FOR CCI USE ONLY
Approved by the Beth Israel Deaconess Medical Center Committee on Clinical Investigations:

Consent Approval Date: 08/17/2018

Protocol Number: 2015P000282

BETH ISRAEL DEACONESS MEDICAL CENTER
APPROVED BY THE
COMMITTEE ON CLINICAL INVESTIGATIONS
06/23/2020
APPROVAL EXPIRATION DATE

INFORMED CONSENT FORM TO TAKE PART IN A RESEARCH STUDY

SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: Efficacy of Open-label vs Double-blind Treatment in IBS
PRINCIPAL INVESTIGATOR: Anthony Lembo, MD
PROTOCOL NUMBER: 2015P000282

INTRODUCTION:

- This is a research study;
- Your participation is voluntary;
- A research study includes only people who choose to take part;
- You may or may not benefit from participating in the study. However, your participation may help others in the future as a result of knowledge gained from the research;
- You may leave the study at any time;
- If you choose not to take part, or if you leave the study, your decision will in no way harm your relationship with any member of the research team or any other individuals at Beth Israel Deaconess Medical Center.

Please read this consent form carefully and ask the investigators or study staff to explain any words or information that you do not clearly understand. Once you read this consent form and understand what your participation in this study will involve, you will be asked to sign this form if you wish to take part. You will be given a signed copy of the form to keep for your records.

DISCLOSURE OF SPECIAL INTERESTS OF BIDMC AND INVESTIGATORS

This study is being conducted by Dr. Anthony Lembo. It is being funded by the National Institute of Health (NIH). Neither BIDMC nor Dr. Lembo have any additional interests in this research project.

WHOM TO CONTACT IF YOU HAVE QUESTIONS OR PROBLEMS

If you have any questions, concerns or complaints about this research or experience any problems, you should contact Anthony Lembo, MD at [617] 667-2138.

PURPOSE

Irritable bowel syndrome (IBS) is a gastrointestinal disorder characterized by chronic abdominal pain or discomfort and altered bowel function (i.e., constipation, diarrhea, or alternating constipation and

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diarrhea).

Evidence exists that indicates that placebos and peppermint oil can have beneficial effects in patients with IBS. In addition, in a previous study, it was shown that patients can be successfully treated for IBS with both open-label and blinded placebo. Blinded means that patients do not know which medication they are receiving. A placebo is a pill that looks like the peppermint oil pills, but contains no active material.

The main purpose of this study is to harness the placebo effect and study the effects of peppermint oil in IBS.

STUDY PARTICIPANTS
You have been asked to be in the study because you have irritable bowel syndrome.

Approximately 400 people will take part in this study at Beth Israel Deaconess Medical Center.

DESCRIPTION OF STUDY DETAILS
If you agree to be in this study, you will be asked to read and sign this consent form. After you sign the consent form, the following things will happen:

Visit 1:
Screening procedures are tests and procedures that will be done to determine if you are eligible to take part in the research study. For this research study, the screening procedures include a medical history review and physical exam.

If you are eligible for participation after the medical history review and physical exam including vital signs, you will be randomly assigned (like the flip of a coin) to receive either 1) placebo delivered openly (open-label) or 2) placebo or peppermint oil delivered double-blind or 3) continuation with your previous treatment with no additions. Both placebo and peppermint oil will be taken three times daily before meals for six weeks.

You will not be able to choose the study group to which you will be assigned.

Open-label means that both you and the study clinician will know whether you are receiving placebo or peppermint oil. Double-blind means that neither you nor the study clinician will know whether you will be receiving the placebo or peppermint oil. However, this information can be learned in case of an emergency.

After you receive your group assignment, the following procedures will occur:

- Completion of questionnaires related to your gastrointestinal symptoms, overall health and well-being, and personal characteristics

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- Dispensation of study treatment
- Collection of blood for genetic analysis.
- You will also be asked to keep a daily symptom diary for the seven days prior to Visit 2 and the seven days prior to Visit 3

Visit 2:
Visit 2 will occur three weeks after Visit 1. At Visit 2, the following procedures will occur:

- Completion of questionnaires related to your gastrointestinal symptoms, overall health and well-being, and personal characteristics
- Physical exam
- Updates on medical history
- Dispensation of study treatment

Visit 3:
Visit 3 will occur three weeks after Visit 2. At Visit 3, the following procedures will occur:

- Completion of questionnaires related to your gastrointestinal symptoms, overall health and well-being, and personal characteristics
- Vital signs
- Physical exam
- Updates on medical history
- Collection of blood for genetic analysis.

