Human Subjects Protocol

VA Puget Sound IRB

Combined Treatments to Optimize Functional Recovery in Veterans with Chronic Low Back Pain
[MIRB # 01676]

Funding Agency: VA RR&D

Principal Investigator: Pradeep Suri MD MS

V7.0

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Abstract

Objective:
Combining procedural and behavioral treatments may have great potential for achieving large magnitude treatment effects for CLBP in Veterans. This is a pilot clinical trial to evaluate the effects of treatment combinations among Veterans with chronic lower back pain (CLBP) with four possible treatment arms: lumbar medial branch nerve radiofrequency ablation (LRFA), targeted steroid injections to the facet nerves with simulated LRFA, video telehealth tablet- and PC-based Activity Tracker-Informed Video-Enabled Cognitive Behavioral Therapy (AcTIVE-CBT), and telephone-based self-directed CBT and education (TBSCE).

Research Design and Methodology:
The proposed research uses a 2 x 2 factorial randomized control trial (RCT) design to examine the individual and combined effects of LRFA and AcTIVE-CBT. The primary outcome is participant-reported back-related functional limitations (mobility and activities of daily living [ADLs]) at 3 months, as measured by the Roland-Morris Disability Questionnaire. Secondary outcomes include activity tracker-assessed step counts, back pain intensity, reduction in opioid use, and quality of life. The randomized control trial will include up to 30 patients from the VA Puget Sound Health Care System (VAPSHCS) Pain Clinic aged 18 and older with a history of CLBP and eligibility for a LRFA procedure, of whom we expect 20 participants will be randomized and complete 3-month data collection. Appropriate LRFA candidates will be offered to participate according to the same criteria used for determining LRFA eligibility in usual clinical care (including responses to 2 sets of medial branch blocks [MBBs]). The provision of LRFA, targeted steroid injections to the facet nerves, AcTIVE-CBT, and TBSCE treatments are not considered to be research, since these treatments are usual clinical care or modifications to usual clinical care. All aspects of treatment will involve credentialed providers already working at VAPSHCS. These clinical treatments will be coordinated within the framework of the study procedures and processes.

Participants will schedule a date for their lumbar procedure (LRFA or targeted steroid injections to the facet nerves with simulated LRFA). Computer-generated concealed block randomized assignment lists will be created, and baseline study assessments will take place on the day of the lumbar procedure. AcTIVE-CBT and TBSCE treatments will take place over 3-months post-randomization. Participants would be blinded to whether they are receiving the study ‘interventions’ or ‘controls’, over the first 3 months of follow-up. Follow-up study assessments will happen 1 month, 2 months, and 3 months post-procedure. The main outcome time point is 3-month follow-up. After the 3-month main study period, participants will be offered the option to either be unblinded to their treatment allocations or to remain blinded to their assigned treatments for up to 9 additional months of optional monthly study outcome assessments. Unblinded participants may make subsequent treatment decisions as they wish, so optional assessments after the study period may be affected by unblinding and other changes in treatment and are not truly randomized comparisons. Participants who did not receive LRFA during the main 3-month period of follow-up may elect to pursue LRFA as part of normal clinical care.

Relevance to VA Mission:
The potential for learning about effective treatment combinations for CLBP yielded by this research is directly relevant to the clinical care of Veterans with this condition. These findings may inform clinical care practices, and/or future research to more definitively characterize the specific and combined effects of the treatments studied here.

List of Abbreviations

VA	Veterans Affairs
CLBP	Chronic Low Back Pain
AHRQ	Agency for Health Research and Quality
RCT	Randomized Control Trial
LRFA	Lumbar Radiofrequency Ablation
AcTIVE-CBT	Activity Tracker-Informed Video-Enabled CBT
CBT	Cognitive Behavioral Therapy
PC	Personal Computer
VAPSHCS	VA Puget Sound Health Care System
MBB	Medial Branch Block
TBSCE	Telephone-Based Self-directed CBT and Education
ADLs	Activities of Daily Living
PI	Principal Investigator
Co-I	Co-investigator
TREWI	Telerehabilitation Enterprise-Wide Initiative
VAPS	VA Puget Sound
CPRS	Computerized Patient Record System
RFA	Radiofrequency Ablation
PM&R	Physical Medicine & Rehabilitation
UW	University of Washington
ACGME	Accreditation Council for Graduate Medical Education
HIPAA	Health Insurance Portability and Accountability Act
NRS	Numerical Rating Scale
ICF	Informed Consent Form
ERIC	Epidemiologic Research and Information Center
TICS	Telephone Interview for Cognitive Status
RMDQ	Roland-Morris Disability Questionnaire
PROMIS	Patient-Reported Outcomes Measurement Information System
NIH	National Institutes of Health
AE	Adverse Event
ANOVA	Analysis of Variance
DMC	Data Monitoring Committee
SAE	Serious Adverse Event
CRF	Case Report Form
ED	Emergency Department
ICU	Intensive Care Unit
UAP	Unanticipated Problem
ADE	Adverse Device Effect
UPIRTSO	Unanticipated AND Related Problem Involving Risk to Subjects or Others
PHI	Protected Health Information
HSR&D	Health Services Research & Development

Contents

Protocol Title:

Combined Treatments to Optimize Functional Recovery in Veterans with Chronic Low Back Pain

Lay Title: Selecting **E**ffective **C**ombinations of **T**reatment for **L**ow **B**ack **P**ain (SELECT LBP or 'SELECT')

1.0 Study Personnel

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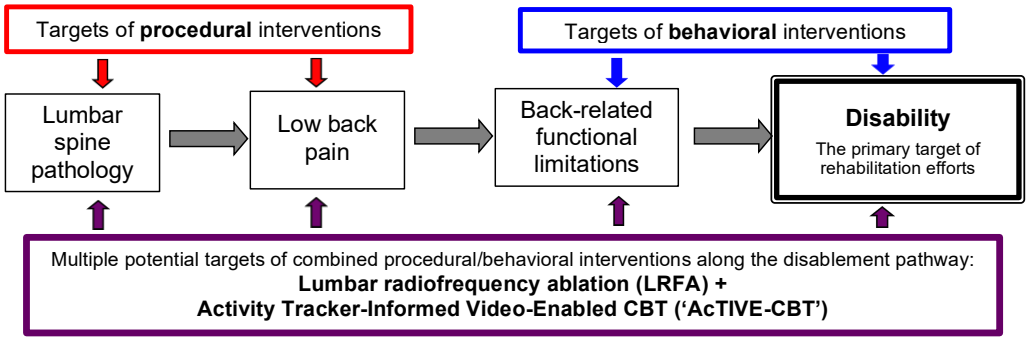
2.0 Introduction

Back pain is the most common pain location and reason for chronic opioid use in Veterans.[12,16] It is also the most common reason for new VA disability compensation after tinnitus and hearing loss.[32] Due to the high prevalence of disabling back pain in Veterans and the functional impact of CLBP in particular, improvement in treatments for CLBP has tremendous potential for improving functional recovery in the Veteran population, perhaps greater than that for any other health condition.

A major barrier to mitigating the impact of CLBP on the Veteran population is the fact that most CLBP treatments have only small magnitude effects. In a review commissioned by the Agency for Health Research and Quality (AHRQ), we found improvements in pain of ≤10% for most first-line rehabilitative treatments for CLBP, such as exercise therapy (including physical therapy), yoga, and tai chi.[6] Improvements in functional limitations were generally even smaller than improvements in pain.[6] For these reasons, **combining pain treatments in future VA research emerged as a core recommendation in 2016 from a VA State of the Art conference on non-pharmacologic pain management (SOTA #13)**.

Similar suggestions were also made in 2016 by other US agencies including AHRQ,[6] the Patient-Centered Outcomes Research Institute,[28] and joint research initiatives by the National Institutes of Health, VA, and Department of Defense.[27]

Figure 1. A conceptual model of back-related disability, and potential targets of CLBP treatments



An important unanswered question is "*Which treatments should be combined?*". In the context of the stepped-care model of pain treatment applied in the VA and many US settings,[1,34] it may be impractical or unethical to combine first-line CLBP treatments (such as physical therapy) with second-line treatments (such as invasive spine procedures or surgeries), since failure of first-line treatment is typically a prerequisite for invasive second-line CLBP treatments. Another vital consideration is which intervention combinations are most likely to produce larger magnitude treatment effects than that of individual treatments alone. In approaching this question, we applied the theoretical framework of the Nagi disablement model, in which back pain is considered an impairment on the pathway to disability (**Figure 1).** Functional recovery and minimizing disability are the end goals of rehabilitative care. We reason that combining treatments that target distinct points in the disablement pathway are more likely to achieve large effects on functional recovery, as compared to treatments targeting the same underlying mechanisms (which might lead to redundancy and diminishing returns). **Procedural interventions** for CLBP aim primarily to address proximal stages in the disablement pathway, such as the underlying lumbar spine pathoanatomy and low back pain. In contrast, **behavioral interventions** for CLBP also target factors over which patients have some control, such as the way patients think about pain, or how pain affects their behavior. By modifying these things, behavioral interventions may affect distal stages in the disablement pathway and achieve effects on functional recovery that are not necessarily dependent on an improvement in pain. **Therefore, we theorize that a combination of procedural and behavioral treatments may have the greatest potential for realizing large magnitude treatment effects for CLBP in Veterans.**

Towards this end, this study will use a 2 x 2 factorial randomized controlled trial (RCT) design to investigate the individual and combined effects of **1) lumbar medial branch nerve radiofrequency ablation (LRFA),** a commonly used procedural intervention to target low back pain severity, and **2) a telehealth tablet- and personal computer (PC)-based Activity Tracker-Informed Video-Enabled Cognitive Behavioral Therapy** program **(**which we call ***"AcTIVE-CBT"*)**, a behavioral intervention designed primarily to target functional limitations both secondary to, and independent of, improvements in pain. AcTIVE-CBT is a modification of standard CBT delivered by video telehealth, which places a greater emphasis on increasing physical activity, and uses current activity tracker technology to support physical activity and an active lifestyle more broadly. For each of these 2 treatments, we will compare outcomes with another standard of care treatment that either poses 1) less risk, or 2) less inconvenience to the Veteran participant, but with potentially comparable or equivalent treatment benefits. **The factorial RCT design of this study will inform as to whether 'stacking' disparate CLBP treatments can result in greater treatment effects than that of each treatment alone.** This study will produce valid

effect size estimates that will inform a definitive future large-scale multicenter RCT to determine the efficacy of LRFA, AcTIVE-CBT, or combined LRFA + AcTIVE-CBT, for Veterans with CLBP.

LRFA is a minimally invasive non-pharmacologic procedure offered at many VA pain clinics, and it is standard care at the VAPSHCS Pain Clinic. It can be used in patients for which CLBP is isolated as coming from the lumbar facet joints, defined by pain relief ('positive responses') to local anesthetic medial branch blocks (MBBs) along the dorsal ramus medial branch nerves (which we refer to informally here as the 'facet nerves').[7,17,22,23,30] Unlike most CLBP treatments, LRFA may result in large-magnitude improvements (≥75% for pain and functional limitations) in properly selected patients.[10] However, LFRA is a neurodestructive procedure involving the temporary destruction of the facet nerves, and there is conflicting evidence regarding its efficacy.[2,5,9,11,18,19,21,26,29-31,33] In particular, it is unknown whether LRFA achieves greater improvements in functional limitations when compared to other active procedure treatments such as injections targeting the facet joints that do not destroy the facet nerves.[17] In this proposed research, outcomes for participants receiving the LRFA procedure will be compared to outcomes for participants receiving a simulated LRFA procedure, in which targeted steroid injections are administered to the involved facet nerves that would otherwise have been destroyed (that is, no nerve destruction is performed).

Although cognitive-behavioral therapy (CBT) is an accepted treatment with demonstrated efficacy for CLBP, [3,4] conventional CBT is not widely available, particularly in rural areas,[14] and incurs substantial travel burdens for Veterans. Our AcTIVE-CBT modification to standard CBT will allow rehabilitation psychologists to deliver CBT directly to Veterans in their homes using video-enabled tablets or PCs, facilitating greater compliance and access. The AcTIVE-CBT intervention also applies unique approaches to promote sustainable behavior change towards a more active lifestyle, including use of the Fitbit activity tracker to provide accurate, objective feedback on activity levels and step counts to Veterans and providers and inform goal setting and progress. Such an approach may facilitate the improvements in functional limitations and activity that have been elusive in RCTs of procedural interventions such as LRFA. An important unanswered question is whether still more efficient (i.e. fewer treatments) programs of CBT and more convenient options for CBT (self-paced and self-directed programs) may result in similar improvements, at still greater efficiency and ease for Veteran access. In this proposed research, outcomes for participants receiving AcTIVE-CBT will be compared to outcomes for participants receiving 'telephone-based self-directed CBT and education' or TBSCE, a brief and efficient form of telehealth CBT. The TBSCE treatment involves a single telephone-based counseling session between the Veteran participant and a psychologist with a structured 3-month plan of education and lessons pertaining to principles of CBT and training to develop active habits of CBT guided by printed materials that we will provide. The structured plan is designed to be self-paced and convenient, allowing for some flexibility while covering all the main components of traditional CBT. These will be supplemented by a supportive contact at the approximate midpoint of the 3-month period and ad hoc availability of the psychologist if requested by the participant.

