The BEST Trial: Biomarkers for Evaluating Spine Treatments

Study Consent

Protocol Number: 00057948

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Consent to Participate in a Research Study
Adult Participants

Sponsor / Study Title:	**National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) / "The BEST Trial: Biomarkers for Evaluating Spine Treatments"**
Protocol Number:	**00057948**
Principal Investigator: (Study Doctor)	**«PiFullName»**
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CONCISE SUMMARY

The purpose of this research study is to evaluate four treatments for chronic low back pain and to determine whether participant characteristics may predict the effectiveness of different treatment options.

Participants will complete:

- a pre-enrollment screening by telephone,
- an enrollment visit, during which they will be evaluated for participation in the study, and
- a 2-week online, self-directed, educational program to learn about the study (the "run-in" period).

After the 2-week run-in period, each participant will be re-evaluated to see if they are eligible to continue in the study. If participants are still eligible, they will complete:

- in-person visits to collect data via questionnaires and other assessments,
- two back-to-back 12-week study treatment periods, and
- a 12-week follow-up period after the end of the last study treatment.

Participants will be assigned to one of four study treatments for the first 12-week study treatment period. For the second 12-week study treatment period, participants will either continue with the same treatment as the first period, receive another treatment in addition to their first-period treatment, or be assigned to a new treatment. The maximum time participants will be in the study is 38 weeks.

Potential benefits to participating in this study include improvement in your chronic low back pain. There is no guarantee of this benefit.

Potential risks to participating in this study are similar to those encountered in a standard clinical practice and are deemed as having no more than a moderate risk level. Risks include worsening of your chronic low back pain, injury, and emotional or physical discomfort. This is not a full list of risks. Refer to the sections below for a more detailed list of risks.

The information provided in this section is discussed in more detail later in this consent form.

What are some general things you should know about research studies?

You are being asked to take part in a research study. Joining the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty or loss of benefits to which you are otherwise entitled.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Deciding not to be in the study or leaving the study before you complete the study activities will not affect your relationship with the study investigator, your health care provider, or the study site. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the study investigator or staff members who may assist them any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to study four treatments for chronic low-back pain to learn whether or not certain treatments work better for people with certain characteristics.

The study's main goal is to find a way to match treatments to low-back pain patients based on their characteristics and how they responded to treatments they have used before.

You are being asked to be in the study because you have reported having low-back pain for at least 3 months and on at least half the days in the past 6 months. You have also reported that your low-back pain is the worst pain you are experiencing.

To participate in this study, you also need to be willing to receive any treatment in this study for which you are eligible.

Are there any reasons you should not be in this study?

You should not be in this study if you are pregnant at the time of the screening phone call or enrollment visit.

In addition, the study investigator can stop you from participating in this study or in certain study activities if you have a condition that would mean you cannot safely participate.

How many people will take part in this study?

Approximately 820 people at up to 15 institutions in the United States will take part in this study.

How long will your part in this study last?

Participants will be in the study up to 38 weeks. Refer to the table below for the time needed for each study activity. This time includes a 2-week run-in period, two 12-week study treatment periods, and a final 12-week follow-up period.

What will happen if you take part in the study?

You will complete several study events before you begin a study treatment. See the table below for details about these study events.

Enrollment and Run-in period

Study Events	Description	Approximate Time Required	Activities During Event
In-person visit	If you are eligible to participate based on the pre-enrollment screening phone call, you will complete an in-person visit to begin the study.	75 minutes	• Review of this consent form • Measurement of waist circumference • Introduction to study website • Discussion of your current low-back pain treatments • Questionnaires • Scheduling future visits
Two-week run-in period	During this period, you will have access to online materials to learn about the study and you will answer online questionnaires.		• Online questionnaires • Review of online study materials • Text messages or e-mails from study staff
Check-in Phone Call	After the two-week run-in period, study staff will call you to discuss your eligibility to participate in the study.	10 minutes	• Questionnaires

After you complete the run-in period, you may no longer be eligible for the study.

