FODMAP diet, may lead to reduced levels of the bioavailability of tryptophan and possibly impact mood perception however, proof of concept studies are needed.

6.   Conclusion

Irritable Bowel Syndrome (IBS) is the most commonly diagnosed Gastrointestinal (GI) condition in the United States [48]. In 2012, it was estimated that 10% of Americans meet the diagnosable criteria for IBS, translating to 30 million people [48]. IBS is an umbrella term that incorporates a spectrum of chronic or recurrent symptoms including abdominal pain, bloating, distension, excessive wind and altered bowel habits when anatomical abnormalities and inflammation have been excluded [12]. A low-FODMAP diet is now considered an effective strategy for managing symptoms of IBS in Australia, with interest expanding across the world [12]. FODMAPs' ability to increase GI symptoms are centered around FODMAPs' three common functional properties; They are 1) poorly absorbed in the proximal small intestine, allowing substrate to reach the distal small intestine and proximal colon 2) small and osmotically-active, which increases the liquidity of luminal content due to osmosis and 3) rapidly fermented by gut microbiota, increasing the amount of gas present in the colon. Dietary adherence is crucial to the success of a low-FODMAP diet, however most people do not find the diet easy to incorporate into their life [8,10]. Several limitations of a low-FODMAP diet pertaining to dietary quality and health benefits have been suggested. Malabsorbed FODMAPs provide multiple benefits including a natural laxative effect due to their osmotic effects, a prebiotic effect with beneficial fermentation by-products [12] and production of a low glycemic response compared to other CHO [21]. Additionally malabsorption of certain

51

FODMAPs has been linked to increases in undesirable mood states [98-100]. Not one study has looked exclusively at healthy adults, changes in intake or looked at overall diet quality as compared to established guidelines. A study is needed looking at dietary quality of low- vs. high-FODMAP diets and should consider adherence and other factors that may influence efficacy and potential impact of the diet.

Appendix B

Methods

Study Design

The study was done by the Energy Balance Lab (EBL) at The University of Rhode Island (URI) in the spring/summer 2013. It was a randomized, single-blinded, cross-over study comparing two dietary conditions in a free-living setting; a low-FODMAP and a high-FODMAP diet. In order to ensure that the diet was single-blinded, the study was entitled "The Carb Study" and the two conditions were labeled "Diet 1" and "Diet 2" representing the low-FODMAP and high-FODMAP diets respectfully. The diet instruction booklet that corresponded to each dietary condition was developed specifically for this project based on multiple published articles [1,5,23,24]. The selection process was randomized, with a coin flip determining which group the first participant would begin. Each of the two conditions lasted 3 days: Tuesday, Wednesday, and Thursday. An eleven day wash out period where subjects consumed their normal diet separated the two conditions. The subjects had baseline measurements and measurements after completing each diet measured on Tuesday and Friday mornings after a 10 hour fast. In total, there were five visits: an initial assessment (visit 1), two baseline testing (visit 2 & 4), two post-diet testing (visits 3 & 5).

Recruitment

The majority of the subjects were recruited from a list of "Potential Study Volunteers" comprised of adults who were candidates or participants in previous,

nutrition-related studies and expressed a desire to be contacted for future studies. A mass email was sent from the EBL team to any adult on this list. In addition to this list, classroom announcements were made in three nutrition classes made up of primarily nutrition students or students in other health-related fields. The estimated attrition rate was expected to be low and was based on a study done by Dr. Melanson (The PI) with a similar demographic and study design (25). In total, 20 participants began the intervention, the attrition rate was 20% and the final sample size was 16. Of the four who did not complete, one subject dropped out due to a hospitalization that involved antibiotic treatment and three subjects did not report to the lab for an appointment.

Subjects

Overall, 18 healthy subjects, free of any gastrointestinal illness completed the study. Gastrointestinal illness included celiac disease, IBS, lactose or gluten intolerance, diverticular disease, colitis such as Crohn's disease or ulcerative colitis or stomach ulcers. Additional exclusion criteria included any food allergies, being a current smoker, being on a weight loss diet, pregnant or lactating, type 1 or 2 diabetes, adrenal disease, kidney or bladder problems a thyroid disease or currently taking any appetite suppressant medications.

Initial Assessment/Screening

During visit 1, potential participants completed an initial assessment and a screening which assured their status as a healthy adult clear of any GI complications. Once subjects were declared eligible, demographic measurements and assessment of

body fat percentage using the BOD POD Body Composition System (Life Measurement Instruments, Concord, Calif., USA) was performed. BODPODs are used to estimate % fat via air displacement plethysmography (ADP). The procedure has been described in full in a previous study[105]. In brief subjects are weighed in minimal clothing. They are then placed in the BOD POD where measurements of body volume are made. Once multiple measurements are made, if the body volume is within 150 ml, the BOD POD then measures thoracic lung volume. From the body mass, body volume and thoracic lung volume obtained, the BOD POD can then determine body density and % fat.

Baseline testing: Fasting

During the baseline visits, subjects reported to the EBL following a 10 hour fast where they completed baseline measurements of height, weight, waist circumference, and an appetite/discomfort questionnaire. In a fasting state, breath hydrogen, capillary glucose and lipid profile was also collected. *(Protocol regarding breath hydrogen, capillary glucose, lipid profile and changes in appetite are discussed in Appendix C however it is important to note that change in these variables are being analyzed as part of another student's thesis.)*The appetite/discomfort questionnaire was a 10 cm visual analogue scale (VAS) for subjects tor rate hunger, satiety, desire to eat and thirst. The use of VAS scales is considered a reliable and valid measurement of appetite [106]. The appetite/discomfort scale used is a five question, VAS-format scale that considered hunger, satiety, thirst and abdominal discomfort.

Baseline testing: Test Meal

Following these baseline measurements, subjects consumed a high-FODMAP test meal consisting of: two slices of whole wheat toast, one with 1 tbsp of honey and one with 1 tbsp of sugar free, no sugar alternative jam, 12 oz of 2% milk and 40 grams of raisins. The Test meal contained 1.141 grams of polyols, 28.494 grams of fructose, .661 grams of galactose and 18.234 grams of lactose, totaling 47.86 grams of FODMAPs. The amount of FODMAP was determined using the 2012 version of the Nutrition Data System for Research (NDS-R) from the Nutrition Coordinating Center (NCC) at the University of Minnesota. The test meal was comprised to have approximately 50 grams of FODMAPs. It is of note that NDSR, like most nutrition databases, does not quantify oligosacchardies such as FOS and GOS, thus, the grams of total FODMAPs is most likely slightly higher due to FOS commonly found in wheat. This number was based on standards used in breath hydrogen testing of lactose intolerance [99] and fructose intolerance [98].

Baseline testing: Postprandial testing

Thirty minutes postprandial, subjects completed the same appetite/discomfort and repeated the same collection methods as fasting measurements described above. A third and final round of testing using the same procedures was conducted 60 minutes postprandial. The break between these three testing points was allocated to subjects receiving dietary instructions for their intervention, and completion of a 24-hour recall. The total time of these visits was approximately 75 minutes.