The expected age range of study participants is 18 years of age and older. We expect the general health status of the subject population to be about average for Veterans' ages. Patients with severe and major active medical or psychiatric comorbidities will not be eligible for the study due to not being clinical candidates for the lumbar procedures and/or CBT and/or candidates for the study procedures. We will not include patients from special classes of subjects or vulnerable populations such as pregnant women,

children, cognitively impaired persons, or prisoners due to possible coercion. We will not otherwise make any exclusions based on gender, sex, race, ethnicity, or any minority group designation. VA employees may be enrolled in the study; however, if enrolled, they cannot complete assessments on their VA paid time. 'Assessments' or 'questionnaires' as referred to in this Protocol are delivered as interviews and do not fall under the definition of "surveys" as used in the Survey Guidance document. As such, OASC and local VAPS HR will not be notified if a VA employee enrolls in this study.

3.0 Objectives

Study Aim: To estimate the individual and combined treatment effects of 1) LRFA (vs. simulated LRFA with targeted steroid injections to the facet nerves) and 2) AcTIVE-CBT (vs. a telephone-based self-directed CBT and education control) in up to 30 Veterans at 3-month follow-up. The primary outcome is participant-reported back-related functional limitations (mobility and ADLs) as measured by the Roland-Morris Disability Questionnaire at 3 months. Secondary outcomes include daily step counts, back pain intensity, reduction in opioid use, and quality of life.

Hypotheses: 1) Each individual treatment will result in improvements in back-related functional limitations and secondary outcomes compared to control, and 2) Combined treatment will produce greater treatment effects than each of the individual treatments alone.

4.0 Resources and Personnel

- This research will be conducted by Dr. Pradeep Suri and the following individuals entirely at VA Puget Sound Health Care System (VAPSHCS)
- Dr. Suri is the PI and will be responsible for study planning and broad oversight; supervising study procedures; integrity of data collection; interpretation of findings; and all subsequent steps including manuscript preparation and submission. He will have access to protected health information.
- Dr. Williams is co-I and will be responsible for study planning and oversight of any aspects related to CBT; supervising study procedures; interpretation of findings; and subsequent steps including manuscript preparation and submission. She will have access to protected health information.
- Dr. Nishio is co-I and will be responsible for study planning and oversight of any aspects related to LRFA or simulated LRFA with targeted steroid injections; interpretation of findings; and subsequent steps including manuscript preparation and submission. He will not have access to protected health information.
- Dr. Soares is co-I (non-key personnel) and will be responsible for some aspects of oversight related to LRFA or simulated LRFA with targeted steroid

injections; and subsequent steps including manuscript preparation and submission. He will not have access to protected health information.

- Dr. Dawson is co-I (non-key personnel) and will be responsible for some aspects of LRFA or simulated LRFA with targeted steroid injection procedures; and subsequent steps including manuscript preparation and submission. He will not have access to protected health information.
- Dr. Hsu is co-I (non-key personnel) and will be responsible for some aspects of LRFA or simulated LRFA with targeted steroid injection procedures; and subsequent steps including manuscript preparation and submission. She will not have access to protected health information.
- Dr. Korpak is the study biostatistician. She will be involved in data analysis; and in manuscript preparation and submission. She will not have access to protected health information.
- Mr. Timmons is the study biostatistician. He will be involved in performing data analysis and be involved in manuscript preparation and submission. He will not have access to protected health information.
- Dr. Moore will function as the data manager. She will obtain data from the Corporate Data Warehouse and assemble that data into a format ready for analyses. She will not have access to protected health information.
- Ms. Fox is the data analyst. She will obtain data from the Corporate Data Warehouse and assemble that data into a format ready for analyses. She will not have access to protected health information.
- Mr. Morelli is the data administrator. He will obtain data from the Corporate Data Warehouse and assemble that data into a format ready for analyses. He will not have access to protected health information.
- Mr. Forsberg is the biostatistician. He will be involved in performing data analysis and in manuscript preparation and submission. He will not have access to protected health information.
- Ms. Marshall is the program manager. She will supervise other administrative staff below. She will not have access to protected health information.
- Mrs. Garcia is the Fitbit coordinator. She will be involved in administrative tasks and coordination of Fitbit-related tasks. She will have access to protected health information.
- Ms. Tanus is the research coordinator. She will be involved in recruiting subjects; obtaining informed consent; and administering questionnaires/interview procedures. She will have access to protected health information.
- Ms. Jang is the research assistant. She will be involved in recruiting subjects; obtaining informed consent; and administering questionnaires/interview procedures. She will have access to protected health information.

- Ms. Libbing is the research assistant. She will be involved in recruiting subjects; obtaining informed consent; and administering questionnaires/interview procedures. She will have access to protected health information.

5.1 Study Design

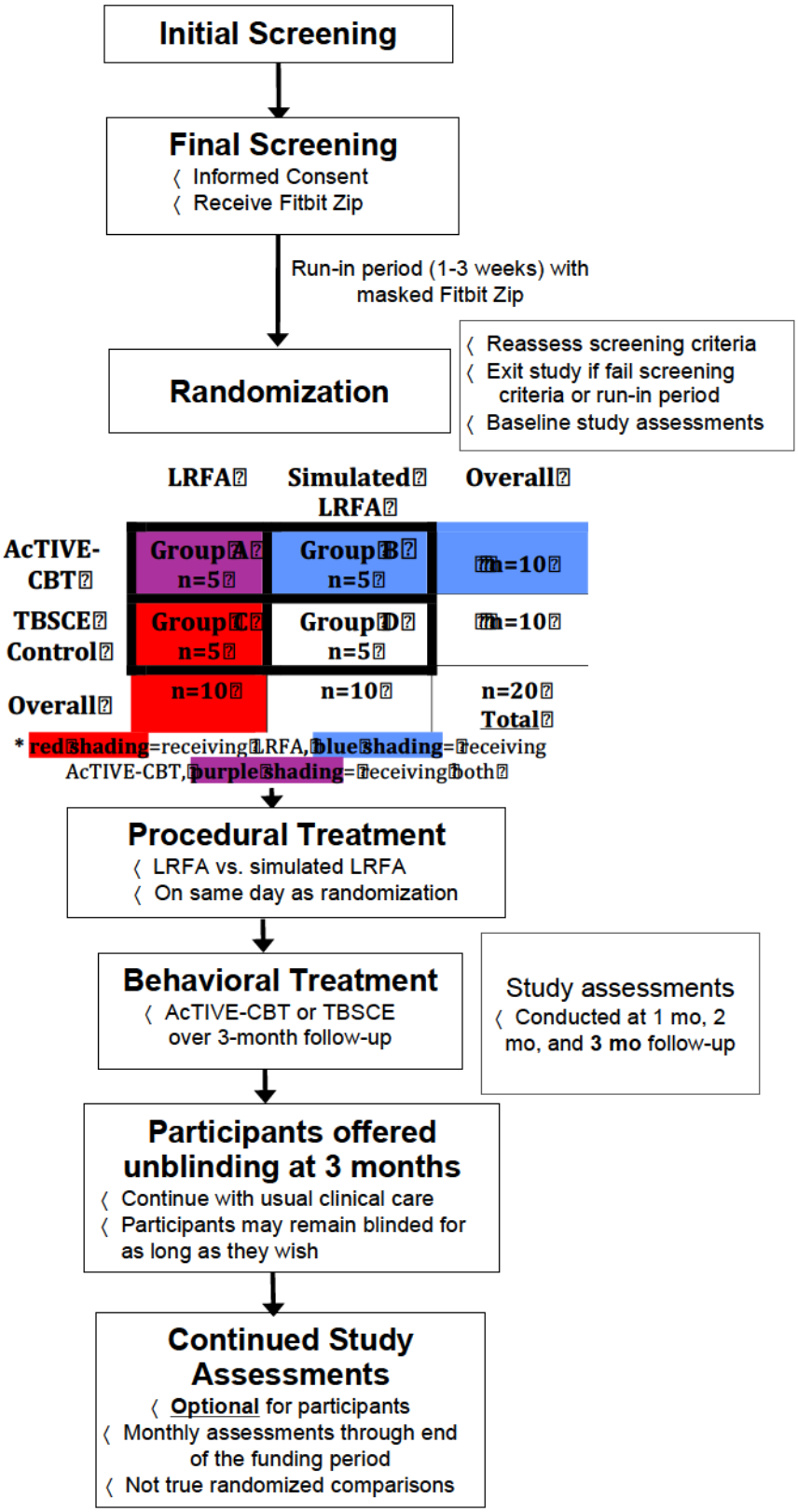
We will conduct a 2 x 2 factorial pilot RCT to investigate the individual and combined effects of 1) lumbar radiofrequency ablation (LRFA) vs. simulated LRFA control with targeted steroid injections to the facet nerves, and 2) Activity Tracker-Informed Video-Enabled Cognitive Behavioral Therapy (AcTIVE-CBT) vs. TBSCE. For simplicity of language, henceforth in this protocol we frequently refer to simulated LRFA with targeted steroid injections to the facet nerves as 'simulated LRFA'. All treatments that will be allocated as part of this research are standard-of-care, "active" treatments expected to improve function and pain in those with CLBP. The study will recruit up to 30 Veterans, with the goal of having 20 Veterans with chronic low back pain (CLBP) who provide complete data for the main study outcome at 3-month follow-up post-randomization (the Roland-Morris Disability Questionnaire), with a minimum of 4 completers of the main 3-month follow-up outcome in each of the 4 'cells' for treatment (see **Figure 2**). Participants would be blinded to whether they are receiving the study 'interventions' or 'controls', over the first 3 months of follow-up. Following the main period of data collection of 3 months of follow-up post-randomization, for those participants who wish to continue with the study, we will continue to collect observational data monthly thereafter for the duration of the funding period (up to 9 additional months); such data collection will continue with or without unblinding to participant group assignments per the randomization, according to what the participant decides. Unblinded participants may make subsequent treatment decisions as they wish, so optional assessments after the study period may be affected by unblinding and other changes in treatment and are not truly randomized comparisons. Participants who did not receive LRFA during the main 3-month period of follow-up may elect to pursue LRFA as part of normal clinical care, and those who receive TBSCE may elect to pursue standard video telehealth CBT (a typical 'extended' course of CBT).

All aspects of intervention and control treatments will be conducted within the context of existing standard of care clinical processes at the VAPSHCS Pain Clinic, the Rehabilitation Care Services division, and the VAPSHCS Telerehabilitation Enterprise-Wide Initiative (TREWI) program (which offers video and telephone telehealth services for a variety of target conditions, including CBT for CLBP). Both LRFA and targeted steroid injections to the facet nerves are commonly performed and standard of care procedures for chronic low back pain in the US.[17,24,25] Although there are no significant differences with respect to improvement in functional limitations between LRFA and targeted steroid injections in randomized controlled trials, [17,20] targeted steroid injections to the facet nerves likely have a lower risk profile than LRFA, given that no nerve destruction occurs.

CBT is also widely accepted as standard of care treatment for chronic pain and CLBP, although there are major limitations on the availability of this treatment in the US, and for Veterans.[3,4] The AcTIVE-CBT and TBSCE treatment arms in this study correspond to extended and brief courses of CBT, respectively. We

expect that the two telehealth treatments to be used in this study, if effective, will be a step toward providing better options to mitigate these limitations in availability for Veterans and non-Veterans alike.

Figure 2



Description of Risks and Risk vs. Benefit

Anticipated risk with this study is minimized because, from the standpoint of interventional spinal procedures offered as part of this study, eligible participants for this study will be identified from among patients receiving MBBs for the purpose of obtaining LRFA in the future. Thus, no individuals who were not already seeking to obtain LRFA as part of usual clinical care services offered at VAPS will be candidates for this study. Potential physical risks from participating in the study involve the same therapeutic risks that would normally be involved with undergoing the LRFA procedure in usual clinical practice (if patients are randomized to the LRFA procedures), or less expected risk than LRFA (if they are randomized to the simulated LRFA procedure, which includes targeted facet nerve injections but will not involve the nerve destruction that is part of LRFA). In other words, risk with simulated LRFA may be less than LRFA, since simulated LRFA does not involve the destruction of the facet nerves. Potential benefits of the study include receiving benefit in CLBP and functional limitations from simulated LRFA and targeted steroid injections and not having to undergo nerve destruction with LRFA.

There are no physical risks associated with the AcTIVE-CBT and TBSCE treatments. There is potential benefit in terms of improving CLBP and functional limitations with both treatments; benefits in the TBSCE treatment ('brief CBT') will involve substantially fewer treatment sessions and may be more convenient than AcTIVE-CBT ('extended CBT').