If you are eligible after you complete the run-in period, you will begin the first treatment period for the study. The specific events during this period are described below.

You may have the option to participate in additional assessments beyond the required study events over three in-person visits if the assessments are supported by the clinic at the time of your enrollment. These additional assessments will provide more information about your characteristics and your low-back pain. These additional assessments are in *italics* in the tables below. Please see below for more details about these additional assessments and the time required.

Baseline Visit and First Study Treatment Period

Study Events	Description	Approximate Time Required	Activities During Event
Baseline in-person visit	You will participate in this activity if you are still eligible for the study based on the above check-in phone call. You will be randomly assigned (like flipping a coin) to a specific study treatment at this visit.	Approximately 4 hours	• Questionnaires* • Physical exam • Magnetic Resonance Imaging (MRI) scan of the spine • Motion Assessments • Collection of blood • Take-home stool collection kit • Assignment to first study treatment • Scheduling future visits
Additional baseline assessments	*You may have the option to undergo a set of assessments that will provide more information about your characteristics and your low-back pain.*	*Approximately 5 hours for all additional assessments*	• *Motion assessments* • *At-home activity monitoring* • *Advanced MRI scan of the spine* • *Brain MRI* • *Sensory testing (pressure, temperature)*
First study treatment period	You will receive a study treatment for up to 12 weeks.	The time required will depend on the treatment.	Activities will depend on the treatment.
Check-in phone call	Study staff will call you to check in halfway through the 12-week treatment.	10 minutes	• Questionnaires

* Some questionnaires will be available to complete online prior to the visit, and others will be completed in-person.

After the completion of the first 12-week treatment, you will begin the second treatment period for the study. The events in the second treatment period are described below. Note that if the first

treatment is working well for you, you may be asked to continue the same treatment alone or in combination with a new treatment. If the first study treatment is not working for you, you will be assigned to a different study treatment altogether.
If you are assigned to a different treatment for the second treatment period, you should not continue the first treatment outside of the study.

Second Study Treatment Period

Study Events	Description	Approximate Time Required	Activities During Event
In-person visit	After you complete the first period of treatment, you will attend another in-person study visit.	1 hour	• Questionnaires* • Physical exam • Motion Assessment • Collection of blood • Assignment to second treatment
Additional assessments	*You may have the option to undergo a set of assessments that will provide more information about your characteristics and your low-back pain.*	*Approximately 4 hours for all additional assessments*	• *Motion assessments* • *Brain MRI* • *Sensory testing (pressure, temperature)*
Second study treatment period	You will either continue the first treatment, add another treatment in addition to the first, or be assigned to a new treatment.	The time required will depend on the treatment.	Activities will depend on the treatment.
Check-in Phone Call	Study staff will call you to check in halfway through the second treatment period.	10 minutes	• Questionnaires

***** Some questionnaires will be available to complete online prior to the visit, and others will be completed in-person

After completion of the second 12-week period of treatment, you will complete several final activities for this study. See the table below for more details about these activities.

Follow-up Visits

Study Events	Description	Approximate Time Required	Activities During Event
In-person visit	After the second treatment period, you will attend another in-person study visit.	40 minutes	• Questionnaires* • Physical exam • Motion Assessment • Collection of blood
Additional assessments	*You may have the option to undergo a set of assessments that will provide more information about your characteristics and your low-back pain.*	*Approximately 4 hours for all additional assessments*	• *Motion assessments* • *Brain MRI* • *Sensory testing (pressure, temperature)*
Check-in Phone Call	Study staff will call you to check in 4 weeks after the end of the second treatment period.	10 minutes	• End of study check-in
Follow-up Texts, Emails, and/or Phone Call	You will receive texts or emails from the study staff. Study staff will call you to follow up 12 weeks after the end of the second treatment period.	10 minutes	• Questionnaires*

* Some questionnaires will be available to complete online prior to the visit, and others will be completed in-person

How will I be contacted by study staff?