Baseline Testing: Diet Instructions and Diet Booklet

56

During baseline visits, subjects met with a member of the research team educated in the FODMAP diet who provided each subject with a16 page diet instruction booklet labeled either "Diet 1" or "Diet 2". The booklets contained detailed lists of recommended and restricted foods. A brief, 15 minute diet explanation was also provided which included identifying encouraged and discouraged foods, brief tips and reiteration of the impotence of adhering to the diet for the purpose of the study's success. "Diet 1" corresponded to the low-FODMAP diet and "Diet 2" was the high-FODMAP diet.

Post-Diet Testing

An almost exact replica of baseline testing protocol was used for post-diet testing. The only addition was the addition of an "opinion regarding the diet" 6 question mixed VAS and free response questionnaire (Appendix D). The only exemption was that no dietary instructions were provided during the POST-Intervention. At the end of the POST-diet visit, subjects were told to either follow their normal diet (visit 3) or were informed that the study was completed (visit 5). The subjects received a $20 incentive on visit 3 and a $60 incentive on visit 5.

Post-diet testing: Diet opinion

The diet opinion scale (Appendix D) used during the POST-Intervention was developed for this project and had not been used in a previous study. The questionnaire was developed based on a questionnaire created by Gearry et al.[10] using items identified by Shepherd et al.[11] as potential barriers to adhering to a low-FODMAP diet. Of note,

since the completion of this study, a questionnaire with similar items has also been used by De Roest et al.[8].

Additional Questionnaires

In addition to in-lab data collected, subjects were given three days worth of questionnaires assessing appetite, symptoms and mood. The appetite questionnaire used was the same questionnaire described earlier, however the abdominal discomfort scale was omitted. It was filled out pre- and post-meals, mid-afternoon, mid-evening and before bed, for a total of nine times throughout the day. The mood and the symptom questionnaires were filled out daily, before bed. The mood questionnaire used (Appendix D) was a non-validated VAS questionnaire developed by the EBL and used in only one previous study [31]. The format was an eight question, VAS scale. The Symptoms questionnaire (Appendix D) was a new, 3-item, mixed VAS, yes/no and free response questionnaire developed by a gastroenterologist at Rhode Island Hospital that had not been used before in a study.

Instruments and methods for answering research questions

Dietary Quality

During visits 2, 3, 4 and 5, trained researchers conducted a 24 hour food recall corresponding to all food and beverage items consumed the previous day. The 24-hour food recall consisted of participants recalling every food or beverage item that they ate on the previous day, from midnight to midnight. Nutrition calculations were performed using the Nutrition System for Research (NDS-R) software version 12 developed by the

Nutrition Coordinating Center, University of Minnestoa, Minneapolis. NDS-R utilizes a multiple pass method described in full elsewhere [26]. Briefly, pass one included obtaining a quick list of foods consumed in the past 24 hours. In pass two, participants are asked to produce details regarding foods on their quick list including portion sizes and amounts eaten. In pass three the list is recited and participants are asked if any information was forgotten.

Foods that were not in the NDS-R database were cited as "missing foods" and corrected after the interview was completed. Resolution of a missing food usually required finding an NDSR substitute (very similar food or a generic version of a food) in the database and matching that substitute for CHO, protein, fat and kcals. Matching was defined as within 1-3 grams for each macronutrient and within 10 kcals for energy. For some foods, the FODMAP content was considered too variable for a substitution (for example ice cream brands and gluten free products). These foods were emailed to NDSR, who then provided an accurate nutrient breakdown for those items.

Dietary Quality: Healthy Eating Index 2010

From this NDSR output file, a single dietary quality score entitled The Healthy Eating Index 2010 (HEI-2010) was obtained through calculations described in greater detail in Appendix E. The HEI is a measure of dietary quality determined by how well an individual's diet compares with federal dietary guidelines, and based directly on the Dietary Guidelines for Americans (DGA) [29]. The DGA are issued every 5 years by the United States Department of Agriculture (USDA) and the US Department of Health and Human Services [29]. The HEI-2010 is the most up-to-date version, modified from the HEI-

2005 and based on the release of the 2010 DGA and revised USDA Food Patterns [29]. The actual score computed was a single number ranging from 0-100 with higher numbers representing better rated diets. The categories considered included total fruit, whole fruit, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, and empty calories [29]. The change in HEI-2010 score from PRE-, to POST-Intervention was used to define change in dietary quality score.

Dietary Adherence

NDS-R output files were used to sum total intake (g) of fructose, lactose and the sugar alcohols (erythritol, inositol, isomalt, lactitol, maltitol, mannitol, pinitol, sorbitol and xylitol.) These items were used to define FODMAP intake. It is important to note that because NDS-R (as well as most other nutrition database systems) cannot calculate consumption of GOS or FOS, this number obtained does not translate to total FODMAP intake. Dietary adherence therefore, was defined according to available FODMAP items. Adherence to the low-FODMAP diet was defined as a reduction of FODMAP from baseline to day three of each diet. Adherence to the high-FODMAP diet was defined as an increase in FODMAP from baseline to day three of the diet. There are currently no set values to define high or low-FODMAP diets

Comparing Mood with FODMAP Intake, Symptoms and Breath Hydrogen

As mentioned previously, mood and symptom questionnaires were obtained for each day of the 3 day intervention. Participants completed these questionnaires at night,

just prior to bed. The scores of interest were the scores obtained on the third day of the

intervention. FODMAP intake for that same day was reflected on the 24 hour food recall

obtained during the Post-Diet testing. This allowed for comparison of participants' mood

scores to 1) their intake of FODMAP, 2) their reported symptoms 3) their HEI-2010

scores on the same day and at the end of the three day intervention. Appendix F show

questionnaire data from mod variables that did not make it into the manuscript results.

Statistics

This was a secondary data analysis from a larger study powered on blood glucose.

Statistical analyses were performed using SPSS (v22). All variables met criteria for

normality. Baseline comparisons between subjects assigned to the two orders were

conducted using t-tests and X^2 tests. Primary outcomes (grams FODMAP and HEI-2010

scores) were assessed using separate 2 (treatment) x 2 (time) x 2 (order) mixed factorial

ANOVA followed by within-treatment paired t-tests (baseline and intervention). Eta^2 was

calculated to estimate effect size using Cohen's categories of small (.1), medium (.6) and

large (.14)[32]. Energy intake (kcal/day) was assessed using similar analyses. All other

inferential analyses of dietary components were performed using a 2 x2 repeated

measures ANOVA where the independent variables were treatment (low- vs. high-

FODMAP) and time (baseline vs. intervention). Paired t-tests compared mood, symptoms

and compliance factors between treatments and Pearsons bivariate correlations explored

relationships between variables. P value <0.05 was considered statistically significant.