Other specific risks of the clinical treatments as routinely provided in usual clinical care are provided below in plain language typical of what is included in the consent form. Although in some situations, the risks associated with usual clinical care that take place within the contexts of a research study might not be described in the research protocol itself, in this instance we describe in detail the risks associated with LRFA. This is done for two main reasons: 1) To avoid any situations in which study participants might not be aware of the attendant risks/benefits of LRFA, a procedure they have sought for treatment of CLBP as part of their normal clinical care. This is relevant because in routine clinical care patients often have misconceptions about what LRFA involves and what the extensive typical screening process for LRFA typically involves; and 2) Because simulated LRFA with targeted steroid injections in the context of this study represents a less invasive (not neurodestructive) procedure which may eliminate or avoid the need for LRFA, and thus, an accurate sense of risk/benefit and relative risk/benefit relies on knowledge of both procedures.

Physical risks:

The LRFA procedure entails applying anesthetic around the nerve to the facet joint and applying heat to selectively destroy the nerve that supplies the facet joint. This may result in relief of pain (the goal of the procedure) until the nerve regenerates over the course of several months, after which time low back pain related to the facet joints would be expected to resume.

LRFA involves the use of x-rays to guide the procedure, and the x-ray radiation amounts involved with LRFA are low. The average amount of radiation exposure from these x-rays will be between 1-8% of the average exposure any person receives from the environment per year. Common risks of LRFA include having no reduction of pain, numbness at the procedure site, temporarily increased back pain, lowering of your blood pressure, facial flushing, or increases in blood sugar levels. Less commonly patients can have nausea; bleeding, persistent redness, or swelling at the procedure site; temporary changes in mood or hormone levels; or brief (lasting minutes to hours) numbness, weakness, or paralysis of the back or legs. In rare instances, cardiac arrest; irregular heartbeat; seizure; nerve injuries; infections; unexpected allergic reactions; bone problems such as bone necrosis; permanent areas of numbness, weakness, worsened pain, or paralysis; spinal cord damage; stroke; and death have been reported with LRFA.

If a participant were to receive simulated LRFA with targeted steroid injections to the facet nerves without

destroying the facet nerves as part of this research study, the possible physical risks are the same as LRFA, but are generally expected to be less likely than that which would be involved in LRFA, since the nerves are not destroyed. Targeted steroid injections to the facet nerves involve the use of x-rays to guide the procedure, and the x-ray radiation amounts involved are low. The average amount of radiation exposure from these x-rays will be between 1-8% of the average exposure any person receives from the environment per year.

Common risks of simulated LRFA with targeted steroid injections to the facet nerves include no reduction of pain, temporary increased back pain, lowering of your blood pressure, facial flushing, or increases in blood sugar levels. Less commonly, patients can have temporary changes in mood or hormone levels, bleeding, persistent redness, or swelling at the procedure site, or brief (lasting minutes to hours) numbness, weakness, or paralysis of back or legs. In rare instances, cardiac arrest; irregular heartbeat; seizure; nerve injuries; infections; unexpected allergic reactions; bone problems permanent areas of numbness, weakness, worsened pain, or paralysis; spinal cord damage; stroke, and death have been reported with procedures of this type.

Psychological risks:

Any physical changes as a result of the LRFA or simulated LRFA procedures may in theory result in psychological distress that is expected to be short-term, since any LRFA-related side effects are usually short-term and self-limited.

Psychological risks with AcTIVE-CBT or TBSCE are the same risks involved in 'usual care' behavioral treatments for pain (such as conventional CBT, mindfulness-based stress reduction, hypnosis, etc.). Participants may experience fatigue and/or boredom while completing the research interviews and/or the AcTIVE-CBT or TBSCE control treatment sessions. Some participants may also experience mild anxiety, frustration, and/or stress while reporting on their mood and psychologic symptoms, during assessment procedures, and/or during the course of treatment. The two types of behavioral treatment (AcTIVE-CBT or TBSCE control) involve discussions between the provider/research staff and the participant about pain and related topics that may make some individuals feel uncomfortable. However, the AcTIVE-CBT or TBSCE control treatments are not expected to involve any serious or long-term risks to an individual's health.

Social, Legal, Privacy, and Other Risks:

There are research risks to participants' privacy associated with inappropriate disclosure of data. Specifically, there is a risk that a participant's identity and participation in the study may be discovered by an outside party. However, we will take various steps as described elsewhere in the study documents to ensure that the likelihood of such risk is negligible.

Description of Study Population/Expected Enrollment/Vulnerable Populations:

We expect to recruit up to 30 Veterans in the proposed study in order to obtain 20 Veterans who complete 3-month follow-up for the primary outcome (improvement in functional limitations), and at least 4 out of 5 participants in each cell of the 2x2 contingency table (see Figure 2) completing 3-month follow-up for the primary outcome. All Veteran participants will be patients recruited from VAPSHCS who are seeking to have the LRFA procedure for CLBP. There are no other categories of participants allowed in the study. Further details of inclusion/exclusion criteria are provided below in Table 4 (this is placed below in Section 5.4 as specified by the Protocol Template format). The expected age range of study participants is 18 years of age and older. We will not include patients from special classes of subjects or vulnerable populations such as pregnant women, children, cognitively impaired persons, or prisoners, due to possible

coercion. We will not otherwise make any exclusions based on gender, sex, race, ethnicity, or any minority group designation.

Randomization:

MBBs will be performed as per usual clinical care processes in the VAPSHCS Pain Clinic. Following usual clinical practice after the 2nd set of MBBs, once a participant is determined eligible based on the Final Screening criteria, including responses to the 2nd set of MBBs, he/she will be scheduled for a procedure slot when LRFA ***or*** simulated LRFA will be performed. The specific procedural treatment to be received (LRFA vs simulated LRFA) will not be known to the participant or the research staff at the time of scheduling.

Description of randomization procedures below mention the "treating interventional spine provider" and the "2nd interventional spine attending physician". The "treating interventional spine provider" is the provider who is in charge of a patient's procedural care in the course of usual practice in the VAPSHCS pain clinic. The "2nd interventional spine attending physician" will be another VAPS interventional spine attending physician who is separate from the "treating interventional spine provider" previously mentioned. Both these physicians will participate in the LRFA and simulated LRFA procedures as described further below; however, the 2nd interventional spine attending physician will be engaged as part of the research procedures, and the treating interventional spine provider will not be engaged as part of the research procedures. Further description of these two different roles is provided below.

The randomization process involves:

1. Treatment assignments will be stored centrally electronically in a secure database at VAPSHCS. Envelopes containing the treatment assignments (hardcopies) will also be pre-generated.
2. We will utilize computer-generated permuted-block randomization to achieve roughly balanced groups. We will use random blocks that are not divulged to the research staff involved in recruitment in order to avoid bias in the recruitment process. Randomization will be stratified by MBB block responses (50-79% vs. ≥80%).
3. Reminder emails will be sent to the clinical assistant (Pati Irish) and the 2nd interventional spine attending physician the day before the scheduled procedure to remind them that they will need to obtain the randomization allocation on the day of the procedure, prior to the procedure. The 2nd interventional spine attending physician is the second interventional spine attending physician-other than the treating spine provider, who will be in the room during LRFA or simulated LRFA and take part in these procedures. Similar emails will be sent on the morning of the procedure.
4. Prior to the lumbar procedure, the clinical assistant **and** the 2nd interventional spine attending physician will open the envelopes which reveal the procedural and behavioral treatment allocations. A non-blinded research staff member will be present to facilitate this and be aware of the treatment allocations. These assignments contained in the envelopes will direct the 2nd interventional spine attending physician whether to perform a standard LRFA or the simulated LRFA, and whether the participant will receive AcTIVE-CBT or TBSCE. A primary function of the clinical assistant is to make sure that the 2nd interventional spine attending physician knows and performs the allocated treatment on the day of the procedure.
5. On the day of the procedure, once the randomization status is known, the non-blinded research staff member and the PI, Dr. Suri, will communicate regarding the participant's assignment to AcTIVE-CBT or TBSCE. Dr. Suri will then place clinical orders in CPRS for telehealth CBT for pain. These orders will specify whether the order is for a brief course of CBT for pain with education and self-directed plan for progression (TBSCE) or an extended course of CBT for pain (AcTIVE-CBT). The non-blinded research staff member will also communicate directly with the treating CBT provider to clarify that the patient is a study participant. The participant will then be scheduled for

the first session of AcTIVE-CBT or TBSCE, which generally will take place within 1-3 weeks of the procedure date whenever possible.

6. On the day of the procedure, prior to revealing each participant's randomization assignment, we will ensure that we have completed the following aspects of data collection and/or report forms: participant contact Information, the Screening Log (described further below)
   Informed Consent (Attachment T – Consent, described further below), and baseline questionnaires **(**the baseline study assessment, pre-randomization, described further below in 'Study Measures').
   The Screening Log is a tracking document used for internal study purposes.

Description of LRFA and simulated LRFA control procedures:

After the treatment allocation for a given participant is known to the clinical assistant and 2nd interventional spine provider, that participant will undergo their lumbar procedure (LRFA or simulated LRFA). Two experienced board-certified pain medicine attending physicians, one of whom is the participant's 'treating' physician who performed the screening MBBs (the 'treating interventional spine provider'), will perform each LRFA procedure. To permit provider blinding, the treating interventional spine provider will place LRFA electrodes at each spinal level to be treated, and will then leave the procedure room, subsequently remaining blinded to allocation. The 2nd interventional spine attending physician (unblinded, not involved in data collection or further care of the participant) will then administer the allocated LRFA treatment or simulated control. For the LRFA group, this involves making a radiofrequency lesion, repositioning the electrode, and making a 2nd RFA lesion, at each medial branch target. For the simulated LRFA group, this involves the placement of electrodes as would normally be done during LRFA, but without making RFA lesions.

The 2nd interventional spine attending physician who will conduct most LRFA and simulated LRFA procedures in this study will be Dr. Bosco Soares, a board-certified Physical Medicine and Rehabilitation (PM&R) physician with subspecialty accreditation in Pain Medicine. For study participants whose treating physician is Dr. Soares, the 2nd interventional spine attending physician will be Dr. Nishio or Dr. Dawson. Drs. Nishio and Dawson are board-certified anesthesiologist physicians with subspecialty accreditation in Pain Medicine. Drs. Soares, Nishio, and Dawson teach LRFA procedures to Pain Medicine fellows in the UW Accreditation Council for Graduate Medical Education (ACGME)-accredited Pain Medicine fellowship. As shown in Table 2, Dr. Soares will not be blinded to randomization unless (for a given participant) he is the treating interventional spine provider, in which case he WILL be blinded. Conversely, Dr. Nishio will be blinded to randomization status, unless (for a given participant) he is acting as the 2nd interventional spine attending physician (Dr. Nishio will often be the 2nd interventional spine attending physician in those instances when Dr. Soares is the treating interventional spine provider).Similarly, Dr. Dawson will be blinded to randomization status, unless (for a given participant) he is acting as the 2nd interventional spine attending physician (Dr. Dawson will sometimes be the 2nd interventional spine attending physician in those instances when Dr. Soares is the treating interventional spine provider).

LRFA Technique:

The LRFA technique to be used in this research is consistent with current practices among our VAPSHCS LRFA providers and with the highest clinical standards available, including those detailed in the Spinal Intervention Society Practice Guidelines for Spinal Diagnostic and Treatment Procedures, 2nd edition. Briefly, LRFA involves initially positioning a spinal needle at each 'facet nerve' (medial branch of the dorsal ramus) that will be ablated, in the same manner in which medial branch blocks are typically performed, and administering local anesthetic to the nerve and the immediately surrounding muscles, covering a volume consistent with the expected size of the region to be ablated. The needle is then left in place, serving as a pointer to the nerve target site. A radiofrequency electrode is then placed along the course of the medial branch, using a fluoroscopic declined view approach with cross-table obliquity as needed to achieve electrode placement parallel to the medial branch, to the target point marked by the spinal needle tip. Once the electrode is positioned, sensory stimulation is performed at 50 Hz up to 1 millivolt until the patient reports axial and no extremity sensation to further confirm appropriate location of the electrode. The intensity of sensory stimulation where the patient reports sensation will be noted by the clinical assistant and 2nd interventional spine attending physician. Motor stimulation is performed at 2 Hz up to 4 volts (but typically no more than 2 volts) to confirm that there is no motor stimulation of the ventral nerve root causing muscle contraction. If there is motor stimulation of the ventral nerve root, the electrode is repositioned and the stimulation sequence is repeated until the correct electrode position is confirmed. If unable to achieve sensory stimulation, a lesion would not be attempted at that level. Once the electrode is in correct position and stimulation testing completed, a lesion is generated by raising the temperature at about 1°C per second, from 37°C to an operating temperature between 80°C and 85°C, which is maintained for 90 seconds. The electrode will then be repositioned slightly by withdrawing or repositioning parallel to the 1st ablation site, or by rotating the electrode, and a 2nd lesion will be made. If at any time during the raising of the temperature, or during the coagulation, the patient reports adverse sensations, the generator will be immediately turned off and the sensation evaluated. Depending on provider preference as part of routine clinical care, local corticosteroid injections may be used to decrease the likelihood and/or severity of a post-LRFA 'neuritis', worsening of back pain that can be due to the nerve ablation/lesioning itself. This process is then repeated for each medial branch nerve that is targeted (typically 2 or more medial branches per LRFA procedure).

