Title: Evaluate and Compare the Clinical Efficacy of the Mediterranean Diet to the Low-FODMAP Diet in Treating Irritable Bowel Syndrome

NCT05807919

Date of IRB Approval : August 1, 2023

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: A Randomized Clinical Trial Evaluating Two Different Dietary Approaches to Treat Irritable Bowel Syndrome

Names, degrees, and affiliations of the principal investigator and study coordinator (if applicable):

Principal Investigator: Prashant Singh, MD, Division of Gastroenterology, Department of Internal Medicine, University of Michigan
Study Coordinator: Samuel W. Chey, MPH, Division of Gastroenterology, Department of Internal Medicine, University of Michigan

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find childcare, or make other plans. In your decision to participate in this study, consider all these matters carefully.

Data and biospecimen collection
This research collects health-related information and biological samples (blood, stool) to better understand Irritable Bowel Syndrome. This study will allow researchers to evaluate the human microbiome (the bacteria that live in your intestines) and blood based biomarkers in relation to Irritable Bowel Syndrome at certain time points before and after completion of the study intervention.

Randomization
This study involves a process called randomization. This means that the dietary wing you are assigned in the study is not chosen by you or the researcher. The study design divides study participants into separate groups, based on chance (like the flip of a coin), to compare different treatments or

procedures. If you decide to be in the study, you need to be comfortable not knowing which study group you will be in until you have completed the study.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include no improvement of your current Irritable Bowel Syndrome. More detailed information will be provided later in this document.

This study may offer some benefit to you now or others in the future by leading to symptom improvements, establishing new treatment options for Irritable Bowel Syndrome. More information will be provided later in this document.

We expect the amount of time you will participate in the study will be 5-7 weeks (1-3 weeks of screening, 4 weeks of intervention).

You can decide not to be in this study. Alternatives to joining this study include consultation with your gastroenterologist or primary care provider, exploration of alternative studies through UMhealthresearch.org, or request presentation of other active studies managed by the FGID research group.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

-2. PURPOSE OF THIS STUDY

2.1 Study purpose:

Diet and lifestyle change are current recommended first-line treatments for symptom relief in patients suffering from Irritable Bowel Syndrome (IBS). We know that IBS symptoms can be made worse by consuming certain types of foods and beverages. A number of different dietary approaches are currently utilized to treat IBS, but many of these approaches have not been scientifically evaluated.

Recent studies have suggested that one of these new dietary approaches performs at an equal level to historical dietary approaches for IBS. This study seeks to evaluate the degree of effectiveness for two different diets (Diet A and Diet B), one historical and one new, that include different types and amounts of food(s). Both diets are predicted to help with your IBS symptoms, but this study hopes to determine if these diets are comparable in their effectiveness to treat IBS.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

You can take part in this study is you are:

- Male or female, at least 18 years of age, but not older than 70 at the time of enrollment
- Able to provide informed consent
- Diagnosed with IBS-Diarrhea(IBS-D) or IBS-Mixed(IBS-M)
- Weekly average of worst daily (in the past 24-hours) abdominal pain score of ≥3.0 on a 0 to 10-point scale
- At least 80% compliance in daily diary entries during a 7-day screening period.
- Must be comfortable eating only food that is provided by the study for a 4-week period

You should NOT have any of the following:

- Diagnosed (or history of) conditions including Inflammatory Bowel Disease (Crohn's Disease, Ulcerative Colitis), Microscopic Colitis, Celiac Disease, or poorly controlled Diabetes Mellitus (Hemoglobin A1c ≥8%)
- Unexplained symptoms including rectal bleeding, weight loss, or nighttime symptoms (pain, diarrhea, bleeding, etc…)
- Adherence to ANY dietary IBS treatments including a gluten-free diet, low-FODMAP diet, low-fat diet, or Mediterranean diet within the past 6 months
- Known allergies to eggs, seafood, peanuts, tree nuts, or milk
- History of an eating disorder that required medical or behavioral treatment within the past 10 years
- History of prior small bowel or colonic surgeries (excluding removal of appendix or gallbladder if either procedure was performed over 6 months before study enrollment)
- Usage of an oral antibiotic within the past 3 months
- Have any planned significant changes to dietary or exercise regimen approaches within 30 days prior to screening or during the study
- Currently pregnant or breastfeeding

3.2 How many people are expected to take part in this study?

We expect to enroll 40 participants into this study at the University of Michigan

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

You will be considered for this study if you have active IBS-D or IBS-M symptoms and meet eligibility criteria listed in section 3.1. If eligible, you will be asked to take part in the following:

Screening (Virtual Meeting and Research Office Visit): After you provide written consent, we will obtain the following information virtually that includes:

- Age, sex, race, related medical history, prior IBS treatments,
- Use of concurrent medications and supplements
- Duration of your IBS symptoms
- Instructions for online questionnaire submissions
- Completion of detailed dietary history
- Instructions to begin and complete the baseline screening phase