Required Resources

Department computers with NDSR and SPSS were already set up and working in the

EBL. All necessary laboratory equipment including the Alere Cholestech LDX System

and the Quintron Model CM Clinical Microlazer were already set up and working in the

EBL. Food models were already available in the EBL

Appendix C: Protocol for breath hydrogen, blood glucose and blood lipid collection
Breath Hydrogen Collection Protocol
Warm Up Period
1.   Turn on system 15 minutes (at least) prior to use.
2.   Following the warm up period, adjust the front panel labeled "parts per million" until it reads "000"
Calibration
           Materials needed- Reference gas, SivRite cartridge, syringe, stopcock
1.   Pull "out" valve stem so that pilot light turns GREEN
2.   Using a syringe with stopcock, extract 20 ml of reference gas (concentration of 98 ppm).
3.   Place the SivRite cartridge directly into the flush port.
4.   Inject the reference gas into the machine via the SivRite cartridge. *(if reference gas cannot be injected, check to make sure A-the valve stem is pulled all the way out and B- the stopcock is open.)*
5.   After the gas has been flushed, push the valve stem "in" until the GREEN light changes to RED and observe the meter response.
6.   Once the meter response becomes stable, adjust the "calibrate" knob until it reads "098".
7.   Pull the valve stem "out" and the meter response should read "000".
8.   If meter response does not read "000", re-zero the instrument and repeat calibration process.
9.   Continue process until instrument is properly calibrated
Collection of Sample:
           Materials needed- Breath Collection kit (including mouth piece, collection bag and discard bag), SivRite cartridge, syringe, stopcock
1.   Ask subject to take deep breath and hold breath for 15 seconds.
2.   After 15 second has passed, have subject exhale normally into collection bag.
3.   Label Sample bag (Subject ID and Pre or Post meal).
Analyzing a Sample
1.   Using a syringe with stopcock, extract 20 ml of the sample gas from the collection bag.
2.   Pull the valve stem "out" so that the pilot light turns GREEN
3.   Connect the SivRite Cartridge to the flush port.
4.   Inject 20 ml of the sample gas into the machine via the SivRite Cartridge
5.   Push valve stem "in" until the light turns RED
6.   Record the H2 concentration (ppm) presented in the meter response
7.   Pull Valve stem "out" so that light turns GREEN and release the sample from the port
8.   Using the syringe, back flush 40 ml of room air into the machine.
9.   Repeat analysis using an additional 20 ml taken from the original collection bag.
10.   Take the average of the two numbers
           This process can be done after the participant has left. Samples are good for 2-3 hours in the breath collection bag
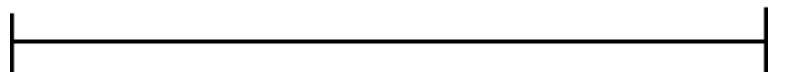
Appendix D: Questionnaires

Opinion regarding the diet questionnaire

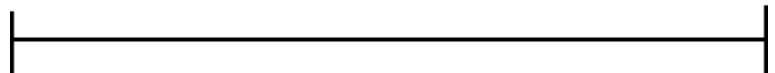**SUBJECT #:** _____ **DATE:** _____ **DIET: 1   2**

These questions relate to your personal opinion regarding the diet you had been asked to follow. Please rate yourself by placing a small "**x**" across the horizontal line at the point which best reflects your present feelings.

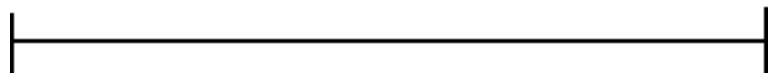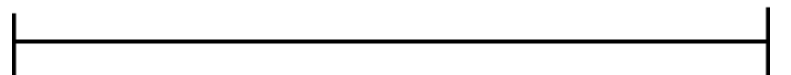1.   How easy/difficult had it been to implement the diet?

|————————————————————————————|

        very easy   very difficult

2.   How easy/difficult had it been to adhere to the diet?

|————————————————————————————|
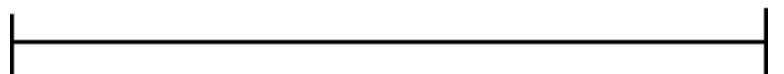
        very easy   very difficult

3.   How easy/difficult was it to obtain the appropriate food?

|————————————————————————————|

        very easy   very difficult

4.   How would you rank the overall taste?

|————————————————————————————|

        did not like it at all   liked it very much

5. What were the biggest challenges in following this diet?

_____

_____

_____

_____

6. What did you like about this diet?

_____

_____

_____

_____
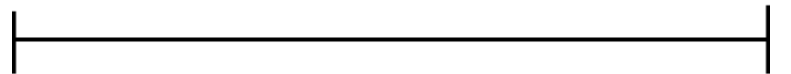
The Mood Questionnaire

SUBJECT:.#: _____   **DATE:** _____   **DIET: 1   2**

*Please fill this once a day before bed
These questions relate to your "mood state" at this time. Please rate yourself by placing a small "**x**" across the horizontal line at the point which best reflects your present feelings.
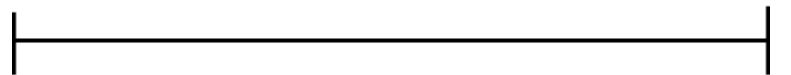
1.   How alert do you feel?

|———————————————————|

      very little   very much

2.   How sad do you feel?

|———————————————————|
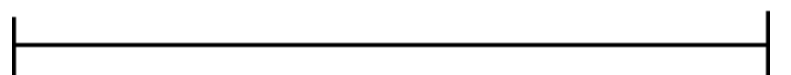
      very little   very much

3.   How tense do you feel?

|———————————————————|
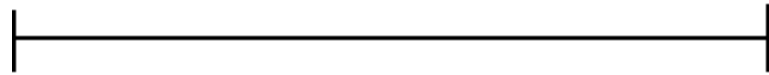
      very little   very much

4.   How much of an effort is it to do anything?

|———————————————————|
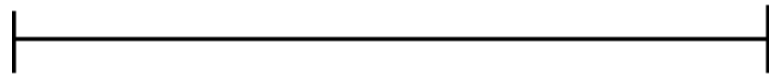
      very little   very much

5. How happy do you feel?

| |
| very little   very much |

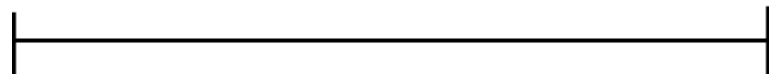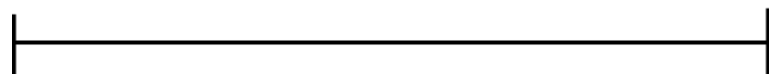6. How weary do you feel?

| |
| very little   very much |

7. How calm do you feel?

| |
| very little   very much |

8. How sleepy do you feel?

| |
| very little   very much |

The symptom questionnaire

<u>Abdominal Symptoms Questionnaire</u>

Please fill out this form every evening (preferably prior to going to bed) for each of the 3 days prior to your next scheduled visit.

1.   A) Are you currently suffering from any abdominal pain?   Yes   No

B) If yes, how severe is the abdominal pain?

|————————————————————————|

          No pain   Severe Pain

C) Please enter the number of days that you get the pain in every 10 days?
          *For example, if you enter 4 it means that you get pain 4 out of every 10 days. If   you get pain every day, enter 10.

          Number of Days with pain: [   ]

2.   A) Do you currently suffer from abdominal distension*?   Yes   No
     (Bloating, swollen or tight tummy)
        (*Women, please ignore distension related to periods)

B) If yes, how severe is you abdominal distension/tightness?

|————————————————————————|

          No distension   Very Severe

3.   How satisfied are you with your Bowel Habit?

|————————————————————————|

          Un-happy   Very Happy

Appendix E: Calculating the Healthy Eating Index 2010 (HEI-2010)

Calculation for the HEI-2010 was based off of a protocol developed by the Nutrition Coordinating Center (NCC) at the University of Minnesota based off of methods described in a previous study _ENREF_106[30]. It is important to note that it is only possible to estimate an approximation of the HEI-2010 score using NDSR.