In addition, between Visit 1 and Visit 2 and also Visit 2 and Visit 3, there will be a brief contact to check-in on the status of the study.

Approximately 57 patients will be randomly asked to participate in an open-ended interview that will be focused on why patients chose to participate and their thoughts about placebo and the study overall. This would occur at Visit 3 and will last for approximately 30 minutes. If you are asked to participate in the interview, it would be audio-recorded to allow for transcription.

I agree to allow my interview to be audio-recorded.
☐ Yes ☐ No

_____ _____
Signature of Subject Date

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Future Use of Blood

Any blood from Visit 1 or Visit 3 that is remaining after the genetic analysis will be saved and stored frozen at BIDMC. There is no limit on the length of time your blood will be kept. The stored blood will not contain any identifiable information, but will contain your research study subject code. We may keep all remaining blood for research indefinitely unless you decide to withdraw your samples by contacting the PI (Anthony Lembo, MD at 617.667.2138). The samples may be used for future analysis related to IBS as more information becomes available. This analysis could include analyzing proteins, DNA, RNA or other genetic biomarkers that are part of future scientific discovery. It is possible that this may be part of a separate unrelated study. The samples may be used by the study team and their collaborators. If the samples are used by collaborators, your samples will be sent with your research study subject code, but not any identifiable information. Collaborators will not have access to the link between your code number or any of your protected health information You will not be informed of any future findings and there is no additional risk to you associated with storing the samples. De-identified information related to your diagnosis, treatment and study results will also be saved. However, it is not known how or if this information will be used in the future.

I agree to allow storing information and the remaining blood for future analysis.
☐ Yes ☐ No

_____ _____
Signature of Subject Date

RISKS AND DISCOMFORTS

As a result of your participation in this study, you are at risk for side effects listed in this section. You should discuss these with the investigator and with your regular doctor if you choose.

Blood Drawing

The risks and discomforts of blood drawing from a vein include the possibility of pain or bruising at the site of the blood draw; occasional feeling of lightheadedness; and rarely, infection at the site of the blood draw.

RISKS ASSOCIATED WITH SURVEYS/QUESTIONNAIRES

Some of the questions we will ask as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions and you may take a break at any time during the study. You may stop your participation in the study at any time.

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LOSS OF CONFIDENTIALITY

There is the potential for loss of confidentiality by participating in this study. Every effort will be made to protect the confidentiality of your identifiable information.

This research involves the possible identification of genetic information about you (and individuals genetically related to you. Additional information about this gene and your present or future health may be discovered at a rapid pace.

You will not have the option of being advised of the results of the research that relate to your biological samples.

CERTIFICATE OF CONFIDENTIALITY

A Certificate of Confidentiality has been obtained from the Department of Health and Human Services. This will help further protect information that may identify you. The Certificate prevents the investigator from being forced to disclose information that may identify you for use in court.

A Certificate of Confidentiality does not prevent you or anyone you tell from voluntarily releasing information about yourself or your involvement in this research. The investigator may not withhold information if you give your health insurance company or employer permission to receive information about your participation in this research. This means that you and your family must also actively protect your own privacy.

Finally, the investigator can take steps, including reporting to authorities as required by law, to prevent serious harm to yourself or others.

There is a possibility that information that identifies you will be given to the Beth Israel Deaconess Medical Center oversight officials or to officials of the Department of Health and Human Services. This Information may be used for audits or evaluations, or to ensure that research work is being done correctly. However, these officials are also obliged to protect your privacy.

CONFIDENTIALITY

Information learned from your participation in this study and from your medical record may be reviewed and photocopied by the Food and Drug Administration (FDA) and/or other federal and state regulatory agencies, accreditation agencies, the Committee on Clinical Investigations, the Human Subjects Protection Office and others involved in research administration of the Beth Israel Deaconess Medical Center with protection of confidentiality so far as permitted by applicable law. Information resulting from this study and from your medical record may be used for research purposes and may be published; however, you will not be identified by name in such publications.

A copy of this consent form and information collected during this research may become part of your medical record, if the information is relevant to the care you receive at Beth Israel Deaconess

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Medical Center. Medical records are considered permanent records; therefore, information cannot be deleted from the record. Medical records are available to health care professionals at Beth Israel Deaconess Medical Center and may be reviewed by staff when carrying out their responsibilities, as well as by external parties such as health care insurers and others in certain circumstances. If you are not currently a patient at Beth Israel Deaconess Medical Center and do not have a medical record at Beth Israel Deaconess Medical Center, one may be created for you for your participation in this research. You may also be required to register as a patient of Beth Israel Deaconess Medical Center in order to participate in this research.