Portions of the study will involve study staff contacting you by phone and e-mail. You will have the option to receive some study information via text messaging. Study-related e-mail and text messages will consist of reminders and notifications about study activities or reminders to contact the study team. These messages may contain personal information about you and may be

sent or received by the study team's personal electronic devices or in a method that is not able to be encrypted (protected). There is the risk that your information could be shared beyond you and the study team. By signing and dating the consent on the last page of this form you are giving permission for the study team to contact you by phone, email, and if preferred, text message. If you do not want to receive un-protected communication that may contain personal information, then you should not consent to participate in this study.

After the study is complete and all research activities concluded, or you withdraw from the study, you will no longer receive un-encrypted (un-protected) communication specific to this study.

If you do not want to receive study-related texts, please initial below.

_____☐ I do NOT consent to receiving study-related text messages

Study Treatments

You will be assigned to one or multiple of the following treatments during your participation in this study. Neither you nor the study investigator will choose the treatment. You will be assigned to study treatment(s) by chance (like flipping a coin). Please see below for more details about each treatment.

- Acceptance and Commitment Therapy
    - This treatment consists of 12 sessions designed to help individuals interrupt pain avoidance behavior patterns in favor of more open, aware, and engaged behavior. Treatment methods include mindfulness exercises, metaphor and identification of values. Four of the 12 sessions will occur face-to-face with a therapist online. The other eight sessions will be self-directed online with ongoing therapist support using an online messaging system.
- Duloxetine
    - For this treatment, you will be prescribed duloxetine, which is an FDA-approved treatment for chronic low-back pain. You will take duloxetine for at least 11weeks of the 12-week treatment period.
- Enhanced Self-Care
    - This treatment will involve online "modules" that provide education about chronic low-back pain and skills to help you manage your pain. You will also be able to monitor your walking activity using a Fitbit that will be provided by the study. The program will continue for approximately 12 weeks. After the first four weeks of this program, the remaining 8 weeks will be tailored to your characteristics and needs.
- Evidence-based Exercise and Manual Therapy
    - For this treatment, a trained Physical Therapist or Chiropractor will provide exercises and hands-on treatment to your joints and muscles. You will complete 10 sessions during an 8-week period: two sessions per week for the first two weeks and 1 session per week for 6 weeks.

At three points during the study, you will be asked to provide blood. 32 mL (about seven tubes) of your blood will be drawn by a qualified study staff member.

At one point during the study, you will be asked to provide a stool sample. You will be provided with a kit, instructions, and a return shipping label. You will be asked to collect the sample at home and send it by mail to the lab.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. The information learned from this study will assist the researchers and clinicians in learning how to improve treatment for chronic low-back pain.

The benefits to you from being in this study may include improvement in the amount of pain that you experience, increased mobility, and/or better ability to perform physical, mental, cognitive, emotional, recreational, and social activities as a result of lessened pain. You may also benefit by gaining new knowledge about your pain condition or by learning new pain self-management techniques. Your mood might improve as a result of interacting with study staff and personnel. Your participation may also offer long-term benefits to your general health, such as establishing and maintaining healthy habits like exercise. However, there is no guarantee that you will receive any direct benefit from being in the study.

What are the possible risks or discomforts involved from being in this study?

You may experience one or more of the risks listed below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study.

Risks Associated with Study Procedures

Breach of Confidentiality

We will make every effort to protect your confidentiality, but there is a small possibility that your data could become known to others. Since study data will be transmitted electronically, there is always the risk that a transmission could be intercepted and decoded. We will meet or exceed all standards of electronic security using only secure servers and encryption. We will protect your information, but there is a chance it will be seen by someone not authorized to see it.

Risks Associated with Phenotypic Assessments

Questionnaires

You will complete questionnaires regarding your pain, medication use, and history of chronic low-back pain and other health conditions. You may find the questions tiring, tedious, or embarrassing. You may choose not to answer a specific question or to decline to complete a questionnaire at any time, however there are some questionnaires that are required for study participation.