Steps:

Step one of calculating the total HEI-2010, involved calculating each of the individual index components. Step two included taking that number and conforming it to the unit of measure used in the index (such as servings converted to cups). Step three involved comparing intake of each item to the score rubric (table 1). Step 4 involves summing the individual scores to produce a single HEI-2010 score. Two decimal points were used for every spot.

Table 4: Healthy Eating Index-2010 components and standards for scoring

Component	Optimum Score	Standard for maximum score	Standard for minimum score of zero
Total Fruit[a]	5	≥0.8 cup eq/1,000 kcal	No fruit
Whole Fruit[b]	5	≥0.4 cup eq/1,000 kcal	No whole fruit
Total Vegetables[c]	5	≥1.1 cup eq/1,000 kcal	No vegetables
Greens and Beans[c]	5	≥0.2 cup eq/1,000 kcal	No dark-green vegetables or beans or peas
Whole Grains	10	≥1.5 oz eq/1,000 kcal	No whole grains
Dairy[d]	10	≥1.3 cup eq/1,000 kcal	No dairy
Total Protein Foods[e]	5	≥2.5 oz eq/1,000 kcal	No protein foods
Seafood and Plant Proteins[ef]	5	≥0.8 oz eq/1,000 kcal	No seafood or plant proteins
Fatty Acids[g]	10	(PUFAs+MUFAs)/SFAs >2.5	(PUFAs+MUFAs)/SFAs ≤1.2
Refined Grains	10	≤1.8 oz eq/1,000 kcal	≥4.3 oz eq/1,000 kcal
Sodium	10	≤1.1 gram/1,000 kcal	≥2.0 grams/1,000 kcal
Empty Calories[h]	20	≤19% of energy	≥50% of energy

[a] Includes 100% fruit juice.
[b] Includes all forms except fruit juice.
[c] Includes any beans and peas not counted as Total Protein Foods.
[d] Includes all milk products, such as fluid milk, yogurt, cheese, and fortified soy beverages.
[e] Beans and peas are included here (and not with vegetables) when the Total Protein Foods standard is otherwise not met.

Calculation based on individual index component:

Total Fruit

1.   The following items were extracted from output file 9 from NDSR and summed up to give total fruit (servings): Citrus juice, fruit juice excluding citrus juice, citrus fruit, fruit excluding citrus fruit, avocado and similar, fried fruits and fruit-based savory snacks

2.   Total fruit (serving) was than divided by two to produce total fruit (cups)

3.   Total energy expenditure (taking from NDSR output file 04) was first divided by 1000.

4.   Then total fruit (cups) was divided by the results of step 3

5.   The result of step 2 was then multiplied by the optimum total fruit score (5) and divided by the standard for maximum total fruit score (.8) to yield the total fruit score. A maximum of 5 and minimum of 0 was used

Whole Fruit

1.   The following items were extracted from output file 9 from NDSR and summed up to give whole fruit (servings): citrus fruit, fruit excluding citrus fruit, avocado and similar, fried fruits and fruit-based savory snacks

2.   Whole fruit (serving) was than divided by 2 to produce total fruit (cups)

3.   Total energy expenditure (taking from NDSR output file 04) was first divided by 1000

4.   Whole fruit (cups) was divided by the results of step 3

5.   The result of step 2 was then multiplied by the optimum whole fruit score (5) and divided by the standard for maximum whole fruit score (.4) to yield the whole fruit score. A maximum of 5 and minimum of 0 was used

Total Vegetables

1.   The following items were unconditionally extracted from output file 9 from NDSR and summed up to produce total vegetables (servings): Dark-green vegetables, deep yellow vegetables, tomato, white potatoes, fried potato, other starchy vegetables, other vegetables, friend vegetables and vegetable juice.

2.   Legumes (cooked dried beans) was extracted and added to the total vegetable component score <u>only</u> if the "total protein foods" (including legumes (cooked dried beans)) max score (>2.5 oz eq/1000 kcals) was reached.

70

3.   Total vegetables (serving) was than divided by 2 to produce total vegetables (cups)

4.   Total energy expenditure (taking from NDSR output file 04) was first divided by 1000.

5.   Then total vegetables (cups) was divided by the results of step 4

6.   The result of step 3 was then multiplied by the optimum total vegetable score (5) and divided by the standard for maximum total vegetable score (1.1) to yield the total vegetable score. A maximum of 5 and minimum of 0 was used

Greens and Beans

1.   Dark green vegetables (servings) from output 09 was extracted and used as the greens and beans score

2.   Legumes (cooked dried beans) was extracted and added to the total vegetable component score only if the "total protein foods" (including legumes (cooked dried beans)) max score (>2.5 oz eq/1000 kcals) was reached.

3.   Greens and beans (serving) was than divided by 2 to produce greens and beans (cups)

4.   Total energy expenditure (taking from NDSR output file 04) was first divided by 1000.

5.   Then greens and beans (cups) was divided by the results of step 4

6.   The result of step 3 was then multiplied by the optimum total vegetable score (5) and divided by the standard for maximum total vegetable score (.2) to yield the total vegetable score. A maximum of 5 and minimum of 0 was used

Whole Grains

1.   The following items were extracted from output file 09 from NDSR and summed up to produce whole grains (oz equiv): Grains, flours and dry mixes-whole grains, loaf-type bread and plain rolls- whole grain, other bread (quick breads, corn muffin, tortillas)-whole grain, crackers-whole grain, pasta-whole grain, ready-to-eat cereal (not presweetened)-whole grain, ready-to-eat cereal (presweetened)-whole grain, cakes, cookies, pies, pastries, donnish, doughnuts and cobblers-whole grain, snack bars-whole grain, snack chips-whole grains, popcorn, and flavored popcorn.

2.   Total energy expenditure (taking from NDSR output file 04) was first divided by 1000.

3.   The result of step 1 was then multiplied by the optimum whole grains score (10) and divided by the standard for maximum total vegetable score (1.5) to yield the whole grains score. A maximum of 10 and minimum of 0 was used.

Diary

1.   The following items were extracted unconditionally from output file 9 from NDSR and summed up to give total fruit (servings): milk-whole, milk, reduced fat, milk, low fat and fat free, milk, nondiary, ready-to-drink flavored milk, whole, ready-to-drink flavored milk-reduced fat, ready-to-drink flavored milk-low fat and fat free, sweetened

71

flavored milk beverage power with non-fat dry milk, artificially sweetened flavored milk beverage with non-fat dry milk, cheese-full fat, cheese-reduced fat, cheese-low fat and fat free, cheese-nondairy, yogurt-sweetened whole milk, yogurt-sweetened low fat, yogurt-sweetened fat free, yogurt- artificially sweetened whole milk, yogurt- artificially sweetened low fat, yogurt-artificially sweetened fat free, yogurt-nondairy, pudding and other diary deserts, artificially sweetened pudding and other diary deserts, dairy-based sweetened meal replacement/supplement, diary-based artificially sweetened meal replacement/supplement

2. Frozen diary deserts was also obtained from output file 09, then times by three and added to the score obtained in step one to produce the total diary score

3. Total energy expenditure (taking from NDSR output file 04) was first divided by 1000.

4. Then total diary (cups) was divided by the results of step 3

5. The result of step 4 was then multiplied by the optimum total diary score (10) and divided by the standard for maximum total fruit score (1.3 cups) to yield the diary score. A maximum of 10 and minimum of 0 was used

Total Protein Score

1. The following items were extracted unconditionally from output file 9 from NDSR and summed up to total protein (oz equiv): beef, lean beef, veal, lean veal, lamb, lean lamb, fresh pork, lean fresh pork, cured pork, lean cured pork, game, poultry, lean poultry, fried chicken-commercial entrée and fast food, fish-fresh and smoked, lean fish-fresh and smoked, fried fish-commercial entrée and fast food, shellfish, fried shellfish-commercial entrée and fast food, cold cuts, lean cold cuts and sausage, organ meats, baby food meat mixtures, eggs, egg substitute, nuts and seeds, nuts and seed butters and meat alternative.