Simulated LRFA with targeted steroid injections technique:

The simulated LRFA control will be performed in an identical fashion to LRFA as above, except that 1) after electrode positioning, a neurodestructive lesion is <u>not</u> made; 2) a targeted corticosteroid injection will be administered at each targeted medial branch prior to the 1st *simulated* lesioning; 3) a pre-recorded audio recording of the procedure will be played by the clinical assistant (out of view of the patient, immediately adjacent to the RFA machine) in order to simulate the beeping and other sounds of the machine and to ensure the appropriate length of the simulated procedure, and 4) the 2nd interventional spine attending physician will turn on sensory stimulation for a short period of at least 3 seconds towards the end of the simulated lesion time, maintaining stimulation intensity no higher than the level where sensory input was initially noted by the patient during testing. The electrode will remain in place for the full 90 seconds that lesioning would normally require, but without heat application. The

electrode will then be repositioned to simulate a second lesion, also of duration 90 seconds. This process would then be repeated for each medial branch nerve that is targeted (2 or more medial branches per simulated LRFA procedure). Targeted corticosteroid injections will consist of a total injectate quantity per patient not to exceed the equivalent of 40-80 mg triamcinolone, divided equally among medial branch sites to be targeted. Lower doses of corticosteroid may be used as per the providers' clinical discretion.

Description of AcTIVE CBT vs. TBSCE CBT treatments

The AcTIVE-CBT treatment involves eight 60-minute treatment sessions spaced over 3 months, delivered via clinical video telehealth methods by clinical psychologists to Veterans in their homes. Psychologists will refer to Fitbit output during the initial evaluation and each treatment session, including reminders and tips about Fitbit use, evaluating step count homework, and tracking overall progress towards goals; the protocol for AcTIVE-CBT is provided as Attachment KK – AcTIVE-CBT Workbook. The TBSCE treatment involves an initial 60-minute telephone education session by a psychologist including education on CBT principles; the provision of an educational book for CBT self-management ('Managing Pain Before It Manages You' by Margaret A. Caudill PhD) and orientation to the workbook;[43] and a structured plan for weekly reading and homework using the workbook[43]. The content of TBSCE interactions in the one initial 60-minute session is as per Attachment MM, but can be adapted to follow psychologists' typical practices for patients beginning CBT for pain who are interested in the treatment but are unable to continue with further sessions. In addition, the psychologist providing TBSCE will contact the participant at the approximate midpoint of the 3-month follow-up period to reinforce key concepts as needed, encourage continued participant-directed use of the plan for weekly reading and workbook use, and answer questions. The psychologist will also be available by phone to address any areas of concern or participant questions during follow-up. TBSCE represents a focused yet 'active' treatment beyond what is normally provided after LRFA. Around the time of the start of behavioral treatments for participants in both the AcTIVE-CBT and TBSCE arms, research staff will provide a written summary of certain data elements from Visit 0 and 1, reflecting the same type of information that would be obtained during an initial clinical evaluation for CBT. This written information will be shared in the form of Attachment NN ('Brief Summary Baseline Data' form). The purpose of this is to provide information to the therapist that will be useful in understanding the participant's baseline status and thus providing effective clinical care. These data elements will include report of pain intensity, number of pain locations, treatment expectancy, hours missed from work or volunteer activities, CLBP-related functional limitations, and past treatments for CLBP. The Brief Summary Baseline Data form (Attachment NN) will be generated by research staff and sent to the clinical therapist using the secure VHA Privacy Act/HIPAA Envelope or fax or encrypted email. If a fax is sent, once the fax receipt has been confirmed at the destination location (confirmed by the therapist), the original form will be destroyed via placement in a designated shredding bin (by the research staff member). If the therapist is located at Seattle campus, the research staff can come to the clinical area for a direct handoff of the Brief Summary Baseline Data form. Once the form is handed to the clinical therapist, the therapist can review this information and record whatever information they would normally do as per their usual clinical practice, in the medical record. The clinical therapist will then destroy the form via placement in a designated shredding bin, not retaining the record for future use, so as to limit potential risk for privacy issues.

In order to avoid imparting biases regarding which treatment is the 'intervention' and which the 'control', AcTIVE-CBT is referred to as 'extended CBT' in the Informed Consent documents and all discussions with the patient, and TBSCE treatment is referred to as 'brief CBT' in the Informed Consent documents and all discussions with the participant.

The AcTIVE CBT and TBSCE control conditions will both be delivered by licensed Clinical Psychologists with specific expertise in cognitive-behavioral therapy and its application to the treatment of chronic pain. Both treating psychologists have appointments within Rehabilitation Care Services at VAPSHCS and are approved for clinical telehealth service modalities. Both study psychologists will be instructed by Dr. Williams in the aspects of clinical CBT treatment to be provided for participants in this study, but are considered clinical staff providing standard-of-care clinical services for chronic pain, and thus not actively engaged in the research procedures. Participants receiving a given treatment (AcTIVE CBT or TBSCE) will generally receive the same information; however, we expect some variation in the amount of time spent on each topic and the specific language used to convey materials. As per usual clinical practice, psychologists will tailor the information in whatever way is indicated to ensure understanding of the content, and to provide individualized support based on personalized goals, barriers, and abilities. If patients specifically request to have one or more in-person sessions of either AcTIVE-CBT or TBSCE in lieu of video telehealth or telephone (respectively), therapists will accommodate such requests as their clinical schedules and availability allow.

ACTIVE-CBT

Psychologists providing the AcTIVE-CBT intervention will receive reports on a participant's Fitbit output and compliance in advance of each treatment session. We will strive to schedule the AcTIVE-CBT sessions at consistent days/times within the week if possible, to facilitate routine and attendance. We will also attempt to schedule sessions evenly across the 3-month follow-up period, to ensure adequate practice time for patients between sessions. AcTIVE-CBT sessions will generally begin with a review of the Fitbit-related output provided by research staff, to gauge activity since the prior session. Sessions will typically include activity plans, expectations, and goals for the next session and long-term. The schedule, scope, and content of treatment as part of the AcTIVE-CBT are similar in scope and content to typical CBT for chronic pain as provided in the RCS service line, but have been specifically tailored for low back pain based on the results of recent successful RCT.[3,4] Some key differences between AcTIVE-CBT and the standard video-based CBT treatment available at VAPSHCS include a greater focus on encouraging walking and physical activity, using the Fitbit Zip units, and greater emphasis on understanding flare-ups and relapse prevention. The components of AcTIVE-CBT are presented in Table 1 below and details of the treatments are found in the patient workbook (Attachment KK – AcTIVE-CBT Workbook). Please note that patient workbook is distinct from the therapist/psychologist manual (Attachment JJ – AcTIVE-CBT Manual). AcTIVE-CBT is meant to be responsive to clinical needs and realities, and if needed, the timing, order, and intensity of these components may vary slightly depending on the specifics of the individual participant, but all will be covered during the 3-month treatment period. AcTIVE-CBT may include audio content. These materials were previously submitted to the IRB with the initial submission. This audio content can be provided to participants in CD format and/or by accessing the content on the VA Seattle ERIC website. The audio content is not copyrighted and we have obtained permission from the audio content creators to use the content without restriction. We have also obtained permissions from the

VAPSHCS privacy officer (Weivoda), information systems security officer (Biggs), area manager for end user operations for IT (Gibson) (see correspondence submitted, including also the IRB Director [Marsh]).

TBSCE

Participants in the TBSCE arm will also receive the Fitbit Zip units, but education and treatment will not be specifically structured around the Fitbit. TBSCE will begin with a 60-minute educational session by a rehabilitation psychologist conducted over the telephone. It will be followed by one brief phone call (10-20 minutes in length) from the rehabilitation psychologist to the participant between 1-2 months after the initial TBSCE session. TBSCE steps follow the structured CBT program included in the book "Managing Pain Before It Manages You" by Caudill, supplemented by a workbook that we have developed for TBSCE. The Caudill book taken together with the workbook are sufficiently detailed that a participant can independently learn the concepts and complete exercises. The workbook includes many of the same topics covered in the AcTIVE-CBT treatment, but in a different order, and without a specific focus on physical activity. Participants will be encouraged to set weekly goals for working through the sessions in the book and completing the assigned readings. At the introductory phone consultation, psychologists will advise participants in setting up a specific written schedule for completing the workbook sections and activities over the 3-month period that the participant will record in their treatment manual (with specific dates when completion of content for a session is expected to be completed). Long-term activity goals and weekly activity goals will be discussed, and these will also be recorded by the patient in the patient treatment manual (Attachment LL – TBSCE Manual (Instructions)). Weekly workbook homework will include: 1) education on chronic pain, 2) theories of pain and diaphragmatic breathing, 3) progressive muscle relaxation and visual imagery, 4) automatic thoughts and pain, 5) cognitive restructuring, 6) stress management, 7) time-based pacing, 8) pleasant activity scheduling, 9) anger management, 10) sleep hygiene, and 11) relapse prevention and flare-up planning.

We may make non-substantive changes to AcTIVE-CBT and TBSCE manuals, workbooks, and provider scripts as the study proceeds. Any substantive changes will be submitted to the IRB for further review.

Quality Assurance

After each session of AcTIVE-CBT, therapists will complete a brief checklist to document the content areas covered in each session (see Attachment OO). These checklists will be used to assess the quality of the AcTIVE-CBT treatment and that major content areas have been covered. Checklists will be retained in a locked file cabinet in the therapist's locked treatment room/office until the last treatment session is completed. After the last treatment session is completed, the therapist will send the checklist to research staff using the secure VHA Privacy Act/HIPAA Envelope or fax or encrypted email. If a fax is sent, once the fax receipt has been confirmed at the destination location (confirmed by discussion or email with research staff), the original checklist will be destroyed via placement in a designated shredding bin (by the therapist). If the therapist is located at Seattle campus, the research staff can come to the clinical area for a direct handoff of the checklist.

Checklists will be collected by research staff and used to track treatment quality/content covered for each participant. These checklists will be treated in the same manner as study questionnaires, using the same methods for data security.

Table 1: Overview of Content in AcTIVE-CBT and TBSCE treatments*		
	AcTIVE-CBT	**TBSCE**
General descriptions and content prior to first session with psychologist	All sessions conducted by video telehealth and psychologist-delivered. Participant will receive basic instruction on Fitbit Zip use from research staff prior to randomization. Participant will receive ongoing research staff support regarding Fitbit use post-randomization, including telephone contacts by research staff at approximately 2 weeks, 6 weeks, and 10 weeks post-randomization. Research staff will produce regular reports on participant Fitbit output and compliance prior to each treatment session, which will be made available to the psychologist and the data relayed to participants during the treatment sessions.	TBSCE is an active yet lower-dose intensity treatment as compared to AcTIVE-CBT. TBSCE will include pain education and CBT-related education and guidance through Dr. Margaret Caudill's CBT '***Managing Chronic Pain***' workbook (referred to as ''*Caudill'* below) Participant will receive basic instruction on Fitbit Zip use from research staff prior to randomization. Participant will receive ongoing research staff support regarding Fitbit use post-randomization including telephone contacts by research staff at approximately 2 weeks, 6 weeks, and 10 weeks post-randomization.
Session 1	Welcome and Introductions; Pain and the Brain **60 min. session by rehabilitation psychologist**	Welcome and Introduction; Introduction to Materials (TBSCE Manual and 'Managing Pain Before It Manages You' workbook by Caudill); Overview of the Treatment Structure; Questions Reading Assignments • Chapter 1 (Beginning to Take Control of Your Pain) • Chapter 2 (Understanding Pain) Topics: • Education about different types of pain • Self-assessment about how you currently cope with pain. **60 min. telephone session by rehabilitation psychologist**
Session 2	Getting Active! Goal-Setting, Pacing, and Managing Flare-Ups **60 min. session by rehabilitation psychologist.**	Reading Assignments • Chapter 3 (The Mind-Body Connection) Topics: • Pain as a form of Chronic Stress • Relaxation Response
Session 3	Thoughts, Feelings, and Pain **60 min. session by rehabilitation psychologist**	Reading Assignments • Chapter 4 (The Body-Mind Connection) Topics: • Increasing activities • How doing activity improves your mood • Pleasant activities
Session 4	Challenging Automatic Thoughts: Part I	Reading Assignments:

	60 min. session by rehabilitation psychologist	• Chapter 5 (The Power of the Mind, pages 97-112) Topics: • How to use powerful cognitive techniques to change your mood. • Recognize your "self-talk", or "automatic thoughts" • Recognize thought distortions
Session 5	Challenging Automatic Thoughts: Part II **60 min. session by rehabilitation psychologist**	Reading Assignments: Chapter 5 (The Power of the Mind). Topics: • How to use powerful cognitive techniques to change your mood. • Recognize your "self-talk", or "automatic thoughts" • Recognize thought distortions **10-20 min psychologist contact by phone conducted between 1-2 months after the initial TBSCE session, to encourage progress with written materials and self-directed progression.**
Session 6	Thinking about Thoughts: Review and Trouble-Shooting **60 min. session by rehabilitation psychologist**	Reading Assignments: Chapter 6 (Adopting Healthy Attitudes) Topics: • Health attitudes
Session 7	Pain Beliefs and Behaviors: Skill Review and Sleep **60 min. session by rehabilitation psychologist**	Reading Assignments: Chapter 8 (Effective Communication) Topics: • Assertiveness • Active Listening
Session 8	Maintaining Gains and Coping with Setbacks **60 min. session by rehabilitation psychologist**	Reading Assignments: • Chapter 9 (Effective Problem Solving) • Chapter 10 (The End of The Beginning) Topics: • Setting Goals • Applying your coping skills to problems • Relapse Prevention • Coping with Pain During Flare-Ups
*See the AcTIVE-CBT manual and workbook, and the TBSCE manual (for participants) for details of treatment. The timing, order, and intensity of these components may vary depending on the specifics of the individual participant, but all will be covered during the 3-month treatment period. Changes made to content above during the study period; updates to the protocol document and attachments will not be routinely submitted to the IRB for further review unless the changes made are substantive.		