Once virtual tasks have been completed, we will complete the following during your in-person research office visit:

- Blood drawn, approximately 2 tablespoonful (30 mL)
- Blood Pressure, temperature, weight and height will be taken.
- Pregnancy test will be obtained in women of childbearing age if no reliable method of contraception is being utilized (e.g. Intrauterine device(IUD), birth control pills(OCP),implant)
- Provision of two stool collection kits (requires half a cup, or 6-8 oz., of stool per kit) to be used per study instruction and returned within 24 hours from collection using pre-paid packages – one sample is to be collected before the initiation of the dietary phase, and the second to be collected on the final day of the dietary phase
- Complete questionnaires assessing your IBS and general health symptoms
- Initial instruction and education to prepare for your Day 0 visit

Blood Samples: We will collect and store your blood samples labeled only with a study ID number and date of blood draw. We plan to test your blood samples for certain biomarkers in future research. We will also utilize blood samples to collect and store information about certain compounds within your blood. Specifically, we will be analyzing certain biomarkers within our blood that provide information on how easily compounds can pass through your intestines.

Stool Samples: The study team will provide you with a collection kit(s) and ask you to collect a stool sample in-person or from-home using a pre-paid shipping sleeve. We will be collecting and analyzing the stool microbiome (the bacteria found in your large intestine and stool).

Baseline Screening: You will be required to complete a baseline-screening period to evaluate and confirm your symptoms through the submission of daily online questionnaires as instructed during your virtual or research office visit. The baseline screening period will be completed over 7-days in most cases but can extend up to 21 days depending on the degree of patient's reported symptoms and overall compliance. If symptoms and other thresholds for eligibility are confirmed, you will be invited to proceed in study participation.

Day 0 Visit (Completed from Home): If you satisfy the inclusion/exclusion criteria, complete your baseline screening period, and fully complete your screening visit, you will be randomized into either

Diet A or Diet B. Neither you nor the study team members interacting with you will know what study cohort they have been randomized into. For some research studies, such as the one you are being asked to join, it is important that you do not learn the results of certain tests. Whether you intend it or not, sometimes learning this information may make you change your actions and behaviors in ways that could impact the outcome of the study.

Days 1-28 (Completed from Home): You will complete a four-week dietary intervention. All meals will be provided by the study through Modify Health (Atlanta, GA, USA), a national food service that specializes in IBS-friendly meals and will be shipped several times per week to your mailing address. You will be provided with 3 meals (approximately 2000 kcal) plus 2 snacks per day. You will complete daily online symptom questionnaires throughout the dietary intervention period per instructions provided during the screening visit.
The intent of the diet is that you should NOT supplement the meals with foods not provided by the study. Any consumption of foods not provided by the study team during the 4-week dietary period may only occur if given explicit and prior authorization from the study team. The consumption of some beverages/drinks not provided by the study team is allowable on a case-by-case basis.

Day 28, End of Treatment Visit (Research Office Visit): After you have finished the treatment period, a final visit will be completed to obtain and distribute the following:

- Review of adverse events and concomitant medications
- Blood drawn, approximately 2 tablespoonful (30 mL)
- Collection of post-treatment stool sample
- Complete questionnaires assessing your IBS and general health symptoms
- Provision of de-brief information on the treatment type received

Future Research: We would also like your permission to keep some of your blood, stool, and medical information collected in the main study, so that we may study it in future research. These data/samples will be stored at the University of Michigan. The future research may be similar to this study or may be completely different.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

As a subject participating in this research study, you have certain responsibilities, such as providing your accurate medical history, ensuring that you arrive at all of your pre-scheduled appointments, following sample collections as instructed/directed, and reporting any adverse events you may have during the study.

For some research studies, such as the one you are being asked to join, it is important you do not learn the results of certain tests. Whether you intend or not, sometimes learning this information may make you change your actions and behaviors in ways that could impact your study outcomes.
Once all tasks outlined above in section 4.1 have been completed, you will have finished study participation.

4.2 How much of my time will be needed to take part in this study?

The first screening visit may require approximately one hour and 30 minutes to complete, in addition to time needed to collect the stool sample at home.

Online questionnaires completed throughout the study will require approximately 5-7 minutes to completeper entry, or approximately 3.5 hours total through the entire study participation period.

The final-post treatment visit may require approximately 1 hour to complete, in addition to time needed to collect the stool sample from home.

4.3 When will my participation in the study be over?
Your participation in the study will end upon satisfying all study phases described in section 4.1.

The entire study is expected to last about 5-7 weeks (1-3 weeks of screening, 4 weeks of intervention).

4.4 What will happen with my information and/or biospecimens used in this study?
With appropriate permissions, your biospecimens and collected information may also be shared with other researchers, here, around the world, and with companies.