2. From the NDSR output file 09, (legumes x2) was added <u>only if</u> the score from step 1 was less than <2.5 oz/1000 kcals.

3. Total energy expenditure (taking from NDSR output file 04) was first divided by 1000.

4. Then total protein score (oz) was divided by the results of step 3

5. The result of step 4 was then multiplied by the optimum total diary score (5) and divided by the standard for maximum total protein score (2.5 oz) to yield the diary score. A maximum of 5 and minimum of 0 was used

Seafood and plant protein

1. The following items were extracted unconditionally from output file 9 from NDSR and summed up to seafood and plant protein (oz equiv): fish-fresh and smoked, lean fish- fresh and smoked, fried fish-commercial entrée and fast food, shellfish, fried shellfish- commercial entrée and fast food, nuts and seeds, nut and seed butters, meat alternative

2. From the NDSR output file 09, (legumes x2) was added <u>only if</u> the score from step 1 was less than <2.5 oz/1000 kcals.

3. Total energy expenditure (taking from NDSR output file 04) was first divided by 1000.
4. Then total protein score (oz) was divided by the results of step 3
5. The result of step 4 was then multiplied by the optimum total diary score (5) and divided by the standard for maximum total protein score (.8 oz) to yield the diary score. A maximum of 5 and minimum of 0 was used

Fatty acids

1. From NDSR output file 04 the sum of all PUFAs and total MUFAs were extracted and added together
2. From NDSR output 04 the sum of all SFAs were added together
3. The result of step 1 was divided by the result of step 2
4. The following equation was used to determine the fatty acid component score (result of step 3-1.2)*10/1.3. A minimum of 0 and a maximum of 10 was used

Refined Grains

1. The following items were extracted from output file 9 from NDSR and summed up to give refined grains (oz equiv):grains, flour and dry mixes-some whole grains, grain, flours and dry mixes-refined grain, loaf-type bread and plain rolls-some whole grain, loaf-type bread and plain rolls-refined grains, other bread (quick bread, corn muffins, tortillas)- some whole grain, other breads (quick bread, corn muffins, tortillas)-refined grain, crackers-some whole grains, crackers-refined grains, pasta-some whole grain, pasta-refined grains, ready-to-eat cereal (not presweetened)- some whole grains, ready-to-eat cereal (not presweetened)-refined grain, ready-to-eat cereal (presweetened)-some whole grain, ready-to-go cereal (presweetened)-refined grain, cakes cookies, pies, pastries, danish, doughnuts and cobblers-some whole grain, cakes cookies, pies, pastries, danish, doughnuts and cobblers-refined grains, Snack bar-Some whole grain, snack bars-refined grains, snack chips-some whole grains, snack chips-refined grains, baby food grain mixtures-refined grains
2. Total energy expenditure (taking from NDSR output file 04) was first divided by 1000.
3. Then total protein score (oz) was divided by the results of step 3
4. The following formula was then applied =2.5-((the result of step 3)-1.8).
5. The following formula was then used to yield the final refined grain score ((the result of step 5)*10/2.5). A minimum of 0 and maximum of 10 was used.

Sodium

1. The total amount of sodium (mg) extracted from output 09 from NDSR was obtained and multiplied by 1000 to yield sodium in g
2. Total energy expenditure (taking from NDSR output file 04) was first divided by 1000.
3. The following formula was then applied =.9-((result of step 2)-1.1)

4.　　　The following formula was then used to yield the final refined grain ((result of step 3)*10/0.9) a minimum of 0 and a maximum of 10 was used

Empty calories

1.　　　From NDSR output file 04:
a.　　　Saturated fat (g) x 9 kcals/gram=kcals from saturated fat
b.　　　Total trans fat (g) x 9 kcal/gram= kcal from trans fat
c.　　　Added sugar (by total sugar (g)) x 4 kcal/gram=kcal from added sugar
2.　　　From NDSR output file 04, alcohol consumption was determined by the following steps:
a.　　　Total daily energy intake (kcals) X 0.013 (g/kcal allowable alcohol)= allowable alcohol (g)
b.　　　If alcohol (g) is > than allowable alcohol (g), then:
i.　　　[alcohol (g) – allowable alcohol (g)] x 7 kcal/g = kcal from excess alcohol
3.　　　Sum the results of 1-a,-b,-c and 2-b-i
4.　　　Based on the total energy intake from output file 04, the following equation was used
a.　　　[kcals from empty calories/total kcals] X 100 = % energy from empty calories
5.　　　Then, the following equation was used: 100-(result of step 4-a)
6.　　　The following formula was then used to yield the final empty calorie score: ((the result of step 5-50))*20/31. A minimum of 0 and a minimum of 20 was used

Calculating the total HEI-2010
1.　　　The results of each individual component scores was added together to yield the HEI-2010

Appendix F: Tables & Other Results

Table 5: Differences in mood and GI distress scores between the low and high-FODMAP diet (n=16)

	Low-FODMAP	High-FODMAP	Δ	t
Alert	4.44±2.51	6.03±2.80	-1.58	-1.904
Sad	2.46±2.14	4.14±3.44	0.32	0.740
Tense	4.14±2.57	3.44±2.46	0.71	0.937
Effort Needed	4.73±2.59	4.04±2.52	0.69	1.437
Happy	6.19±1.76	6.55±1.68	-0.36	0.621
Weary	5.86±3.01	3.88±2.61	**1.98**	**2.894***
Calm	5.49±2.38	5.68±2.31	-0.19	-.241
Sleepy	7.00±2.23	6.74±1.98	0.27	.469
Ab. Pain	.61±1.40	.31±.99	0.3	.885
Ab. Distention	.98±1.86	.58±1.86	0.39	.573
Satis. With BM	6.23±1.56	6.36±2.44	-0.08	0.889

*=p<.05
Differences between low- and high-FODMAP diet compared using a Paired ttest