Blinding Strategy:

Blinding with respect to the lumbar procedures (LRFA vs. simulated LRFA):

1. Participants and treating interventional spine providers will be blinded to the status of LRFA vs. simulated LRFA. The PI Dr. Suri and Dr. Williams will not be blinded, since they are the overseeing study clinicians. Further details are provided below in Table 2.
2. For blinding purposes, both LRFA and simulated LRFA will be performed in an identical fashion with the exception of medial branch lesioning, which will not be done in the simulated LRFA group, as described above. Duration and sounds of both the LRFA and simulated LRFA procedures will be similar. Both LRFA and simulated LRFA will apply all safety precautions normally used in our facility such as not using general anesthesia, and the use of both sensory and motor stimulation to avoid incorrect electrode placement (described further below).
3. During the procedure (LRFA or simulated LRFA), the treating interventional spine provider will make initial placements of all LRFA electrodes to be used in that procedure as he/she would do normally for LRFA. Once the treating interventional spine provider has placed all LRFA electrodes, the treating interventional spine provider will leave the room and subsequently remain blinded to the procedure allocation (i.e. the randomization to LRFA vs. simulated LRFA). The 2nd interventional spine attending physician will take over the procedure once the treating interventional spine provider leaves the room; the 2nd interventional spine attending physician will *not* be blinded to the procedure allocation. After the treating interventional spine provider leaves the room, the 2nd interventional spine attending physician will either use the radiofrequency machine in the appropriate manner for standard LRFA by lesioning the nerve, or administer the therapeutic MBB (for the control procedure) and apply the simulated LRFA lesion. During simulated LRFA, a recording will be played (Attachment X – Simulated LRFA Recording), by either the 2nd interventional spine attending physician or the clinical assistant, to simulate the typical sounds of LRFA. Additionally, the 2nd interventional spine attending physician will turn on sensory stimulation for a short period of at least 3 seconds towards the end of each simulated lesion time, maintaining stimulation intensity no higher than the level where sensory input was initially noted by the patient during testing. The 2nd interventional spine attending physician will then make a slight repositioning of the LRFA needle to a 2nd location, and administer the 2nd lesion (or the simulated 2nd lesion). If the simulated LRFA procedure is performed, the 2nd interventional spine attending physician or clinical assistant will turn on the audio recording of the LRFA at any times that the lesioning of the nerves would normally occur. Additionally, the 2nd interventional spine attending physician will again turn on sensory stimulation for a short period of at least 3 seconds towards the end of each simulated lesion time, maintaining stimulation intensity no higher than the level where sensory input was initially noted by the patient during testing.
4. The patient and the treating interventional spine provider are therefore blinded to the procedural treatment received. We will employ several strategies to ensure patients are not able to determine which intervention they receive based on the sounds and length of the procedure:
    i. We will enroll only patients who have not had prior LRFA
    ii. The electrode will remain in place for the full 90 seconds (and repositioned to simulate a second lesion) for each simulated lesion site.
    iii. We will use a pre-recorded audio recording of an LRFA procedure in order to simulate the sounds made by the machine during the ablation. We will pre-test this recording several times in the pain clinic in advance of the first randomization.
    iv. We will use a brief period of sensory stimulation during the simulated LRFA lesion as described above.
5. In some clinical situations, it may be impossible for a 2nd interventional spine attending to be on hand to complete a LRFA or simulated LRFA procedure, and maintain blinding of the treating interventional spine provider. For instance, a clinical situation may call that provider away or detain

that individual. In such an instance, the treating interventional spine provider will become unblinded.

6. In the event that participants who are randomized to LRFA vs. simulated LRFA subsequently wish to go on to receive the treatment they were not randomized to, or wish to go on to another lumbar-related procedure that for some reason necessitates that the participant become unblinded to the treatment they were randomized to, prior to the end of the 3-month main follow-up period of data collection, we will unblind participants to their treatment status. This will be done by informing the treating interventional spine provider of the procedural treatment received (LRFA vs. simulated LRFA) prior to a clinical appointment with the participant. The Veteran participant and their provider will then have the information needed to confer and make a fully informed decision about the next clinical treatment steps that are most appropriate for the Veteran.

Blinding with respect to CBT treatments (AcTIVE-CBT vs. TBSCE):

7. It is not possible to blind patients and rehabilitation psychologists to whether or not they are receiving AcTIVE-CBT or TBSCE. To limit the potential for influencing participants' perceptions of the interventions as more or less likely to be effective, participants will not be specifically told which of the AcTIVE-CBT or TBSCE treatments represents the intervention of interest or the control treatment in the current study. They will however have full advance knowledge of what the treatments will actually entail.

Table 2: Blinding Status of Research Staff

	Blinded/Unblinded and Reason	**When blinded**
Dr. Pradeep Suri (PI)	Not blinded (main study physician responsible for clinical issues)	N/A
Dr. Rhonda Williams	Not blinded (study physician responsible for clinical issues pertaining to mental health)	N/A
Drs. Isuta Nishio, Tim Dawson, Amy Hsu	Yes; blinded when not acting as the 2nd interventional spine attending physician (which he/she will be in cases when another spine provider is the treating interventional spine provider[a])	Entire study, see superscript 'a' to the left
Dr. Bosco Soares	Not blinded; except when he is acting as the treating interventional spine provider (in which instances he will be blinded[b])	Entire study[b]
Dr. Janna Friedly	Blinded and no contact with individual-level study data at any point	Entire study

5.2 Recruitment Methods

We will recruit up to 30 participants from among Veterans seeking evaluation for LRFA in the VAPSHCS Pain Clinic. The eligibility and exclusion criteria (**see Table 4 below**) are specifically defined to capture the medically eligible target population who are likely to benefit from the LRFA procedure, are candidates for cognitive-behavioral therapy (CBT), are capable of describing changes in function and pain that serve as the markers for effectiveness, and are able to be compliant with participation in a research study.

Brief Overview of Recruitment (**see Figure 2**)

Determination of participant eligibility, recruitment, and the major steps prior to randomization include the following:

- Stage 1 Initial Screening: for confirmation of a) clinical eligibility to receive LRFA vs. simulated LRFA with targeted steroid injections, b) clinical eligibility for AcTIVE CBT vs. TBSCE, and c) other aspects related to eligibility to participate in study.
- Stage 2 Final Screening (**Visit 1**): for confirmation of a) continued clinical eligibility to receive LRFA vs. simulated LRFA with targeted steroid injections and appropriate 'positive responses' to the 2nd set of MBBs, b) continued clinical eligibility for AcTIVE CBT vs. TBSCE, and c) other aspects related to continued eligibility to participate in study.
    - Informed Consent is offered if patient passes Stage 2 Final Screening
- Run-in period **(between Visit 1 and Visit 2**): to identify participants likely to have poor compliance with study procedures defined by a) those unable to be contacted by research staff, or b) unable to use the Fitbit Zips. The length of the run-in period will be at least 1 week; this period of time for the run-in is substantially shorter than the typical period involved in current clinical care in the VAPS Pain Clinic between the 2nd/last set of MBBs and the date of LRFA (~ weeks on average), and thus will be nested within usual clinical scheduling practices.
- Randomization (**Visit 2**): to reevaluate whether there have been any changes to the Final Screening Criteria, reassessed on the day of randomization
    - Participants will not be randomized if they fail Final Screening criteria
    - If a study participant is not able to be reached by phone or in-person at least one time during the run-in period, they will not be randomized
    - If a study participant is unable to use the Fitbit Zips, they will be categorized as 'non-Fitbit-compliant'. They will be able to continue in the study, but the randomization will be stratified by 'Fitbit-compliant' vs. 'non-Fitbit-compliant' status.

Those ineligible for the study, those who decline to participate, and those who participate but later are deemed ineligible and are not randomized (i.e. those who fail the run-in period) will continue to be seen in the VAPSHCS Pain Clinic and will continue to receive appropriate care for CLBP, which may include LRFA or cognitive behavioral therapy (CBT) for pain for appropriate patients.

Usual Care for MBBs and LRFA at VAPSHCS:

Usual practice in the VAPSHCS Pain Clinic involves screening patients with CLBP for LRFA eligibility with 2 separate sets of MBBs. This is done because the temporary pain relief that happens with MBBs (temporary anesthetic blocks of the 'medial branch nerves') simulates the type of pain relief that should occur with LRFA (when the nerves are ablated [destroyed]). At VAPSHCS these 2 sets of MBBs are scheduled, on average, about 3 weeks apart. Individuals who have 'positive' responses to MBBs (temporary resolution or marked improvement of CLBP) on both occasions, and meet other clinical criteria, are eligible for LRFA. Those who do not have positive responses to MBBs, or do not meet other clinical criteria, are not eligible for having LRFA because they will not benefit from the procedure. 2 sets of screening MBBs are the highest standard of care for selected LRFA candidates in the US because up to 50% of patients who have positive responses to 1 set of screening MBBs are having 'false positive' responses and would not respond to LRFA. The performance of MBBs in usual clinical practice always requires fluoroscopy (x-rays) to position the spinal needles in the appropriate locations; fluoroscopy is always needed for LRFA for the same reason in usual

clinical practice. At VAPSHCS, LRFA is typically scheduled for a time within 3 weeks after the 2nd set of MBBs.

Usual care in the VAPSHCS Pain Clinic requires that MBB candidates meet several clinical criteria for safety/appropriateness reasons. Exclusion criteria are 1) possible pregnancy or other condition that precludes fluoroscopy use, 2) contraindications to MBBs, such as allergy to local anesthetic or contrast, 3) other contraindications to receiving MBBs, and 4) any contraindications to LRFA itself (for example, patients on anticoagulation which cannot be held or bridged appropriately for the LRFA procedure).

Pre-Screening:

We have a HIPAA waiver to be able to screen patients for preliminary eligibility among those who are scheduled to receive lumbar MBBs for chronic axial low back pain in the VAPSHCS Pain Clinic. Study staff will review Computerized Patient Record System (CPRS) records of all patients scheduled for lumbar MBBs in the VAPSHCS Pain Clinic. This initial medical record screening protocol involves assessment of those criteria from Table 4 which can be assessed by CPRS record review. Ideally, potential participants will be identified prior to the 1st set of MBBs that is typically performed in routine interventional spine clinical care for those with CLBP in the VAPSHCS Pain Clinic. When patients are identified who meet preliminary eligibility criteria on the medical record screening, staff will alert the "treating interventional spine provider" (the interventional spine physician in the Pain Clinic who is performing the MBB procedure). Research staff would contact the treating interventional spine provider via encrypted email, telephone, or in-person to alert them when a particular Veteran who appears to be eligible for the study based on medical record screening protocol will be attending an upcoming appointment. Due to typical clinical procedures in the Pain Clinic, we do not anticipate that providers will attempt to recruit any patients in situations where they have not received an alert from research study staff that a patient has passed pre-screening and may be an appropriate participant. That visit, and the MBB procedure, would take place in the normal fashion for clinical care. Treating interventional spine providers will have available in their clinic rooms a list of the major clinical criteria for study inclusion (Attachment J – Interventional Spine Provider Checklist); this list is a reference to aid the clinician in recognition of eligible participants, and is not used for data collection. After the MBB procedure, if the treating interventional spine provider believes the patient to be eligible for study participation, the provider will briefly introduce the study (this will serve as the introduction by non-study personnel) and can provide a flyer with study information (Attachment K - Recruitment Flyer). If the patient expresses interest in being contacted and learning more about the study, the treating interventional spine provider will alert study staff to initiate contact with the patient. Research staff will initiate contact with the Veteran by one of two methods: 1) in-person contact with the Veteran potential participant while they are in the VAPSHCS Pain Clinic area, either after the 1st set of MBBs, or before/after the 2nd set of MBBs, and/or 2) by telephone (if the potential participant has given verbal permission for subsequent phone contacts by study staff). At the time of an in-person contact with the Veteran participant, research staff will provide each potential participant with a copy of a 'What to Expect' (Initial Contact) informational form (Attachment PP) and a blank copy of the study consent, so the participant can read more about what the study would entail, at their leisure. If initial contact is begun in clinic and later completed by telephone, the 'What to Expect' (Initial Contact) informational form (Attachment PP) and a blank copy of the study consent will be sent by mail to the participant.