Blood Draw

Taking blood may cause some pain, bleeding or bruising at the spot where the needle enters your body. Rarely, taking blood may cause fainting or infection. To minimize these risks, experienced medical personnel will perform the blood draws using aseptic (clean) technique.

Stool Collection

Any stool sample may contain germs that spread disease. It is important to follow the instructions included in the stool collection kit and thoroughly wash your hands to avoid spreading infection.

Some people may feel uncomfortable or embarrassed using the stool collection kit. There should be no pain while collecting the stool sample. However, if you are constipated, straining to pass stool may be painful.

Physical Exam

There are no physical risks but you might experience momentary embarrassment or discomfort. The exam is similar to those that are performed as part of routine medical care.

Biomechanical (Motion) Assessment

You will receive at least one motion assessment, which requires the use of a wearable device to measure your movement and function as related to chronic low-back pain. You may find the wearable device uncomfortable and may experience light low-back muscle fatigue or soreness similar to a light workout the day following the motion assessment. Less common are short-term aggravation of existing low-back symptoms; irritation, pinching, rubbing, or sticking of skin from motion harness components; piercings or other wearable materials (for example, insulin pump) snagging during the motion testing, and loss of balance while performing the motion assessment causing a fall.

Adhesive may be used to attach wearable sensors during assessments. These adhesives may cause short-term, minor skin irritation. Some participants may participate in additional testing by wearing a device on their waist and wrist continuously for seven days, which may be burdensome. These additional assessments may also cause minor physical discomfort or tiredness but are unlikely to cause long-term physical discomfort.

MRI

You will undergo one Magnetic Resonance Imaging (MRI) of your spine during your baseline visit. This MRI will take approximately 30 minutes. Some participants may participate in additional imaging. If you participate in the additional imaging, you may undergo one advanced spine MRI scan that will take approximately 30 minutes and three brain MRIs. Each of the three brain MRIs last approximately 60 minutes and will be given at three separate study visits. During

an MRI, you must lie still on your back in the MRI scanner in a tight space. This may make you anxious.

MRI is safe for most participants but is not recommended for certain groups of people, such as those with certain medical devices (for example, implanted cardiac devices, cochlear implants, or intracranial aneurism clips) or with metal in their body (for example, wire mesh, screws). MRI is not safe for pregnant women. While MRI is safe for most participants, the procedure may cause some participants to feel emotional discomfort, anxiety, and claustrophobia. The noise of MRI requires participants to wear ear protection and may cause peripheral muscle or nerve stimulation.

Quantitative Sensory Testing (QST)

Some participants may receive QST, a set of assessments that test how sensitive you are to pressure and pin prick sensations. These assessments may cause discomfort in the areas of testing, but this discomfort is expected to go away a few minutes after the test is done. These tests will not cause any tissue injury.

Participants who receive QST will also be exposed to cold water that is uncomfortable. The water will not be cold enough to cause any tissue damage. The cold-water part of the QST assessment is not recommended for participants with uncontrolled high blood pressure, uncontrolled heart conditions, or a history of Raynaud's Syndrome.

Genetic Analysis & Information

Genetics and genomics are the study of DNA and RNA. DNA are substances made of smaller pieces called genes. RNA helps uncover the information in the DNA. Your genes influence your risk of getting certain diseases and how your disease progresses. As part of this study, the investigators would like to use your DNA to look for genes and gene products (for example, proteins) that might affect the severity of your chronic low-back pain. DNA and RNA can be studied from the blood and stool samples that you provide. Study investigators will not report back results found during the course of genetic or genomic analyses.

The risks related to genetic analyses can be to individuals or groups. These harms include others viewing you in a negative way or having trouble getting insurance. To reduce this risk, your samples will be stored and labeled with a code. If the results are used for future research, the researchers will not be able to identify you. Genetic results from this study will not be recorded in your medical record.