75

Tables 6: The correlation between selected nutrients, mood score and GI score

	Alert	Sad	Tense	Effort needed	Happy	Weary	Calm	Sleepy	Abd Pain	Abd Distention	Satis. With BM
FODMAP intake	.487**	.098	-.284	.005	.274	-.269	.050	-.243	-.186	-.116	.165
HEI-2010	-.204	.276	.297	.211	-.363*	.222	-.151	.314	-.214	.006	-.048
Total Calories (kcal)	.357*	-.036	-.257	-.096	.224	-.081	.193	-.196	-.047	.078	-.054
Total Fat (g)	.427*	-.075	-.400*	-.288	.125	-.306	.138	-.338	-.180	.042	-.095
% Cal from fat	.121	-.066	-.345	-.368*	-.109	-.448	.033	-.254	-.197	-.089	-.170
Total Protein (g)	.226	.203	-.126	.027	-.196	.022	-.189	-.070	-.230	.166	.016
% Cal From Protein	-.113	.345	.176	.155	-.623**	.139	-.531**	.215	-.212	.033	.161
Total CHO (g)	.313	-.078	-.201	-.007	.344	.029	.300	-.081	.004	.073	.028
% Cal From CHO	.022	-.107	.145	.221	.393*	.282	.235	.153	.192	.109	.134
Starch (g)	.160	-.100	-.178	.028	.296	.084	.290	.104	.052	.123	-.005
Total Fiber (g)	.189	.064	-.172	.081	.057	.139	.314	.080	-.189	.052	-.022
Total Sugar	.381*	-.071	-.156	-.070	.319	-.049	.205	-.257	-.025	-.030	.098
Glucose (g)	.473**	-.056	-.356*	.106	.376*	.086	.350	-.238	-.116	.048	.270
lactose (g)	.390*	-.020	-.217	-.125	.169	-.437*	-.223	-.067	-.168	-.147	.086
Fructose (g)	.314	.118	-.201	.090	.214	.021	.235	-.253	-.088	-.005	.145
total sugar (g)	.381*	-.071	-.156	-.070	.320	-.048	.203	-.256	-.025	-.030	.098
Added Sugars	.288	-.100	-.122	-.159	.237	-.010	.180	-.323	.020	.041	.033
glycemic Index	.040	-.087	.111	.202	.194	.385*	-.120	-.030	.296	.445*	.095
Caffeine	.252	-.295	-.435*	-.388*	.171	-.142	.333	-.376*	-.200	.244	-.159
Abd. Pain	-.384*	-.032	.352	.234	-.002	.377*	-.142	.193			
Abd. Distention	-.093	.051	.065	.019	-.209	.212	.016	.124			
Satis. With BM	.008	.022	.030	.459**	.115	.382*	-.084	.286			

76

Table 7: Healthy Eating index-2010 raw numbers (unadjusted per 1000 kcal)

HEI Component	Low-FODMAP diet			High-FODMAP diet			ANOVA[a]	
	Baseline	**Day 3**	**Δ**	**Baseline**	**Day 3**	**Δ**	**F (1,15)**	η^2
Total Fruit (cups)	0.77±1.02	.93±.88	0.17	.93±1.15	.75±.60	-0.18	0.51	-
Whole Fruit (cups)	.62±.78	.79±.83	0.17	.65±.77	.45±.43	-0.19	1.34	-
Total Vegetable (cups)	1.50±1.41	1.75±1.40	0.25	1.65±1.19	1.13±1.07	-0.52	1.82	-
Greens & Beans (cups)	.21±.59	.40±.57	0.19	.45±.75	.29±.47	-0.17	2.22	-
Whole Grain (oz)	2.07±3.55	1.16±1.33	0.9	2.01±3.15	1.94±2.23	-0.07	0.72	-
Dairy (cups)	2.29±1.67	1.11±1.29	-1.18	2.85±3.44	3.16±3.30	0.3	2.01	-
Total Protein (oz)	4.88±4.99	7.08±5.98	2.19	4.80±4.52	6.06±4.93	1.26	0.15	-
Seafood & Plant (oz)	1.20±2.85	1.49±2.14	0.29	1.99±3.12	1.27±2.86	-0.72	0.37	-
Refined Grain (oz)	6.47±4.65	2.79±3.46	**-3.67****	5.59±4.62	7.20±4.63	-1.61	10.562**	**.41**
Empty calories (kcals)	620.02±455.62	342.08±283.96	**-277.94***	552.56±445.97	610.49±411.47	57.93	8.02*	**.35**

*=P<.05, **=P<.01

A 2 (treatment) X 2 (time) repeated measures ANOVA with post hoc ttest was used.

[a]= the time*treatment interaction F statistic reported

77

Table 8: Correlation between FODMAP intake, mood scores and HEI-2010 scores

Correlation Coefficients (n=15-16)					
FODMAP Intake				FODMAP Intake	
	Low-FODMAP	High-FODMAP		Low-FODMAP	High-FODMAP
Mood variable			HEI- 2010 variable		
Alert	.343	.497	Total Fruit Score	.089	-.241
Sad	.305	-.014	Whole Fruit Score	-.100	-.205
Tense	-.218	-.285	Total Vegetable Score	.303	.187
Effort needed	.189	-.054	Greens and Beans Score	.070	-.023
Happy	.159	.423	Whole Grain Score	-.171	-.296
Weary	-.068	-.282	Dairy Score	.106	**.532***
Calm	.310	-.337	Total Protein Score	-.220	-.328
Sleepy	-.311	-.163	Seafood & Plant Score	.370	-.362
			Fatty Acid Score	.296	.490
			Refined Grain Score	-.054	-.016
			Sodium Score	-.228	-.363
			Empty Calorie Score	-.221	-.420
			Total HEI-2010	-.023	**-.554***

*p<.05

After completion of each diet, Random subjects (low-FODMAP n=9, high-FODMAP n=7) completed a 10 cm VAS scale regarding their opinion of the diet. The median score for "How easy/difficult had it been to implement the diet? " (0=very easy, 10=very difficult) were higher (more difficult) for the low FODMAP diet (median response 6.4, SD= 2.1, range 0.9-8.0, interquartile range 2.1) compared to the high-FODMAP diet (median response 4.8, SD=2.8, range 1.1-8.3, interquartile range=3.4). The median score for the question "How easy/difficult had it been to adhere to the diet?" (0=very easy, 10=very difficult) was higher for the low-FODMAP diet (median responds 5.7, SD= 1.9, range 1.2-7.8, interquartile range= 1.9) compared to the high-FODMAP diet (median responds 4.6, SD= 2.4, range 0.8-7.3, interquartile range= 4.7). The median score for the question "How easy/difficult was it to obtain the appropriate food?" (0=very easy, 10=very difficult) was lower (easier) for the low-FODMAP diet (median responds 2.5, SD= 1.7, range 1.2-5.8, interquartile range 3.2) compared to the high-FODMAP diet (median responds 4.5, SD= 2.3, range .9-5.9, interquartile range 4.7). Median scores for the question "How would you rank the overall taste?" (0=did not like it at all, 10=liked it very much) were lower for the low-FODMAP diet (median score 4.6, SD= 2.4, range 0-8.0, interquartile range 2.2) compared to the high-FODMAP diet (median scores 7.0, SD= 1.5, range 4.7-8.9, interquartile range 2.6).

Two free response questions were also included on the questionnaire. For the question "What were the biggest challenges in following this diet?" responses for the low-FODMAP diet included: 1)lack of variety, 2)changing from his/her normal diet (n=2), 3) food availability, 4)restriction of milk and apples, 6)lack of options in school

79

dining hall, 6)unable to use sweeteners and 7)having to pay close attention to foods eaten.