Additionally, interested Veterans who are given contact information related to the study by the treating interventional spine provider may contact research staff to initiate eligibility screening or assessments at any time.

Screening:

We define chronic low back pain as low back pain present for at least 3 months.[8] Low back pain is defined as occurring between the lower posterior margin of the rib cage and the horizontal gluteal fold. Low back pain intensity is measured using the numerical rating scale (NRS), with NRS ≥ 4 for study inclusion (i.e., NRS must be 4 or higher). See **Table 4** (placed in Section 5.4 as required by the Protocol format) below for a complete and detailed list of inclusion and exclusion criteria, and rationale/indications for exclusion criteria.

Among other criteria, eligible patients will be identified based on their responses to MBBs performed according to routine clinical practice in the VAPSHCS Pain Clinic. Interventional providers in the VAPSHCS Pain Clinic use either lidocaine or bupivacaine anesthetic. Table 3 lists technical details that must be met for MBBs to be counted as 'positive responses'. These criteria will be assessed by research staff, with clarifications as needed by the PI and the treating interventional spine provider. Table 3 and Table 4 assume that the 1st set of MBBs is performed with lidocaine and the 2nd set of MBBs is performed with bupivacaine as per our usual practice. However, clinicians may, for clinical reasons, elect to perform the 1st set of MBBs with lidocaine and the 2nd with bupivacaine, both the 1st and 2nd sets with lidocaine, or both the 1st and 2nd sets with bupivacaine. Any of these combinations are acceptable for the purposes of this study provided that 2 sets of MBBs are used for screening (Table 3).

Table 3. Aspects of medial branch blocks needed to characterize responses

	1st set of MBBs (part of Initial Screening criteria)	**2st set of MBBs** (part of Final Screening criteria)
Anesthetic Type	Lidocaine	Bupivacaine
Anesthetic volume	0.5 cc	0.5 cc
Use of contrast to confirm proper positioning at the medial branch and absence of intra-vascular placement	Yes	Yes
Time window for onset of relief of typical low back pain symptoms	within 30 mins	within 30 mins
Expected duration of pain relief	<12 hours	<36 hours
	End of the duration of pain relief is marked by the point where the ***majority*** of the pre-block pain intensity levels (>50%) have returned. For instance, if a potential participant reports 6/10 pain pre-MBBs, and achieves 1/10 pain post-MBBs, pain relief would be considered to be ongoing at the point where pain intensity was reported as 3/10, but not at the point where pain intensity was reported as 4/10. Depending on the distribution of recruited participants' MBB responses (50-79% vs. ≥80%) after the initial period of recruitment, we may restrict study participation in the participant selection phase in order to oversample participants who have ≥80% relief with MBBs.	
Other follow-up assessments	Phone call 2-5 days after 1st set of MBBs, to assess for return of typical low back pain, with or	Phone call 2-5 days after 2nd set of MBBs, to assess for return of typical low back pain, with or

	without patient referring to their pain diary results. If a clinical phone call or other assessment has been made to assess MBB response by clinical staff or the treating interventional spine provider, the information from that assessment will be used instead of the phone call by study staff.	without patient referring to their pain diary results. If a clinical phone call or other assessment has been made to assess MBB response by clinical staff or the treating interventional spine provider, the information from that assessment will be used instead of the phone call by study staff.
Relief of pain	≥50% improvement in typical low back pain symptoms For both the 1st and 2nd set of MBBs, we will calculate % pain improvement based on patient reported pre-procedure 0-10 pain numeric rating scale score for typical low back pain, minus the post-procedure 0-10 pain numeric rating scale scores for typical low back pain, divided by the pre-procedure 0-10 pain numeric rating scale scores for typical low back pain. Patients will be blinded to the thresholds of % improvement that define a 'positive response'.	

A. Initial Screening: We will pre-arrange permission to approach patients with chronic low back pain presenting to the VAPSHCS system Pain Clinic, who meet the Initial Screening criteria from Table 4 (including but not limited to ≥50% pain improvement with MBBs as performed in routine clinical practice in our institution). Patients who appear to meet Initial Screening criteria will be approached to participate in this trial by research staff.

i. Research staff will identify patients scheduled for a 1st set of lumbar MBBs (either notified at the time of scheduling by the clinic scheduling coordinator or from scanning the upcoming clinic schedule) that appear to meet Initial Screening criteria, as described above. A pre-screening checklist will be used (Attachment L - Screening Checklist).

ii. If a potential participant is identified in pre-screening, research staff will then inform the treating spine provider who is scheduled to perform the 1st set of MBBs, to alert them that an upcoming patient might be a potential study participant. This will remind the treating spine provider to consider whether the patient might be a potential study participant once the normally scheduled clinical evaluation has been completed.

iii. The normally scheduled clinical evaluation, including MBBs, will take place. After the 1st set of MBBs is performed for a patient, as per usual clinical practice, the provider will elicit an initial post-MBB assessment of typical low back pain intensity using a 0 to 10 numerical rating scale (NRS), which will be compared to the pre-MBB assessment of low back pain intensity using a 0 to 10 NRS. Comparison of the post- and pre-MBB NRS scores will yield a proportion for % improvement of typical low back pain. As per usual clinical practice, the provider will also apply the other criteria as described in Table 3 in determining whether a positive response to MBBs is present. Treating spine providers will also have available a 'checklist' of the major clinical eligibility criteria, so they can easily be reminded of the main points that would identify a potential study participant. If they feel such is clinically appropriate, and participants are interested in learning more about the study, the provider will notify the research staff member that a potential participant can be approached. Research staff will be stationed in an adjacent, yet separate, clinical area, and will be available to talk to the potential participant in a private area, to learn more about the study. If a potential participant is only interested in receiving written information, they will be provided with a study flyer.

iv. Research staff will describe the study, answer any questions, and elicit information to complete the Initial Screening assessment (see Table 4 for inclusion/exclusion criteria) and collect basic demographic data only. Those patients who are interested in participation and meet study criteria will be followed to determine continued eligibility as per study criteria over time. Potential participants will be informed that they will also be re-contacted by phone within 2-5 days after the day when the 1st set of MBBs was completed, and that at a later time (when and/or after they return for their next routine clinical appointment for their 2nd set of MBBs) they will be reassessed to complete final screening. This includes the outcome of the 2nd set of MBBs that would normally be offered as part of clinical care to patients who have positive responses to a 1st set of MBBs. As part of usual care processes post-MBBs in the VAPSHCS Pain Clinic, patients complete a written pain diary to record low back pain intensity using a 0 to 10 NRS for up to 2 days after the procedure. As part of usual care, patients post-MBBs also receive a follow-up phone call from a nurse coordinator within 1 week of their MBBs (and usually within several days). In addition to phone contacts with potential participants, research staff will refer to this clinical information as needed to ascertain if 'positive' MBB responses have occurred.

v. If a potential participant who is approached after the 1st set of MBBs does not wish to speak to research staff or cannot do so at the time of their clinical appointment, we will offer those individuals a phone call to continue providing information about the study, determine eligibility, and obtain information about positive responses to the 1st set of MBBs. Those who are unsure about providing permission to speak to research staff by telephone will be provided written information about the study, and asked to contact research study staff if they are interested in the study, ideally within 2-5 days of their 1st set of MBBs.

vi. If research staff is unable to make contact with a potentially eligible patient on the day when the 1st set of MBBs is completed, contacts will be made by telephone as mentioned above, by staff within 2-5 days of the 1st set of MBBs. In those cases, research staff will inquire retrospectively about responses to MBBs in the initial hours and days after the 1st set of MBBs. Research staff will refer to clinical information from pain diaries and the nurse coordinator follow-up phone call as needed to ascertain if 'positive' MBB responses occurred and to identify individuals with non-concordant responses to MBBs (for example, pain lasting >24 hours after a 1st set of MBBs using lidocaine). Individuals with non-concordant responses to MBBs will <u>not</u> be eligible for participation.

vii. Participants who decline study participation at any stage in Screening (Initial or Final) may be asked whether they would answer questions (up to 6 questions) about their reasons for non-participation. Such questions would be recorded in a non-identifiable format, without links to any patient identifiers of any kind.

viii. Depending on the distribution of recruited participants' MBB responses (50-79% vs. ≥80%) after the initial period of recruitment, we may restrict study participation in the participant selection phase in order to oversample participants who have ≥80% relief with MBBs (which would affect both the Initial and Final Screening criteria for potential participants).

ix. If a potential participant is identified after their MBBs have already been completed, or not approached at the usual time of an initial or final screening for another reason, we will send the participant an approach letter (Attachment ZZZ – Approach Letter) and a FAQ document with information about the study (Attachment ZZZ2 – Approach Letter FAQ). These documents will prompt the Veteran to contact research study staff if they wish to hear more information about the study, or if he/she is not interested in the study. If we do not hear back from Veterans who are mailed the approach letter and FAQ within 4 business days, we will make attempts to contact the Veteran by telephone until a contact is made, leaving voicemail messages as needed.

B. Final Screening (Visit 1): The final screening process takes place after the potential RCT participant has undergone the 2nd set of MBBs.

i. Initial Screening Criteria will be repeated, as per Table 4.

ii. Eligible participants will be offered Informed Consent. They will be informed that they will be ***likely*** trial participants, unless subsequent selection criteria render them ineligible in the run-in period between the time of Informed Consent, and the day of their LRFA or simulated LRFA procedure when they will be randomized. Further details regarding Informed Consent are provided below.

iii. If participants decide to participate in the study and complete Informed Consent, in most cases, participants will be scheduled for a future date for their lumbar procedure (LRFA procedure or simulated control procedure) at the time of their 2nd set of MBBs, generally within 1-3 weeks, as per usual clinical practice and using usual clinical processes for scheduling. Research staff will coordinate with clinical staff about scheduling specifics as needed in order to facilitate this and make these transitions smooth for the participant. If for an individual participant, their physician elects to not schedule a future procedure date until a later time, research staff will monitor clinical processes and plan around the future procedure date at the time it is decided upon.

iv. After the time when the future lumbar procedure date is decided upon, patients will be scheduled for their 1st assessment with a rehabilitation psychologist for AcTIVE-CBT or TBSCE control, which will generally begin within 1-3 weeks of the LRFA procedure. Such scheduling will also be done through usual clinical processes for scheduling. Research staff will coordinate with clinical staff about scheduling specifics as needed in order to facilitate that this is done smoothly.

v. Participants will be provided with a Fitbit Zip unit and instructed on how to use the unit. We will assign subjects a login name (e.g., FitbitSel165, FitbitSel672, etc.) and a password for the Fitbit website, and guide the participant through processes for using the website so they can become familiarized with how it works. We will create a Gmail account for the participant, which matches the Fitbit login name, to be used for the duration of this study. Fitbit will use the email address provided to send system-generated weekly updates about the subject's activity levels. The Fitbit account will use the participants login name rather than their actual name. The Fitbit website displays the following data to each user: the number, intensity, and timing of steps taken per day, distance covered, and calories burned. We will request participants not to make edits to their Fitbit accounts during their participation in the study, but to contact research staff who will make such changes for them. An example of this might be if a participant forgets their password information or wishes to change their password; if this happens, the participant would call research staff to change to a new password. We will ask the participants to set up their Fitbit profile so that others cannot view their personal information for the 3-month main period of data collection. During the initial set-up we will verify that the Privacy Settings on each participant's Fitbit profile are set so that no one other than the subject can view their personal information (age, height, weight, etc.). Participants will be instructed on how to upload ('sync') their Fitbit data regularly (ideally, every other day, but at least once every 7 days).

vi. After instructing subjects on how to use the Fitbit, we will mask the Fitbit display screen by turning it around in its case, and we will ask subjects to wear the Fitbit with the display screen covered for the duration of the run-in period. This will allow us to establish how many steps they typically take when not receiving feedback from the Fitbit device or website (i.e., their baseline). Data from the first 7-day period during the run-in period where the Fitbit is used on at least 3 out of 7 days, for at least 6 hours during waking hours on each of those 3 days, will constitute the baseline assessment for step counts. During the run-in period, we will ask participants to try to use the website as little as possible or to only use the Fitbit website when syncing the Fitbit, and to try to not view their Fitbit data on the website. On the day of randomization, we will ask subjects to reveal their display screen by turning their Fitbit around

in its case.

vii. Participants will be given a study participation pledge form (Attachment M - Pledge Run-In). The pledge describes the study rules and procedures and states that the subject will do his/her best to follow them. It will remind participants about frequent syncing, maintain the masking, and limiting use of the Fitbit website as possible. Participants will have a chance to read the pledge and ask questions, and confirm verbally that they understand the pledge and agree to its content. Participants can keep the pledge form.

viii. We will also provide participants with the option to meet with designated research staff at VAPSHCS Seattle campus at any time during the first 3 months after randomization that they wish, to review Fitbit related questions, syncing practices, and/or get a refresher demonstration on how to use their devices and the Fitbit website.

ix. As part of routine clinical practice in the Pain Clinic, in order to determine longer-term response to MBBs, and assess for non-concordant responses, participants are provided with a pain diary and asked to record NRS rating for typical low back pain intensity as done during the initial screening.

x. Research staff will call the patient by telephone 2-5 days after the 2nd set of MBBs. At this time, they will review ratings of low back pain intensity since the 2nd set of MBBs, referring to the clinical pain diary as needed. This information will be used to identify individuals with non-concordant responses to MBBs (for example, pain lasting >36 hours after a 2nd set of MBBs with bupivacaine).

xi. If a potential participant is identified after their MBBs have already been completed, or not approached at the usual time of an initial or final screening for another reason, we will send the participant an approach letter (Attachment ZZZ – Approach Letter) and a FAQ document with information about the study (Attachment ZZZ2 – Approach Letter FAQ). These documents will prompt the Veteran to contact research study staff if they wish to hear more information about the study, or if he/she is not interested in the study. If we do not hear back from Veterans who are mailed the approach letter and FAQ within 4 business days, we will make attempts to contact the Veteran by telephone until a contact is made, leaving voicemail messages as needed. In instances where potential participants are identified via approach letters in this manner, baseline study assessments can be completed as needed in in person in coordination with clinical appointments or by telephone, or during in-person research assessments.