Federal law called the Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Risks Associated with Study Interventions and Run-in Activities

Below are the risks for each type of study treatment. Since you will be assigned to up to two of these study treatments, not all of these risks will apply.

Acceptance Commitment Therapy (ACT)

The ACT behavioral intervention includes discussing your pain experience with a trained therapist and may make you feel emotionally uncomfortable. These risks are minimal and are sometimes part of the therapeutic process. To reduce the disabling effects of depression, fear or other feelings, one may need to first recognize these before identifying healthy goals for improvement. You will meet with your assigned study therapist four times and will be able to contact them at any time by email. Your study therapist will thoroughly explain study treatment and what to expect. They will provide ongoing support over the course of study treatment and, if applicable, will monitor you for worsening of depression or anxiety symptoms. You may also reach out to your study staff with any questions or concerns throughout the course of the study.

Duloxetine

Duloxetine is an antidepressant that may be prescribed to you with daily doses ranging from 30 mg to 60 mg. The most common side effects with this drug include:

- Nausea
- Vomiting
- Dry mouth
- Constipation
- Diarrhea
- Fatigue (tiredness)
- Difficulty sleeping
- Dizziness

Severe liver problems, sometimes fatal, have been seen in patients treated with duloxetine.

All of these side effects are thought to be less common if your dosage is slowly increased over time by your provider and many (especially gastrointestinal intolerance) typically get better.

The most serious adverse effect associated with duloxetine is the increased risk of suicidality when starting this medication, especially in people under age 25. If you have a history of bipolar disorder, manic episodes, or suicide attempts you will not be eligible for participation in the Duloxetine study intervention. If you are assigned this study treatment, you will be regularly monitored for clinical worsening, suicidality, or unusual changes in behavior.

If you are having suicidal thoughts call the study doctor at the telephone number listed on the first page of this form. If you feel in crisis, you can call 911 and/or a Nationwide Suicide Hotline that is answered 24 hours a day with a skilled, trained counselor. One example is the National Suicide Prevention Lifeline at 1-800-273-TALK (8255).

If you notice any change in your health or new symptoms after initiating this treatment we would like you to notify the study team, and they will provide counseling on how to proceed.

Allergic Reaction Risk

As with taking any drug, there is a risk of allergic reaction when taking duloxetine. If you have a very serious allergic reaction, you may be at risk of death. Some symptoms of allergic reactions are:

- Rash
- Wheezing and difficulty breathing
- Dizziness and fainting
- Swelling around the mouth, throat or eyes
- A fast pulse
- Sweating

Please seek treatment immediately and tell the study doctor and study staff if you have any of these symptoms.

Enhanced Self-Care (ESC)

The ESC treatment is an educational and self-care digital intervention. If you are assigned to this study treatment, your risks are minimal.

Evidence-Based Exercise and Manual Therapy (EBEM)

If you are assigned to EBEM Therapy, a trained provider will use manual therapy to reduce pain and stiffness, and to improve range of motion. Manual therapy consists of hands-on treatment to increase the movement and flexibility of your joints and muscles. The trained provider will also ask you to do specific exercises to improve muscle strength, flexibility and endurance. Both are considered safe for the treatment of low-back pain. The side effects associated with therapeutic exercise, manual therapy to your joints and muscles are common and benign, such as transient post-study treatment muscle and/or joint soreness which typically resolve within 24 hours. If you receive hands-on study treatment to your muscles, you may have mild muscle soreness at the site of the study treatment during and after study treatment. Skin irritation is also possible if massage lotions and oils are used.

You may be asked to discuss your pain experiences and the impact of low-back pain on various aspects of your life, which may cause emotional distress. EBEM is not recommended for people with high blood pressure or heart conditions.

Run-In Period

During the run-in period, you will be asked to read informational materials delivered to you electronically. Risks are minimal.

What are the risks to a pregnancy or to a nursing child?

If you are pregnant or planning to get pregnant, you should not be in the study.