POSSIBLE BENEFITS

It is not possible to predict whether you will benefit directly from participation in this study. However, your participation may help others in the future as a result of knowledge gained from the research.

OTHER AVAILABLE OPTIONS

Taking part in this study is voluntary. Instead of being in this study, you have the following options:

- There are commonly used treatments available for persons who have IBS including FDA-approved medications to treat pain, spasms and change in bowel habits. Anti-depressants and antibiotics may also help.
- Nutritional interventions may also be helpful
- To not take part in the study.

This research study is not meant to diagnose or treat medical problems. Participation in this research study does not take the place of routine physical examinations or visits to your regular doctor.

We recommend that you discuss these and other options with the investigator and your regular doctor so that you can make a well-informed decision about participating in this study.

IF YOU DECIDE NOT TO TAKE PART IN THE STUDY

Participation in this study is voluntary. You have the right to decide not to take part in this study. If you choose to participate, you have the right to leave the study at any time. Your decision to not participate will not result in any penalties or loss of benefits to you. The investigators will tell you about new information that may affect your willingness to stay in this study.

If you decide not to participate in the study or decide to leave the study early, your decision will not affect your relationship with the research team or any other individual at Beth Israel Deaconess Medical Center.

INVESTIGATORS RIGHT TO STOP THE STUDY

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, or if it would be dangerous for you to continue, or if you do not follow

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study procedures as directed by the investigators. Beth Israel Deaconess Medical Center or the funding source may stop the study at any time.

COSTS AND/OR PAYMENTS TO YOU

COSTS COVERED BY STUDY

You will not be charged for any of the medications, tests or procedures that are a part of this research study.

COST OF RESEARCH RELATED INJURY:

If you are injured as a direct result of your participation in this study you should contact the Investigator at the number provided under the section "Whom to Call if You Have Questions" in this form. You will be offered the necessary care to treat your injury. You or your insurance company will be billed for medical care and/or hospitalization related to this injury. You will be responsible for all co-payments and deductibles required under your insurance. BIDMC will consider reimbursement of injury related expenses not covered by your insurance on a case-by-case basis. At this time there is no plan to reimburse you for items such as lost wages or lost time from work. By signing this consent form you have not given up any legal rights.

PAYMENTS TO YOU:

You will receive a parking voucher or single-use MBTA ticket for each visit. If your scheduled visit occurs outside of MBTA operating hours or if a disability affects your ability to use fixed MBTA routes, transportation costs will be reimbursed with a receipt if within the city of Boston.

OTHER IMPORTANT INFORMATION

A description of this clinical trial will be available on 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.

AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION

As part of this study, we will be collecting, using and sharing with others information about you. Please review this section carefully as it contains information about the federal privacy rules and the use and disclosure of your information.

PROTECTED HEALTH INFORMATION [PHI]

By signing this informed consent document, you are allowing the investigators and other authorized personnel to use [internally at BIDMC] and disclose [to people and organizations outside the BIDMC workforce identified in this consent] health information about you. This may include information about you that already exists (for example: your medical records and other sources of health information, demographic information, the results of any laboratory tests, and mental health records

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if applicable as well as any new information generated as part of this study. This is your Protected Health Information.

PEOPLE/GROUPS AT BIDMC WHO WILL SHARE AND USE YOUR PROTECTED HEALTH INFORMATION
Your Protected Health Information may be shared with and used by investigators listed on this consent form as well as the supporting research team [i.e. research assistants and coordinators, statisticians, data managers, laboratory personnel, pharmacy personnel, administrative assistants], and may also be shared and used by other health care providers at BIDMC who have treated you in the past and have information relevant to the research, or who provide services to you in connection with the research. Your Protected Health Information may also be shared with the members and staff of the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center, which is responsible for reviewing studies for the protection of the research subjects.

PEOPLE/GROUPS OUTSIDE OF BIDMC WITH WHOM YOUR PROTECTED HEALTH INFORMATION WILL BE SHARED
We will take care to maintain confidentiality and privacy about you and your Protected Health Information. We may share your Protected Health Information with the following groups so that they may carry out their duties related to this study:

- Laboratories not affiliated with BIDMC that are involved in conducting tests related to the research
- Statisticians and other data monitors not affiliated with BIDMC
- Centralized data collectors
- Your health insurance company
- The Food and Drug Administration [FDA], the Department of Health and Human Services [DHHS], the National Institute of Health [NIH], the Office for Human Research Protections [OHRP], and other federal and state agencies that may have jurisdiction over the research
- Hospital and Clinical Research Accrediting Agencies
- Data and Safety Monitoring boards that oversee this study (if applicable)

Those who receive your Protected Health Information during the course of the research may not be required by the federal privacy regulations to protect it, and they may make further disclosures to others and use your information without being subject to penalties under those laws.

