RESEARCH PROTOCOL

Date	**3/1/17**
Title	Impact of diet on functional gastrointestinal symptoms; a national population based survey
Principal Investigator	Rachel N. Pauls, MD
Sub-Investigators	Joshua Max, MD
Research Specialist	Eunsun Yook, MS
Department	Department of OB/Gyn, Division of Urogynecology and Reconstructive Pelvic Surgery; TriHealth Digestive Institute, Division of Gastroenterology
Hatton #	**17-006**

Purpose of Study:

- To delineate the role of diet in functional gastrointestinal (GI) symptoms.
- To determine the prevalence of functional GI disorders in the general population.
  - **Primary Aim:** To describe common triggers for food-related GI symptoms.
  - **Secondary Aims:** To assess prevalence of self-reported functional GI disorders and awareness of dietary modification programs for GI symptoms.

Hypothesis or Research Question

- We hypothesize that functional GI symptoms are very common, and may not be associated with formal diagnoses.
- We further hypothesize that certain foods may be triggers for symptoms, and that food 'sensitivity' is common in the population.
- Finally, we hypothesize that the majority of people are aware of gluten-free eating but are less aware of other dietary treatments for GI symptoms.

Background

Hippocrates said "Let food be thy medicine, and medicine be thy food"[1]. This quote rings true today, more than ever before. Functional GI disorders, involving symptoms such as gas/bloating, diarrhea, constipation and abdominal pain, are estimated to impact between 35 and 45 million Americans, an overwhelming 15-20% of the population. These symptoms are responsible for upwards of 20 billion dollars in healthcare costs and extensive loss of quality of life for sufferers[2,3]. Moreover, many patients suffer in silence, with 67% of subjects waiting more than a year before treatment, and 11% waiting over 10 years[4]. Irritable bowel syndrome or IBS is the most prevalent functional GI disorder[5], and several recent studies support the idea that dietary modifications may be key to alleviating this condition[6-16].

Food sensitivities and reported intolerance to lactose, gluten, wheat, and carbohydrates are increasing globally. While the mechanism is unclear, restriction of particular foods or food groups may alleviate functional GI symptoms. Indeed, both gluten-free and low-FODMAP diets

have been shown to reduce symptoms in affected patients, and not exclusively in those with celiac disease or lactose intolerance[16,17].

The low-FODMAP diet was initially described in 2006, and to date, dozens of well-designed studies have confirmed its benefit for IBS[11,13-15,18-27]. FODMAP is an acronym standing for Fermentable, Oligo, Di, and Mono-saccharides and Polyols. These short-chain carbohydrates are poorly digested and can lead to symptoms of gas, bloating, diarrhea and constipation. Other disorders showing benefit from FODMAP restriction include inflammatory bowel disorders (Crohn's disease and colitis), gastroparesis, diverticulitis, post-gastric resection and small intestinal bacterial overgrowth (SIBO)[9,12,28-32]. Benefit from this eating plan has surpassed touted success of medications commonly prescribed for IBS, without the side effects and high cost[1].

Thus, the purpose of this study is to document GI symptoms among the US population, as well as to ascertain awareness and utilization of dietary treatments that exist. Similar research has been conducted on small samples sizes in the United Kingdom[17] but is lacking in the US. This information is important in identifying knowledge gaps and will aid both physicians and dietitians to educate their patients about these programs. Furthermore it is important for health care providers to understand the a priori knowledge and utilization of dietary modifications amongst sufferers of functional GI disorders.

Research Plan

- **Study Design**
  - This cross-sectional survey study will be administered through a secure online server at SurveyMonkey®.

- **Participants**
  - The survey will be administered to men and women between the ages of 18 and 80.
  - Subjects will be recruited via email.
  - A cover email will explain how to access the survey and that participation is voluntary.
  - Email addresses will be obtained through SurveyMonkey®.
  - The investigators will not have access to the email addresses or the subject contact information.
  - Exclusion Criteria:
    - Visual impairment.
    - Inability to read.
    - Inability to understand English.
    - Inability to use a computer to respond to questions.

- **Data Collection**
  - The survey consists of questions regarding GI symptoms[33], strategies for managing symptoms, foods that may trigger symptoms, and awareness of dietary plans for GI symptoms.
  - Demographic information will also be obtained.