If you are currently breastfeeding, you will not be eligible for participation in the Duloxetine study intervention.

If you choose not to be in the study, what other treatment options do you have?

You do not have to be in this research study in order to receive treatment. All of the treatments in this study are available outside of this study. If you do not wish to participate in this study, but would like to pursue treatment for your chronic low-back pain, contact your physician to discuss your options.

What if new findings are made during the study that provides new information?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

Will I receive the results from my MRIs?

The images we are using in this study will be reviewed for study purposes only. Images will not be reviewed for the purpose of providing individual health information to study participants. As a result, you may not be informed of any unexpected findings.

How will information about you be protected?

Your participation in this study will be kept confidential (private) as permitted by law. This includes information you provide in your questionnaire answers and data from your laboratory results. You will be assigned a special study code that will be used on the questionnaires and all study forms. The list that links your name with this special study code will be kept in a secured, private location. Only information needed for this study is recorded. Staff members involved in conducting this study are required to sign a form stating they will protect your information.

Your coded information from the study will be stored securely by the study team and the data coordinating center at the University of North Carolina at Chapel Hill. The data coordinating center provides the study researchers with limited coded information for analysis. All study information is grouped together and information will not be linked to any one person. If reports or results from that data are shared with the study team and the research staff at your site, no one will know what information is yours.

Once the study is over, the study data will be stored indefinitely at a location approved by the National Institutes of Health (NIH).

Participants will not be identified in any report, presentation, or publication about this study.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, the study site will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research

study could be reviewed by representatives of the study site, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

Every effort will be made to keep your being in the study and your personal information private and confidential; but absolute confidentiality cannot be guaranteed. For example, if we learn something that would immediately put you or others in danger, the researchers are required by law to take steps to keep you and others safe. This means that we have to report to the authorities (hospital, police, or social services) any information you tell us that suggests you might be in danger, such as if you tell us that you plan to hurt or kill yourself, hurt or kill someone else, or if you tell us that someone is abusing or neglecting you.

As part of the study, the study team may share the results of your study assessments and parts of your medical record with the groups named below. These groups may include people from the Back Pain Research Consortium (BACPAC), These groups are required to make sure your protected health information (PHI) is kept private.

In addition, your records may be reviewed, under guidelines of the Federal Privacy Act, by the sponsoring agency at the NIH, study monitors acting on behalf of the NIH, investigators and research staff from BACPAC, and by Advarra IRB to make sure that the study staff is doing what they are supposed to and that study participants are protected. If your study records are reviewed, your identity could become known to them.

Under some state laws, confidentiality does not extend to certain communicable diseases, such as TB, HIV, hepatitis, or other illnesses that put others at risk. If the researchers become aware that you have such an illness, they may be required to report it to state authorities.

Audio- and Video-Recorded Data

EBEM sessions, study-related telephone calls, and some ACT face-to-face visits with a therapist might be recorded for quality control purposes. This is to ensure that providers are following study procedures.

You will be notified if a study visit, phone call, or telehealth visit is being recorded. Even if you consent to be recorded, you may request that any recording be stopped at any point during a visit or call. You do not need to agree to be recorded to be in the study.

Video tapes, audio recordings, and any transcripts of these recordings will be stored securely up to seven years after the study is finished. After that time, they will be destroyed.

Please initial one of the lines below to indicate whether you consent to being recorded during this study.

_____ OK to record me during the study

_____ Not OK to record me during the study

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research participants or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Will my study data be included in my medical records?

By signing and dating this informed consent document, you agree that some of the information generated by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you.