Your identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks are:
Diet A and Diet B: Both study diets may cause a change in your stool consistency. While it is expected to help normalize your stool consistency, they can very rarely cause constipation. Both diets may cause weight loss, which is also rare.

Blood Sampling: A trained technician, nurse, or physician will obtain the blood samples. You will be checked closely to see if complications due to blood drawing occur. Complications that may arise as a result of blood collection are typically minimal and may include bruising, swelling, fainting, and infection.

Stool Sampling: Collecting stool samples may be inconvenient for you.

Reproductive Risks and other Issues to Participating in Research: Due to unknown and potential harm to the unborn baby, sexually active women of child-bearing age will be asked to submit a urine pregnancy test to confirm non-pregnancy prior to study enrollment and participation.

Loss of Confidentiality and Privacy: Researchers will try their best to minimize these risks by following good clinical practices in the conduct of this study, and by taking utmost precautions in maintaining your privacy.

Warfarin (blood thinner) doses may be affected by your diet due to alterations in your vitamin K, you may need to make appropriate adjustments while on these diets.

The researchers will also ask you to follow study instructions and to report any changes in your health and medications as the information becomes available to you.

The researchers will try to minimize these risks by:
Blood Sampling: Medical care will be available if the need arises.

Stool Sampling: The researcher will provide you with a collection kit and instructions on collecting the samples properly and conveniently.

Reproductive Risks and Other Issues to Participating in Research: Participants of child-bearing age will be asked to maintain a stable form of birth control (IUD, birth control pills,, implants, hormonal, etc…) while on study or submit negative urine pregnancy test upon request prior to dietary randomization.

Additionally, there may be a risk of loss to confidentiality or privacy. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

As with any research study, there may be additional risks that are unknown or unexpected.**5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?**
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

Efforts taken by the research team to minimize risks and potential side effects are outlined in section 5.1

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one treatment-based study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
Dietary modifications accomplished through study participation could lead to symptom improvements. However, you may not receive any personal benefits from being in this study, but others may benefit from the knowledge gained from this study.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?

There may be other ways of treating your condition. These include: consultation with your gastroenterologist or primary care provider, exploration of UMhealthresarch.org for alternative studies, or request presentation of other active studies managed by the FGID research group.

Although dietary therapy is available as part of this clinical study, you should check with the researchers and/or your primary care physician to discuss your options including how to obtain any alternative treatments and whether they must be managed through a physician or require medical supervision.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information".

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

No, research participation is 100% voluntary and participants are welcome to withdraw their participation from the study at any time.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researcher's telephone number listed in Section 10.1.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
You will not receive payments for participating in the study.
But, this study will provide 4 weeks of catered, pre-made meals and snacks at no-cost.

8.3 Who could profit or financially benefit from the study results?

The company whose product is being studied:
"Modify Health" is supplying the study meals and snacks, and they may benefit from the results of the study.

The researchers conducting the study:
The principal investigators at the University of Michigan, Drs. Singh, Chey, and Eswaran initiated the study and designed the study protocol.

We'd like you to know that Dr. Chey is a consultant for "Modify Health and holds stock options there. However, he is not likely to benefit financially from the results of this study.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the accrued data or discoveries. You will not have rights to these discoveries or any proceeds from them.

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9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?
We are committed to respecting your privacy and keeping your personal informatio confidential. For example, a unique code will be assigned to your research study records in a secure location where only authorized individuals, such as a study doctor or study staff member, will have access to.

Your research information will be stored in a locked cabinet and will not be made part of your regular medical record. Research records will be kept in a separate secure research file that does not include names, registration numbers, or other information that is likely to allow someone other than the researchers to link the information to you.

A description of this clinical trial will be available on http://www.clinicaltrials.gov/, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.

- Study sponsors or funders, or safety monitors or committees, may need the information to:
  - Make sure the study is done safely and properly
  - Learn more about side effects
  - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.

- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, Social Security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities. (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Prashant Singh, MD
Mailing Address: 1500 E Medical Center Drive, Room 3912 Taubman Center, Ann Arbor, MI, 48109
Telephone: 734-936-6400
Study Coordinator: Samuel W. Chey, MPH
Mailing Address: 1500 E Medical Center Drive, Room 3912 Taubman Center, Ann Arbor, MI, 48109
Telephone: 734-764-9226

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies, include the appropriate calling codes.)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Sig-A

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with [NAME OF STUDY TEAM MEMBER OBTAINING CONSENT] _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Sig-D

Consent/Assent to Collect for Unspecified Future Research

This project involves the option to allow the study team to keep your identifiable specimens/data for use in future research. I understand that it is my choice whether or not to allow future use of my specimens. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

_____ Yes, I agree to let the study team keep my specimens for future research.

_____ No, I do not agree to let the study team keep my specimens for future research.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Sig-G

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____