C. Run-in period of Fitbit Use (between Visit 1 and Visit 2)

The purpose of the run-in period is 1) to identify those participants who are able to use the Fitbit a minimum amount which we consider to be 'Fitbit-compliant', so that this variable can be adjusted for analytically , and 2) exclude participants who fail Final Screening criteria or who are determined to be highly unlikely to be able to participate in study procedures (i.e. those who cannot be contacted by phone or in-person at least one time during the run-in period, indicating that they would not be able to complete subsequent telephone questionnaires). During the run-in period, research staff will be available to receive phone calls or visits from the participants so as to help them with any Fitbit related questions they have, or their ability to sync their data. Once it seems that a participant is able to use the Fitbit and sync it (which in many cases may be immediately after Visit 1), the research staff will begin a "test period" of 7 days. The earliest possible start of a test period would be the day after the randomization. If a participant has not synced their Fitbit by day 3 or 4 of the test period, they will receive a telephone call from research staff to offer help and answer questions, and to remind the participant to sync the Fitbit. On days 5, 6, or 7, participants will receive up to one telephone contact/reminder and/or voicemail message left, in order to remind the participant to sync their Fitbit by the end of the 7th day after the start of the test period. If a life issue or barrier presents that interferes with ability to use the Fitbit unit, or the participant encounters a technological hurdle

of some type (such as device failure) the test period may be restarted at any time, and the process repeated. In addition, the test period can be extended as needed due to holidays or absences (either for the participant or research staff) on an ad hoc basis. However, if a full test period elapses without the participant syncing their Fitbit, this would constitute a failure of the run-in period.

i. Research staff will monitor the frequency of participant Fitbit use, and whether they are able to periodically upload their data. Participants who do not use their Fitbit, or do not upload data at least once during the run-in period, will receive reminder phone calls.
ii. Research staff will make telephone contacts as needed with participants to help participants learn how to use their Fitbits.
iii. Participants who do wear their Fitbit unit on at least 3 of 7 days during the test period, for 6 hours at least each day during the participant's regular waking hours will be classified as being 'Fitbit-complaint'. Participants who do NOT wear their Fitbit unit on at least 3 of 7 days during the test period, for 6 hours at least each day during the participant's regular waking hours will be classified as 'non-Fitbit compliant'.
iv. Participants who cannot be contacted at least once during the run-in period will be considered to have failed the run-period. They will be excluded from study participation and will not be randomized.

D. Reassessment of study criteria on the day of randomization (Visit 2):

i. Initial Screening Criteria will be repeated, as per Table 4 (but not including MBBs). Individuals who no longer meet screening criteria will not be randomized and will not be followed further as part of the study.
ii. Randomization will take place as described further below.
iii. The lumbar procedure (LRFA or simulated LRFA) will be performed as per the processes described below.
iv. Subjects will be given a 2nd study participation pledge form. This version of the pledge form will include the items listed on the 1st pledge form, without information pertinent to the run-in period, but will also include additional details that are specific to each participant's CBT allocation (AcTIVE-CBT vs. TBSCE). Specifically, the AcTIVE-CBT pledge form will encourage the participant to use their Fitbit, and try to gradually increase their daily walking while in the study (Attachment O – Pledge Visit 2 Extended). As previously, subjects will have a chance to read the pledge and ask questions, and confirm verbally that they understand the pledge and agree to its content. The participant can keep the pledge form. TBSCE participants will also read a pledge form (Attachment N – Pledge Visit 2 Brief), which is the same as (Attachment O – Pledge Visit 2 Extended), except it does not specifically encourage active Fitbit engagement, and recommends against using the Fitbit Group or Friend functions.
v. At the time the 2nd study pledge form is provided by a research staff member, the staff member will will ask the "Post-procedure questions". These involve 1-4 questions, which inquire about the participant's immediate impression of whether they received LRFA, or simulated LRFA.

E. Approach Letters.

i. In certain situations, potential participants for SELECT may not be captured by the pre-screening and screening processes as described above. Therefore, they may be identified at some point after their 1st set of MBBs have been completed, but when they no longer have an upcoming clinical appointment scheduled when it is possible to approach them in person about the study. In some cases, this may occur between their 2nd set of MBBs and the time of their lumbar RFA procedure. For Veterans who meet this criteria and are identified during the screening process, we will follow the steps below.
ii. If potential Veteran participants are identified as above, the PI will send an encrypted email to the treating interventional spine provider for the potential participant, and/or contact by telephone. The

interventional spine provider will 1) decide whether the Veteran appears to meet criteria for the study, and 2) approves research staff contacting the patient. Either the interventional spine provider will complete the Interventional Provider Checklist, or the PI will complete based on information from the interventional spine provider and/or the medical record.

iii. If the Veteran is a potential participant and approved by the interventional spine provider, research staff will mail an approach letter.
iv. If we do not receive an inquiry from a potential participant within 7 days after the letter was sent, research staff will begin attempts to contact the potential participant. We will leave voicemail messages as needed. If the Veteran is reached, research staff will talk to them at that time or arrange another time to do so, over the phone, or in person. That discussion can be scheduled around the time of an upcoming appointment at the Seattle campus, if convenient for Veteran.
v. At the time arranged to talk, research staff will provide Veteran with basic information as you would at the initial contact (Visit 0). If a Veteran is <u>not</u> interested and wants to stop talking, staff will end the call. If a Veteran is interested, research staff would proceed with the screening checklist as typically done during a Visit 0.
vi. If Veteran passes the screening checklist, we would mail him/her the same info he/she would normally get at a Visit 0 (a What to Expect form [approach letter version] and a blank consent)
vii. If Veteran passes the screening checklist, research staff would try to arrange an in-person Visit 1 in order to complete study procedures and informed consent. Visit 1 would need to happen ***at least*** 2 days before the time when their LRFA is scheduled. Ideally this would be scheduled to coincide with another clinical visits or time when he/she is already coming to the medical center. We will inform Veterans that the Visit 1 would be for ***<u>research</u>***, and that there is no "travel compensation" for this visit. However, there is study-related compensation for completing Visit 1, including informed consent, as well as for our other study assessments. Visit 1 would otherwise take place exactly as described above, including distribution of Fitbits, and a 'run-in period' after visit 1. The run-in requirement for Fitbit use can be waived for Veterans recruited via Approach Letter, if there is insufficient time between Visit 1 and Visit 2 for Fitbit wear and syncing.

F. COVID-19 Pre-Screening Measures

i. SELECT staff will specifically inquire with the Pain Clinic physician treating a patient about whether the patient has active symptoms of fever, cough, or shortness of breath, and/or is potentially at-risk for COVID-19, prior to interactions with a participant/potential participant. SELECT staff will not engage in face-to-face interactions with participants/potential participants if they are thought to have *any* of these symptoms or historical features by the Pain Clinic treating physician. In those cases, we may conduct screening by phone (for participants in the study) or via our existing 'approach letter' pathway (for potential participants- which includes screening by phone). We will apply these procedures until there is further specific guidance from R&D about what to do in response to contacts potentially involving those at-risk for COVID-19, or until such screening is no longer needed.
ii. SELECT staff will only approach patients if they feel comfortable doing so. Until COVID-19 screening at VA Puget Sound is lifted, or until further guidance from R&D regarding patient contact, the Study Coordinator will serve as a back-up for all in-person contact visits, and will conduct in-person contact visits in lieu of any staff who wish to refrain from patient contact during this time. SELECT staff will reach out to the Study Coordinator directly if they wish to refrain from in-person contact.

<u>Patients who Decline</u>:

We will enter data for all patients screened into the study database and assign a screening ID. The system will assign a screening ID for all screened patients, including those who are ineligible or eligible and refused to enroll. Research staff will collect basic demographic information using the demographic information form from all patients who are deemed eligible to participate yet decline to participate. These data will be collected to

determine if there are significant differences between eligible participants who enroll and those who do not. If an eligible patient refuses to participate in the study, research staff member will ask the patient about the reason for declining study participation and record it on the patient Screening Form. Patients who decline but meet eligibility criteria will continue usual clinical care in the VAPSHCS Pain Clinic for interventional spine procedures, including LRFA, as they would normally do.

Understanding the reasons why Veteran patients are not interested in study participation is an essential step towards making the research process acceptable to Veterans in the future. Patients who decline will be asked verbally whether they would be willing to answer up to 6 questions about why they are not interested in study participation. We will inform patients that any answers they provide will be recorded without reference to any identifying information about them, so there would be no way to discern by looking at this information from what patient the information came from. Thus, this type of answering questions is different than what would be in a research study, and we will assure the patient that answering these questions does not constitute participation in the study. We provide the script for these questions as Attachment QQ ('Questions to Non-participants')

Study participants will be compensated for their time spent completing the research procedures for this study, which include the time spent in the Informed Consent process, and completing the study assessments (in person or telephone questionnaires). They are not compensated for the lumbar procedures (LRFA or simulated LRFA with targeted steroid injections) or CBT (AcTIVE-CBT or TBSCE) they receive during the 3 months of main study follow-up, since these are usual clinical care processes appropriate for LRFA-eligible individuals with chronic low back pain. Compensation will be made by checks mailed to participants. Payments will happen after the study visits on the day of randomization, the 3-month follow-up, and again at the end of the optional period of more extended follow-up after 3-months, unless participants express that they would wish instead to be paid monthly. Compensation will be by check, which will usually be mailed to participants within 4-8 weeks after completing each component. However, due to possible delays, participants will be told it could be up to 4 months after completing each component that they will receive payment. Compensation is as follows:

- VISIT 1: Information session, informed consent, and pre-assessment ($ 35)
- VISIT 2: The 'baseline' study assessment, which involves completing questionnaires ($ 25)
- VISIT 3: A questionnaire completed by telephone ($ 10)
- VISIT 4: A questionnaire completed by telephone ($ 10)
- VISIT 5: A questionnaire completed by telephone ($ 25)
- Additional compensation for completing all 3 sets of telephone assessments ($ 15)
- An 'interim survey' questionnaire that may be offered in the event that a participant elects a major change to the interventional spine treatment or behavioral treatment regimen prior to the expected earliest point of unblinding at the 3-month follow-up ($ 10)

<u>Optional study visits</u>

- VISITS 6-14: If participant decides to continue participation in this study after Visit 5, these are study visits that will take place over the telephone ($ 10 for each monthly telephone questionnaire). We will clarify that optional study visits will not take place after the formal end of the study, so some participants recruited late during the study will have fewer "optional" study visits that they can complete.

In sum, participants may be reimbursed up to $120 for completing all study assessments processes over 3 months. In addition, participants may be reimbursed up to a maximum of $30-90 for optional study assessments between months 4 and 12 and an additional $10 if an 'interim survey' is completed.

5.3 Informed Consent Procedures

A Waiver of Informed Consent was obtained to cover screening/recruitment procedures. Informed consent for study participation is as described below.

A. Informed Consent:
We will obtain written consent from potential study participants following the final screening, after completion of the 2nd set of MBBs.