For the question, "What did you like about this diet?" responses from the low-FODMAP diet included 1)trying different foods (2), 2)increasing fruits (1) and vegetables (2), 3) realizing how many carbohydrates he/she consumes, 4) enjoyed options (did not specify if this means as compared to the high-FODMAP diet and 5) enjoyed the high fiber foods and eliminating old foods. For the high-FODMAP diet, reported challenges include 1) changing from normal diet, 2) not eating rice, 3) wanting food not offered on the diet. For "what did you like about this diet?", responses on the high-FODMAP diet include 1)realizing what I eat, 2)able to eat pasta, 3)easier to follow (than the low-FODMAP diet).

Appendix G. Diet Instruction Booklets

Low-FODMAP diet (Diet 1)

Diet 1

Contact Information

Unsure about something?

In a pinch it is probably safer to avoid it but feel free to call us at, Lab Phone 401-874-2067, or e-mail us at carbstudy.URI@gmail.com during the day if you have any questions.

Diet Tips

- "Gluten-free" breads, pastas, and bake mixes are good alternatives to the usual kinds, which contain wheat.
- Even for "Allowed" foods, try not to eat too much in one sitting, but also don't stress over exact serving sizes.
  - For example, you shouldn't eat a whole two-pound bag of grapes in one day, but don't feel like you need to count out exactly how many grapes you can have.
- Check the Ingredients List on food labels and look for any prohibited foods.
- If you're not sure if an item at a restaurant contains a particular prohibited food, ask your server or someone who works there if they have that information.
  - This will be especially useful for foods containing wheat and milk.
  - It may be easier to avoid or limit use of restaurants for the duration of the test diet.

Fruit To Avoid

FRUITS

- Apple
- Apricot
- Avocado
- Blackberry
- Cherry
- Custard apple
- Longon
- Lychee
- Mango
- Nashi
- Nectarine
- Peach
- Pear
- Persimmon
- Plum
- Prunes
- Sugar snap peas
- Canned fruit
- Watermelon
- Concentrated fruit sources
- Large servings of fruit
- Dried fruit
- Fruit juice

82

Fruits To Eat

- Banana
- Blueberry
- Boysenberry
- Carrabolla
- Cantaloupe
- Durian
- Grape
- Grapefruit
- Honeydew
- Kiwifruit
- Lemon
- Lime
- Mandarin
- Orange
- Passion fruit
- Pawpaw
- pineapple
- Raspberry
- Rhubarb
- Rockmelon
- Star anise
- Strawberry
- Tangelo
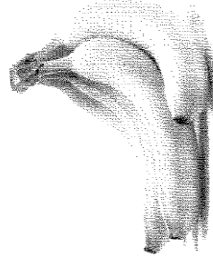
OTHER

Alcohol

Allowed
- Wine (limit one 5 oz serving)
- Beer (limit one 12 oz serving)
- Neutral Grain Spirits (limit one 1.5 oz serving)
  - Ex. vodka, whiskey, gin

Not Allowed
- Rum

One mixed drink with
- 1.5 fl oz (44 mL)
  of 80-proof liquor
  (such as vodka,
  gin, scotch, bourbon,
  brandy, or rum)

5 fl oz (148 mL)
of wine

12 fl oz (355 mL) of
beer or wine cooler

Sweeteners to Eat

Sweeteners
- Any artificial sweetener not ending in "-ol" (in small quantities)
- Sugar (sucrose)
- Glucose

Honey substitutes
- Maple syrup
- Golden syrup
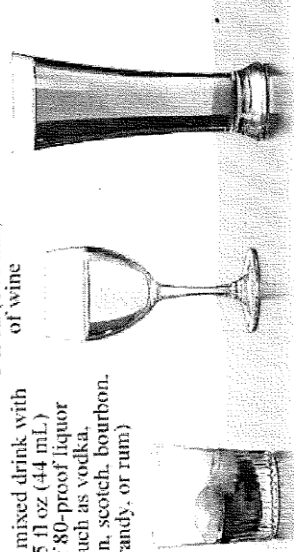
VEGETABLES

Veggies To Avoid

- Artichokes
- Asparagus
- Beetroot
- Broccoli
- Brussels sprouts
- Cabbage
- Cauliflower
- Eggplant
- Fennel
- Garlic
- Green peppers
- Leeks
- Mushrooms
- Okra
- Onions (all types)
- Peas
- Shallots
- Snow peas
- Spring onion
- Sweet corn

Veggies To Eat

- Alfalfa
- Artichoke
- Bamboo shoots
- Bean shoots
- Beets
- Bok choy
- Bell peppers
- Butternut squash
- Carrot
- Capsicum
- Celery
- Chives
- Choko
- Choy sum
- Corn
- Cucumber
- Endive
- Ginger
- Green beans
- Lettuce

- Olives
- Parsnip
- Potato, white
- Pumpkin
- Red pepper
- Scallions (green onions)
- Silver beet
- Spinach
- Spring onion
- Summer squash- yellow
- Swede
- Sweet potato
- Taro
- Tomato
- Turnip

OTHER

Sweeteners To Avoid

Sweeteners

- Corn syrup
- High fructose corn syrup
- Fructose
- Honey
- Isomalt

Sugar Alcohols

- Maltitol
- Mannitol
- Sorbitol
- Xylitol
- any sweetener ending with "-ol"

85

Protein To Eat

All Meat (except breaded meats)

All Nuts (except pistachios)

- Almonds
- Macadamias
- Peanuts
- Pecans
- Pine nut
- Pumpkin seeds
- Sesame Seeds
- Sunflower seeds
- Walnuts

Grains To Avoid

All grains that contain gluten need to be avoided

- Wheat
- Rye
- Barley
- Crackers
- Cookies
- Couscous
- Pasta

Grains To Eat

All gluten-free grains are okay

- **Gluten free bread**
- **Gluten free pasta**
- Arrowroot
- Corn flakes
- Millet
- Oats
- Oat bran
- Polenta
- Phylum
- Quinoa
- Rice: brown and white
- Rice bran
- Sorghum
- Tapioca

PROTEIN

Protein To Avoid

Breaded Meat

Pistachios

All Beans and Legumes

- Baked beans
- Black Beans
- Chickpeas (Garbanzo beans)
- Hummus
- Kidney beans
- Lentils
- Red kidney beans
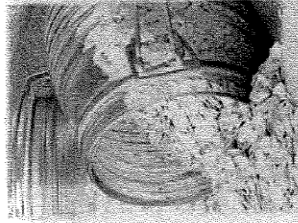
Dairy To Eat

- o
- Hard cheeses
  - o Cheddar
  - o Swiss
  - o Parmesan
  - o Brie
  - o Feta
  - o Camembert
  - o Mozzarella
- Lactose-free Milk
- Lactose-free Yogurt
- Ice cream Substitutes
  - o Galati
  - o Sorbet
- Butter
- Butter substitute
  - o Olive oil
- Almond milk
- Coconut Milk
- Oat Milk
- Rice Milk
- Soy milk
- Kefir

Dairy To Avoid

- Soft un-ripened cheeses
  - o Cottage
  - o Cream
  - o Mascarpone
  - o Ricotta
- Milk from cows, goats or sheep
- Yogurt
- Custard
- Ice cream
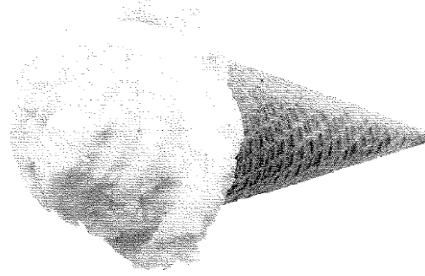
Diet 2

Discouraged Fruits

- Banana
- Blueberry
- Boysenberry
- Carrabolla
- Cantaloupe
- Durian
- Grape
- Grapefruit
- Honeydew
- Kiwifruit
- Lemon
- Lime
- Mandarin
- Orange
- Passion fruit
- Pawpaw
- Pineapple
- Raspberry
- Rhubarb
- Rockmelon
- Star anise
- Strawberry
- Tangelo
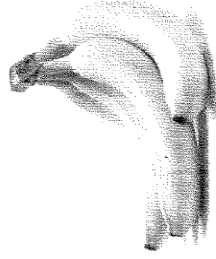
Contact Information

Unsure about something?