Storage and Sharing of Your Data and Samples

Your blood and biospecimen-related data will be stored securely at the study site before being shipped to the NIH-approved central process laboratory for storage and analysis during the study. Participants will collect stool samples at home and ship them to the NIH-approved central process laboratory. At the end of the study, all remaining samples will be stored at sites that the NIH selects for this study. Your data will also be stored securely at the study site, on data servers, and in HIPAA-compliant data management systems. Your data and samples will be stored indefinitely. We will do our best to protect your personal information. Your name and other personally-identifying information will not be kept with the data or samples. Your data and samples will either be stored without a code linking them to you or they will have a code that links to your identifying information. If your data has a code, the key to the code will be kept at the study site in a separate, secure area and will not be shared outside of the study site.

This study is part of the NIH HEAL Initiative focused on understanding and developing new treatments for addiction and pain. Research gives us the best information and progresses more quickly when data is available from many studies and many individuals, and when many researchers can work with the data and samples and analyze them in different ways. Therefore, as well as using your data and samples for the purpose of this and other NIH HEAL Initiative studies, we would like your permission to make the data and samples collected in the study widely available to other researchers. The shared data and samples may be used indefinitely for research not related to this study or the HEAL Initiative, without asking you for additional consent.

Your samples collected for this study contain your DNA. Your DNA and genetic information is unique to you. With your permission, your genetic information may also be used for research unrelated to this study.

If you withdraw from this research study before it is done, we will keep and continue to use data and samples that have already been collected. Your privacy will be protected to the full extent possible.

Please review the information on the potential benefits and risks of storing and sharing your data and samples and then indicate your decision in the box below.

Potential benefits of sharing of data and samples

There is no direct benefit to you from the storage and sharing of data and samples, but sharing may help researchers learn more about low-back pain and other diseases, which may help you or others in the future.

Risks of sharing data and samples

Even though we will protect your privacy as much as possible, there is a very small chance that the data and samples could be identified as yours. The risk of this happening is very small, but may grow in the future as technology changes.

Research using data and samples from this study may lead to new tests, drugs, or devices with commercial value. You will not receive any payment for any product developed from research using your samples and data.

Please indicate your choice regarding data and sample sharing by initialing on one of the lines below:

I agree to the sharing of my data and samples for use in other research studies.

Yes_____ **No_____**

Will you receive results from research involving your specimens?

Most research with your specimens is not expected to yield new information that would be meaningful to share with you personally. There are no plans to re-contact you or other participants with information about research results.

The use of your samples may result in commercial profit. You will not be compensated for the use of your samples other than what is described in this consent form.

You will be asked to sign a separate form ("HIPAA Authorization") to allow researchers to review your medical records.

What will happen if you are injured by this research?

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured then they will help you get the care you need.

If you are injured as a result of taking the study drug(s) or from procedures done for the purpose of this study, you will have to pay for any medical expenses necessary to treat your injury that are not covered by your medical insurance or any other third-party coverage. The study site has not set aside funds to pay you for any such injuries, illnesses, or reactions, or for the related medical care.

By signing and dating this document, you will not lose any of your legal rights or release anyone involved in the research from responsibility for mistakes.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The study investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction to a study intervention, you no longer meet the eligibility criteria for the study or for the intervention to which you have been assigned, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

Will it cost you anything to be in this study?

If you enroll in this study, you will have costs which include travel to/from the clinic and, if applicable, child/dependent care needed while participating in study visits.

The study treatments and assessments will be provided at no cost to you.

Will you receive compensation for being in this study?

«Compensation»

You may receive up to $1,745 for taking part in this study – up to $1,275 for required study activities and up to $470 for other study activities. Please see the table below for more detail. Any payment provided for participation in this study may be subject to applicable tax withholding obligations.

Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If an individual's study payment(s) equals or exceeds $600 per calendar year for U.S. persons, that amount will be reported to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted above, we cannot issue you a payment for participation. However, you may still choose to participate in this study.

The table below describes the payment by study activity completed. The first table describes required activities, and the second table describes additional activities that are not required for participation in the study. Not all participants will participate in the additional activities. The cost of parking and other costs related to participation in study activities may be covered per your study site (if applicable). If you participate in the additional assessments, you will receive additional payments, which are detailed in the second table below. If you terminate early from the study, you will be reimbursed for those portions of the study you completed.