- The survey instrument is attached.

- **Intervention or experimental aspect of the study**
  - There is no intervention.

- **Statistical Analysis**
  - Demographic data will be described using frequency (percentage) for categorical variables and mean (standard deviation) or median (interquartile range) for continuous variables.
  - Categorical data will be analyzed using Pearson's chi-square or Fisher's exact test; continuous data will be analyzed using Student's t-test.
    - A goal of greater than 500 subjects is sought. Sufficient emails will be obtained from SurveyMonkey® to accomplish this sample size.

Ethical Considerations

- **Informed consent**
  - By completing the survey, providers will be giving their consent to participate. No separate informed consent will be administered.

- **Privacy information**
  - The surveys are completely confidential. No identifying information will be obtained.

Cost/Budget

- Approximately $3500 for the use of the email addresses.

Estimated Period of Time to Complete Study	
When will study begin?	2/1/2017
Protocol Development Completed	2 weeks
Admin Review Time	2 weeks
IRB Approval	3 weeks
Data collection	8 weeks
Data analysis	4 weeks
Presentation development (if applicable)	N/A
Manuscript Development (if applicable)	4 weeks
Journal submission process (if applicable)	6 months
Study closure	2 months

References

1. Chey WD. Food: The Main Course to Wellness and Illness in Patients With Irritable Bowel Syndrome. *The American journal of gastroenterology.* 2016.
2. Canavan C, West J, Card T. The epidemiology of irritable bowel syndrome. *Clinical epidemiology.* 2014;6:71-80.
3. Lacy BE, Patel H, Guerin A, et al. Variation in Care for Patients with Irritable Bowel Syndrome in the United States. *PloS one.* 2016;11(4):e0154258.
4. Association AG. IBS in America Survey. 2015.
5. Saha L. Irritable bowel syndrome: pathogenesis, diagnosis, treatment, and evidence-based medicine. *World journal of gastroenterology : WJG.* 2014;20(22):6759-6773.
6. Wong WM. Restriction of FODMAP in the management of bloating in irritable bowel syndrome. *Singapore medical journal.* 2016;57(9):476-484.
7. Maagaard L, Ankersen DV, Vegh Z, et al. Follow-up of patients with functional bowel symptoms treated with a low FODMAP diet. *World journal of gastroenterology : WJG.* 2016;22(15):4009-4019.
8. Nanayakkara WS, Skidmore PM, O'Brien L, Wilkinson TJ, Gearry RB. Efficacy of the low FODMAP diet for treating irritable bowel syndrome: the evidence to date. *Clinical and experimental gastroenterology.* 2016;9:131-142.
9. Halmos EP. A low fodmap diet in patients with crohn's disease. *Journal of gastroenterology and hepatology.* 2016.
10. Halmos EP, Bogatyrev A, Ly E, Liels KL, Muir JG, Gibson PR. Challenges of Quantifying FODMAPs in Enteral Nutrition Formulas: Evaluation of Artifacts and Solutions. *JPEN. Journal of parenteral and enteral nutrition.* 2016.
11. Halmos EP, Christophersen CT, Bird AR, Shepherd SJ, Gibson PR, Muir JG. Diets that differ in their FODMAP content alter the colonic luminal microenvironment. *Gut.* 2015;64(1):93-100.
12. Halmos EP, Christophersen CT, Bird AR, Shepherd SJ, Muir JG, Gibson PR. Consistent Prebiotic Effect on Gut Microbiota With Altered FODMAP Intake in Patients with Crohn's Disease: A Randomised, Controlled Cross-Over Trial of Well-Defined Diets. *Clinical and translational gastroenterology.* 2016;7:e164.
13. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology.* 2014;146(1):67-75 e65.
14. Dugum M, Barco K, Garg S. Managing irritable bowel syndrome: The low-FODMAP diet. *Cleveland Clinic journal of medicine.* 2016;83(9):655-662.
15. Hustoft TN, Hausken T, Ystad SO, et al. Effects of varying dietary content of fermentable short-chain carbohydrates on symptoms, fecal microenvironment, and cytokine profiles in patients with irritable bowel syndrome. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society.* 2016.
16. Elli L, Tomba C, Branchi F, et al. Evidence for the Presence of Non-Celiac Gluten Sensitivity in Patients with Functional Gastrointestinal Symptoms: Results from a Multicenter Randomized Double-Blind Placebo-Controlled Gluten Challenge. *Nutrients.* 2016;8(2):84.
17. Hayes P, Corish C, O'Mahony E, Quigley EM. A dietary survey of patients with irritable bowel syndrome. *Journal of human nutrition and dietetics : the official journal of the British Dietetic Association.* 2014;27 Suppl 2:36-47.
18. Chumpitazi BP, Cope JL, Hollister EB, et al. Randomised clinical trial: gut microbiome biomarkers are associated with clinical response to a low FODMAP diet in children with the irritable bowel syndrome. *Alimentary pharmacology & therapeutics.* 2015;42(4):418-427.
19. Eswaran SL, Chey WD, Han-Markey T, Ball S, Jackson K. A Randomized Controlled Trial Comparing the Low FODMAP Diet vs. Modified NICE Guidelines in US Adults with IBS-D. *The American journal of gastroenterology.* 2016.
20. Hackett C, Kolber MR. Low FODMAP diet. *Canadian family physician Medecin de famille canadien.* 2015;61(8):691.
21. Gibson PR, Shepherd SJ. Evidence-based dietary management of functional gastrointestinal symptoms: The FODMAP approach. *Journal of gastroenterology and hepatology.* 2010;25(2):252-258.
22. Kortlever T, Hebblethwaite C, Leeper J, O'Brien L, Mulder C, Gearry RB. Low FODMAP diet efficacy in IBS patients-what is the evidence and what else do we need to know? *The New Zealand medical journal.* 2016;129(1442):75-83.

23. Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Case Study: Utilizing a Low FODMAP Diet to Combat Exercise-Induced Gastrointestinal Symptoms. *International journal of sport nutrition and exercise metabolism.* 2016;26(5):481-487.
24. Mansueto P, Seidita A, D'Alcamo A, Carroccio A. Role of FODMAPs in Patients With Irritable Bowel Syndrome. *Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition.* 2015;30(5):665-682.
25. McIntosh K, Reed DE, Schneider T, et al. FODMAPs alter symptoms and the metabolome of patients with IBS: a randomised controlled trial. *Gut.* 2016.
26. Marsh A, Eslick EM, Eslick GD. Does a diet low in FODMAPs reduce symptoms associated with functional gastrointestinal disorders? A comprehensive systematic review and meta-analysis. *European journal of nutrition.* 2015.
27. Prichard R, Rossi M, Muir J, Yao C, Whelan K, Lomer M. Fermentable oligosaccharide, disaccharide, monosaccharide and polyol content of foods commonly consumed by ethnic minority groups in the United Kingdom. *International journal of food sciences and nutrition.* 2016;67(4):383-390.
28. Prince AC, Myers CE, Joyce T, Irving P, Lomer M, Whelan K. Fermentable Carbohydrate Restriction (Low FODMAP Diet) in Clinical Practice Improves Functional Gastrointestinal Symptoms in Patients with Inflammatory Bowel Disease. *Inflammatory bowel diseases.* 2016.
29. Uno Y, van Velkinburgh JC. Logical hypothesis: Low FODMAP diet to prevent diverticulitis. *World journal of gastrointestinal pharmacology and therapeutics.* 2016;7(4):503-512.
30. Croagh C, Shepherd SJ, Berryman M, Muir JG, Gibson PR. Pilot study on the effect of reducing dietary FODMAP intake on bowel function in patients without a colon. *Inflammatory bowel diseases.* 2007;13(12):1522-1528.
31. Lis D, Ahuja KD, Stellingwerff T, Kitic CM, Fell J. Food avoidance in athletes: FODMAP foods on the list. *Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme.* 2016:1-3.
32. Durchschein F, Petritsch W, Hammer HF. Diet therapy for inflammatory bowel diseases: The established and the new. *World journal of gastroenterology : WJG.* 2016;22(7):2179-2194.
33. Organisation WG. IBS questionnaire for HCP. 2009.