WHY WE ARE USING AND SHARING YOUR PROTECTED HEALTH INFORMATION
The main reason for using and sharing your Protected Health Information is to conduct and oversee the research as described in this Informed Consent Document. There are many other reasons beyond the research for which BIDMC may use or disclose your Protected Health Information. Not all of these reasons require your express written authorization. For example, we will use and share your Protected Health Information to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities. The various ways in which

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BIDMC may use and disclose your protected health information without your authorization are explained in a document called the Notice of Privacy Practices. If you have not received a copy of BIDMC's Notice of Privacy Practices, please ask us for one and review it before signing this form. In addition to signing this document, you may also be asked to sign a BIDMC General Agreement form acknowledging that you have received the BIDMC Notice of Privacy Practices.

NO EXPIRATION DATE – RIGHT TO WITHDRAW AUTHORIZATION

Your authorization for the use and disclosure of your Protected Health Information in this Study shall never expire. However, you may withdraw your authorization for the use and disclosure of your Protected Health Information at any time provided you notify the Principal Investigator in writing. If you would like to take back your authorization so that your Protected Health Information can no longer be used in this study, please send a letter notifying the Principal Investigator of your withdrawal of your authorization to Anthony Lembo, at 330 Brookline Ave., Boston, MA. Please be aware that the investigators in this study will not be required to destroy or retrieve any of your Protected Health Information that has already been used or disclosed before the Principal Investigator receives your letter, and they are permitted to continue to use and disclose your previously collected information as necessary to complete the research.

REFUSAL TO SIGN

Your clinical treatment may not be conditioned upon whether you sign the Authorization for Research. However, if you choose not to sign this informed consent document and authorization for the use and disclosure of your Protected Health Information, you will not be allowed to take part in the research study.

RIGHT TO ACCESS AND COPY YOUR PHI

If you wish to review or copy your Protected Health Information as it is made part of your medical record, you may do so after the completion or termination of the study by sending a letter to the Principal Investigator requesting a copy of your Protected Health Information. You may not be allowed to inspect or copy your Protected Health Information until this study is completed or terminated.

ADDITIONAL CONTACT FOR QUESTIONS OR CONCERNS

You may contact the Human Subjects Protection Office at [617] 975-8500 in the event that you would like to obtain information or to offer input about the research study. This office is independent of the investigator or investigator's research staff and can also assist with questions relating to your rights as a participant in research, which may include questions, concerns or complaints about your participation in the study.

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THE FOLLOWING PARAGRAPHS CONTAIN SOME STANDARD INFORMATION WHICH GENERALLY APPLIES TO INDIVIDUALS PARTICIPATING IN A RESEARCH STUDY.

CONSENT FORM FOR CLINICAL RESEARCH

I have read the previous page[s] of the consent form and the investigator has explained the details of the study. I understand that I am free to ask additional questions.

If I wish additional information regarding this research and my rights as a research subject, or if I believe I have been harmed by this study, I may contact the Human Subjects Protection Office (HSPO).

I am aware that this is a research project and that unforeseen side effects may occur.

I understand that the Beth Israel Deaconess Medical Center has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or to my insurer unless payment is otherwise provided for in this consent form.

I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive.

I acknowledge that no guarantees have been made to me regarding the results of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form.

_____ _____

Signature of Subject or Legally Authorized Representative (Parent if the subject is a minor) — Date

_____

Relationship of Legally Authorized Representative to Subject

The subject has been given the opportunity to read this consent form and to ask questions before signing, and has been given a copy.

_____

SIGNATURE OF INVESTIGATOR/Co-Investigator DATE

_____

PRINT INVESTIGATOR'S/Co-Investigator's NAME

A signing co-investigator must be listed on the study's approved Research Staffing Form at the time of consent.

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THE FOLLOWING SECTIONS ARE NOT NEEDED FOR ALL STUDIES AND SHOULD BE UTILIZED AS INDICATED:

If the subject is able to speak and understand English but is not able to read or write

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is able to understand English but is not physically able to read or write or see

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is not English speaking and signed the translated Short Form in lieu of the English consent document.

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Signature of Interpreter: _____

Printed name of Interpreter: _____

Date: _____