Payments for Required Study Activities

Study Activity	Payment per activity or day	Maximum number of activities/days	Maximum total for activity
In-person study visits	$100	7	$700
2-week run-in period	$20	1	$20
Blood draw	$20	3	$60
Return stool sample	$20	1	$20
Spine MRI	$90	1	$90
Motion assessment	$20	3	$60
Questionnaires	$25	10	$250
Completion bonus	$75	1	$75

Payments for Additional Study Activities

Study Activity	Payment per activity or day	Maximum number of activities/days	Maximum total for activity
Brain MRI	$90	3	$270
Advanced Spine MRI	$45	1	$45
Return sensors	$50	1	$50
Additional motion assessments	$20	3	$60
QST	$15	3	$45

If you do not complete the study, for any reason, you will be paid for each study visit you do complete.

You will be paid _____ ***["following each completed visit", "monthly", "quarterly", "at the end of your participation in the research study", "following each completed visit or at the end of your participation in the research study, whichever you prefer"]***.

If you have any questions regarding your compensation for participation, please contact the study staff.

Who is sponsoring this study?

This research is funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

Whom to Contact About This Study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the study investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, and/or concerns or complaints regarding this research study, contact:

- By mail:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00057948.

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.

What if you have questions about your rights as a research participant?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 410-884-2900 or by email to adviser@advarra.com.

Required and Optional Study Assessments

All participants in the study will be required to:

- answer questionnaires
- receive a physical exam
- receive a motion assessment lasting approximately 10 minutes at each of 3 separate visits[1,2]
- provide blood samples at 3 separate visits
- receive an at-home stool collection kit to provide a single stool sample
- receive 1 spine MRI lasting approximately 30 minutes[3]

Participants who meet additional eligibility requirements may participate in further assessments *in addition to* the required study assessments as the site's appointment schedule allows.

Participants participating in additional assessments may:

- receive additional motion assessments lasting approximately 50 minutes at each of 3 separate visits[1,2]
- receive an advanced spine MRI lasting approximately 30 minutes[2,3]
- receive a brain MRI lasting approximately 60 minutes at each of 3 separate visits[1,2,3]

- receive sensory testing (pressure, temperature) lasting approximately 60 minutes at each of 3 separate visits[1,2]

[1]Participants should **not** take "as needed" medications for at least 8 hours before these assessments. As needed pain medications include NSAIDs (for example, Motrin, Advil, Aleve), acetaminophen (for example, Tylenol), certain anti-anxiety medications (for example, Valium, Xanax), certain sedatives (for example, Ambien), and opioids.

[2]Participants should **not** consume alcohol the day of the assessment.

[3]Participants must lie flat on their backs for the duration of the MRI.

Please initial one of the lines below to indicate whether you consent to being considered for participating in the additional assessments for this study. Your consent does not guarantee participation in the additional assessments.

_____ YES, I consent to being considered for participation in the additional assessments

_____ NO, I do not consent to being considered for participation in the additional assessments

Access to past and future electronic medical records

As part of this study, investigators would like to study how chronic low-back pain patients use health insurance. To do this, investigators will need to access your electronic medical records and/or your health insurance claims data.

We are asking your permission to access your electronic medical records and health insurance claims data to view claims activity occurring one year prior to your enrollment in this study through one year after you complete this study. This is approximately three years of claims data.

We are also asking your permission to access the data described above at any point from the time of your enrollment in this study through four years after the study ends.

Please initial one of the lines below to indicate whether you consent to access to your electronic medical records.

_____ YES, study investigators may access my electronic medical records and claims data for this purpose and for the time period described above.

_____ NO, study investigators may not access my electronic medical records and claims data for this purpose or for the time period described above.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

_____
Date

_____
Printed Name of Research Participant

_____
Signature of Research Team Member Obtaining Consent

_____
Date

_____
Printed Name of Research Team Member Obtaining Consent