Feel free to call us at, Lab Phone 401-874-2067, or e-mail us at carbstudy.URI@gmail.com during the day if you have any questions.

Encouraged Fruits

- Apple
- Apricot
- Avocado
- Blackberry
- Cherry
- Custard apple
- Longon
- Lychee
- Mango
- Nashi
- Nectarine
- Peach
- Pear
- Persimmon
- Plum
- Prunes
- Sugar snap peas
- Canned fruit
- Watermelon
- Dried fruit
- Fruit juice

Diet Tips

- Aim to have at least 2 "Encouraged" foods at every meal and at least 1 "Encouraged" food for every snack. More is better, if you can!

- Try not to have "Discouraged" foods, in favor of 'Encouraged" foods. To this end, it might be prudent to limit yourself to 1 "Discouraged" food per meal.

- You can eat any foods NOT in this booklet as you normally would.

91
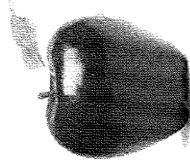
Encouraged
Sweeteners

Sweeteners
- Corn syrup
- High fructose corn syrup
- Fructose
- Honey
- Isomalt

Sugar Alcohols
- Maltitol
- Mannitol
- Sorbitol
- Xylitol
- any sweetener ending with "-ol"
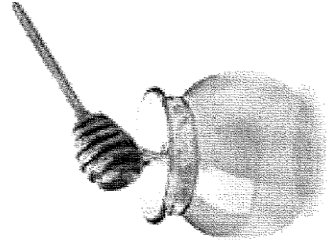
VEGETABLES

Discouraged
Veggies

- Alfalfa
- Artichoke
- Bamboo shoots
- Bean shoots
- Beets
- Bok choy
- Bell peppers
- Butternut squash
- Carrot
- Capsicum
- Celery
- Chives
- Choko
- Choy sum
- Corn
- Cucumber
- Eggplant
- Endive
- Ginger
- Green beans

- Lettuce
- Olives
- Parsnip
- Potato, white
- Pumpkin
- Red pepper
- Scallions (green onions)
- Silver beet
- Spinach
- Spring onion
- Summer squash-yellow
- Swede
- Sweet potato
- Taro

Encouraged Veggies

- Artichokes
- Asparagus
- Beetroot
- Broccoli
- Brussels sprouts
- Cabbage
- Cauliflower
- Eggplant
- Fennel
- Garlic
- Green peppers
- Leeks
- Mushrooms
- Okra
- Onions (all types)
- peas
- Shallots
- Snow peas
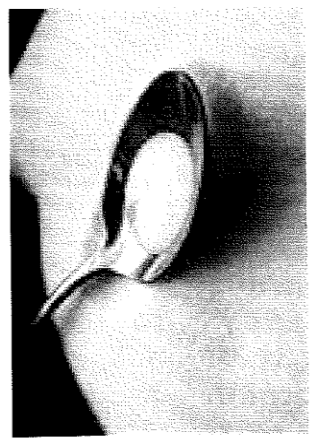- Spring onion
- Sweet corn
- Yam
- Zucchini
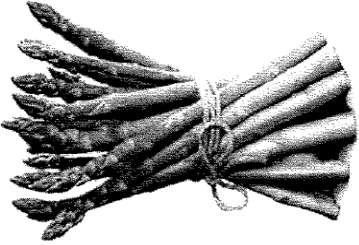
OTHER

Discouraged Sweeteners

Sweeteners
- Any artificial sweetener not ending in "-ol" (in small quantities)
- Sugar (sucrose)
- Glucose

Honeys substitutes
- Maple syrup
- Golden syrup

PROTEIN

Encouraged Protein

Nuts

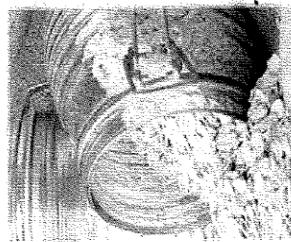- Pistachios

All Legumes

- Baked beans
- Chickpeas
- Hummus
- Kidney beans
- Lentils
- Red kidney beans
- Black Beans

GRAINS

Discouraged Grains

- Arrowroot
- Corn flakes
- Millet
- Oats
- Oat bran
- Polenta
- Phylum
- Quinoa
- Rice: brown and white
- Rice bran
- Sorghum
- Tapioca

GRAINS

Encouraged Grains

- Wheat
- Rye
- Barley
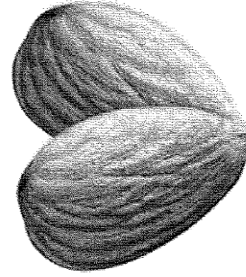- Crackers
- Cookies
- Couscous
- Pasta

PROTEIN

Discouraged Protein

All Nuts (except pistachios)

- Almonds
- Macadamias
- Peanuts
- Pecans
- Pine nut
- Pumpkin seeds
- Sesame Seeds
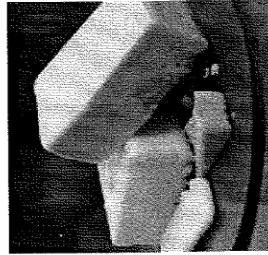- Sunflower seeds
- Walnuts

Encouraged Dairy

Dairy: Cheeses

- Soft un-ripened cheeses
  - Cottage
  - Cream
  - Mascarpone
  - Ricotta

Dairy: Other

- Milk from cows, goats or sheep
- Custard
- Ice cream

Discouraged Dairy

Dairy: Cheeses

Hard cheeses
- Cheddar
- Swiss
- Parmesan
- Brie
- Feta
- Camembert
- Mozzarella

Dairy: Other

- **Lactose Free Milk and Yogurt**
- **Butter substitute**
  - Olive oil
- Almond milk
- Butter
- Coconut Milk
- Green Valley Yogurt
- Ice cream Substitutes
  - Galati
  - Sorbet
- Lifeway Kefir (strawberry or blueberry)
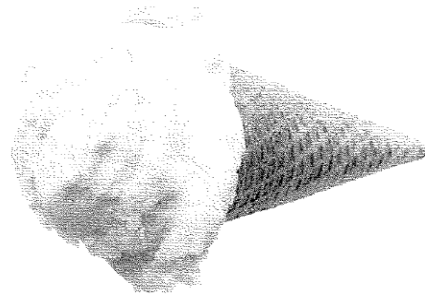- Oat Milk
- Rice Milk
- Soy milk

96

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