During Informed Consent, potential RCT participants will:

i. Receive basic information concerning the overall study goals, which involve simultaneous randomization to 2 types of active treatment: procedural treatments that target the lumbar facet joints, and behavioral treatments based on principles of CBT for chronic pain.
ii. Receive detailed information concerning the study procedures;
iii. Have the opportunity to consider all available options for treatment of pain;
iv. Receive adequate time to raise questions and voice concerns;
v. Be questioned to assure that they understand all information provided;
vi. Provide written voluntary consent to participate in continued screening processes.

B. Detailed Description of Informed Consent:
In the section below, all uses of the word 'patients' prior to completion and signing of the informed consent form (ICF) refers to potential candidates for study participation beyond the Informed Consent. Please see the Informed Consent documents themselves.

Patients will be informed during the consenting process that if they are determined to be fully eligible for the study and choose to participate, they will be randomized to LRFA or a simulated LRFA procedure including targeted steroid injections to the facet nerves, and to two types of telehealth-administered behavioral treatments for pain (one brief, one extended). All treatments (both the procedural treatments and behavioral treatments) are "active" treatments expected to improve pain and/or pain-related functional limitations, and all are standard of care treatments in the US.

Because in routine clinical practice our experience has been that patients receiving invasive lumbar pain procedures such as LRFA and lumbar steroid injections are often unclear of some specifics of these procedures and their risks, our informed consent document differs from typical recommendations in that it enumerates the specific physical risks of these procedures, even though these involve the same risks as performed in routine clinical care. We have chosen this route to ensure that participants are fully informed. However, if the IRB reviewers' have further questions or recommend that these risks of usual care practices are omitted, we will be happy to provide further information and/or revise accordingly.

Study staff will describe that radiofrequency ablation (LRFA) is a widely used therapy for relieving low back pain, but that there remains debate about its effectiveness, whether other less invasive procedures may be equivalent (such as steroid injections) and whether long-term negative sequelae from LRFA can involve the joints, adjacent muscles or intervertebral discs. Patients will be informed that there is some possibility that at least some of the pain-relieving effect of LRFA may not be due to the nerve destruction itself, but due to the local anesthesia used, the direct mechanical effect of the needles/electrodes on the tissues in the back, nonspecific effects, or other things that we do not know yet. Patients will also receive a description of the targeted steroid injections that will be administered as part of the simulated LRFA control procedure, and how these procedures may have therapeutic effects, without possible long-term negative sequelae from nerve destruction (as in LRFA) involved joints, or adjacent muscles or intervertebral discs. Patients will also be informed that there is also

uncertainty about the true effectiveness of targeted steroid injections, similar to the situation with LRFA effectiveness. The risks of the LRFA procedure will be discussed, including that it entails applying heat to a nerve that supplies the facet joint (which destroys the nerve at least temporarily) and applying anesthetic around the nerve to the facet joint. Risks will be noted, including infection, bleeding, nerve damage, pain at the injection site, allergic reaction, and worsening of back pain. The risks of the simulated LRFA control procedure with targeted steroid injections will also be discussed, which generally involve the same possible risks as LRFA, but with a lower expected frequency of such risks since the nerves are not destroyed. Patients will be informed that, if they meet all inclusion criteria and are ultimately randomized, they will have a 50% chance (1:1 randomization) that they will not receive LRFA initially, but will receive simulated LRFA with targeted steroid injections instead. Potential risks of enrolling in the trial and being randomized to the control procedure will be discussed, including the possibility that they may continue to experience back pain. Potential benefits of enrolling in the trial and being randomized to the control procedure will be discussed, including the possibility that the patient may have back pain improvement and avoid the need for LRFA, surgery or other interventions for pain and that closer follow-up than usual will be given.

Study staff will also describe to potential participants that many behavioral treatments for CLBP are available, and some (such as CBT) have evidence of effectiveness. However, we don't know what components of CBT-related treatments create these positive effects. We will explain moreover that CBT, even video-based CBT such as the AcTIVE-CBT intervention, consumes substantial Veteran time which may not result in any effects beyond those of the initial education, the provision of written materials, and the formal structure needed for a patient-directed graded, progressive, education and self-management program. Therefore, this study involves comparing two programs of CBT which are delivered by telehealth methods, intended to make it easier for Veterans to access CBT, without the burdens of travel and transportation to repeated face-to-face appointments. One program is an 'extended CBT' program, which involves a program requiring more appointments and video-based sessions with a psychologist (ACTIVE-CBT). The other program is a 'brief CBT' program, which involves a single telephone-based session with a psychologist, and a structured program for education and for the patient to apply the concepts of CBT independently and at their own pace, using formal written materials, with subsequent check-ins by the psychologist as needed (TBSCE). Patients will be informed that, if they meet all inclusion criteria and are ultimately randomized, they will also have a 50% chance (1:1 randomization) of receiving one of these 2 treatments. The extended CBT treatment (AcTIVE-CBT) will involve eight 1-hour video sessions with a psychologist and the provision of educational materials; and the brief CBT treatment (TBSCE) will involve one 1-hour telephone session with a psychologist and the provision of educational materials, with one follow-up phone call by the psychologists approximately 1-2 months after the 1st session of TBSCE, and focused troubleshooting with any problems that might arise. Both treatments will involve the patient needing to wear a Fitbit activity tracker daily for 3 months. However, the AcTIVE-CBT treatment will involve specific therapy-related interactions surrounding the Fitbit unit. Participants in the AcTIVE-CBT group will be given a 'pledge' form which indicates their intent to try to upload their information to the Fitbit website regularly and consult their Fitbit regularly during the study, to the extent that they are able (Attachment O – Pledge Visit 2 Extended). Participants in the TBSCE group will be given a 'pledge' form which indicates their intent to try to upload their information to the Fitbit website regularly, but will not include prompts for participants to consult their Fitbit during the study, and will ask them not to spend time reviewing their information on the Fitbit website or using the Group or Friend functions, to the extent that they are able, during the first 3 months of the study (Attachment N – Pledge Visit 2 Brief). At the conclusion of the study, unless participants elect not to do so, participants will be provided with an official report containing their study data, including their activity tracker data. Participants may keep the Fitbit unit/s that they use during the study, after study conclusion, irrespective of their group assignment.

In addition, patient consent will include that the study will follow participants for 3 months and collect information on back specific functional status, pain, Fitbit data, health-related quality of life, and other study measures. Potential participants will consent either to data collection for 3 months only, or to also include an ongoing data collection on a monthly basis after the 3-month assessment, for up to 9 additional months, or until the funding period ends (whichever date comes first). Participants may change their mind about the duration of time they wish to participate in data collection at any time during the study.

Potential participants will be informed that, if they choose to participate in the study, they will remain blinded to which study interventional procedure they received (LRFA vs. simulated LRFA) until 3 months. Pledge forms will ask participants to not actively seek out to find answers for which procedural group they are in. At 3 months they will have the opportunity to become unblinded if they wish, and make any usual health care decisions related to CLBP that they wish at that time, with or without the input of their treating physician. This might include having LRFA, irrespective of whether they had already received LRFA or simulated LRFA as part of this study. They will also be informed that if they wish to become unblinded at any time during the study (to seek treatment off protocol for example) or discontinue enrollment in the trial, they can do so. Potential participants will also be told that at 3 months they can be informed about which of the 2 behavioral interventions (AcTIVE-CBT and TBSCE) constituted the official study 'control'. At 3 months they will have the opportunity to become unblinded to this information if they wish, and make any usual health care decisions related to CLBP that they wish at that time, with or without the input of their treating physician. This might include other behavioral treatments including conventional in-person CBT, typical video-based telehealth as offered by the VAPSHCS TREWI program, or others, irrespective of whether they received the AcTIVE-CBT or TBSCE treatment as part of this study. They will also be informed that if they wish to become unblinded at any time (and to pursue usual care outside of the study protocol) or discontinue enrollment in the trial, they will be allowed to do so at their discretion.

The consent process will occur at a time deemed mutually feasible for the Veteran patient and staff member and coordinated on a case-by-case basis. The consent process will take place in a private location (e.g., a medical exam room or private conference room). In most instances, this will take place in the Building 100 Room 7C-130A (in the Pain Clinic clinical area). However, if Room 7C-130A is occupied, this will take place in another unoccupied patient room in the Pain Clinic clinical area, or in Room 7C-14.

A research staff member (see Study Staff Form) will review each section of the IRB-approved ICF, inviting discussion to ensure comprehension. Potential participants will be asked to repeat back understanding of this material as necessary. Individuals will not be permitted to participate if there is any question as to whether a person is able to provide informed consent. Study staff will be trained to ensure competency to discuss informed consent and strategies to ensure there is no coercion. Potential participants will be provided with as much time as needed to review the ICF and ask the research staff member questions about the ICF, their rights as human participants, and participation in the study. Potential participants will be fully informed of all risks and benefits prior to giving their written informed consent and prior to enrollment in the study. To minimize the possibility of coercion or undue influence prospective subjects will be informed that their decision regarding involvement will in no way influence their clinical care and they will be asked if they need some time to consider their involvement before providing consent. All study personnel will have completed the necessary human subjects protections training per VA policy. Informed consent will be conducted in English. Prospective subjects will be asked if they are able to understand English and whether they feel comfortable speaking it.

If during the course of this contact the potential participant has questions that cannot be addressed by research staff, one of the study investigators or the research manager (depending on the nature of the

questions) will follow up with the potential participant to answer the questions. Potential participants may take time to think about participating and render a decision in a subsequent visit.

Research staff will also review a HIPAA authorization form with the potential participant that permits research staff to review CPRS encounters to extract data collected during treatment. The potential participant will then be asked to sign and date the ICF. Research staff will also date and sign the ICF. All participants will be offered a copy of the signed ICF for their personal records. A note of enrollment will be made in CPRS.

Research staff will file original copies of both the consent and HIPAA forms in the Seattle ERIC offices, kept separate from data collected during screening and subsequent data collected during participation in the study. Research staff will provide participants with staff contact information after the consent process. Participants will also be provided the VAPSHCS research brochure.

5.4 Inclusion/Exclusion Criteria

Table 4: Study Inclusion/Exclusion Criteria and Justification

Initial Screening Criteria (pre-screening)		
Inclusion Criteria	**Exclusion Criteria**	**Rationale/ Indications for Exclusion Criteria**
Chronic low back pain of duration ≥ 3 months, defined by: "How long has back pain has been an ongoing problem for you. Response of "> 3 months" defines CLBP.[63]	Clinical suspicion that the *current low back pain symptoms* have a *significant* and *sustained* component that is attributed to lumbar spine-related syndromes including lumbosacral radicular syndrome (radiculopathy), symptomatic lumbar spinal stenosis (neurogenic claudication), with confirmatory imaging findings, spinal instability requiring surgery, or other 'red flag' conditions (infection/ malignancy/ fracture)	Primarily due to appropriateness for the LRFA intervention vs. simulated LRFA
Low back pain intensity numerical rating scale (NRS) ≥ 4 (must be 4 or higher)		
Has failed at 1st line rehabilitative treatments, including physical therapy, yoga, tai chi, chiropractic or osteopathic manipulation, and/or massage.	Pregnant females, prisoners, or the cognitively impaired (see also below)	Primarily due to appropriateness for the LRFA intervention vs. simulated LRFA
Patient is considered as a candidate for unilateral or bilateral LRFA at 2-4 spinal levels (between L1 and S1) 'Positive responses' to 1st set of lumbar MBBs, including 1) ≥50% pain improvement	Prior lumbar RFA	Primarily due to appropriateness for the LRFA intervention vs. simulated LRFA
	Prior lumbar spine surgery involving the levels where LRFA is to be performed, within the past 2	

of typical low back pain, and 2) onset of typical lumbar back pain relief within 30 mins and relief lasting at least 30 mins after the onset of initial pain relief Depending on the distribution of recruited participants' MBB responses (50-79% vs. ≥80%) after the initial period of recruitment, we may restrict study participation in the participant selection phase in order to oversample participants who have ≥80% relief with MBBs.	years Lumbar fusion or instrumentation involving the levels where LRFA is to be performed Onset of the current low back pain symptoms *prior to* a laminectomy/discectomy/foraminotomy involving the levels where LRFA is to be performed, or within 2 years of a prior laminectomy/discectomy/foraminotomy involving the levels where LRFA is to be performed	
Must have access to a computer, tablet, or smartphone with internet access at home or at work (not via a public resource such as the public library)	Prior CBT for chronic pain (a full course focused on pain, ≥4 sessions)	Primarily due to appropriateness for the AcTIVE-CBT vs. TBSCE
Must be able to read English, provide informed consent and complete the assessment instruments accurately	Primary psychotic or major thought disorder (lifetime), any active suicidal/homicidal ideation (past 6 months), unstable or severe psychiatric/behavioral conditions (e.g. delirium, mania, psychosis)	Primarily due to appropriateness for the AcTIVE-CBT vs. TBSCE
	Hospitalization for psychiatric reasons involving psychosis other than suicidal ideation, homicidal ideation, and/or PTSD, in the past 5 years	Primarily due to appropriateness for the AcTIVE-CBT vs. TBSCE
	Cognitive limitations that would prevent participation in AcTIVE-CBT or the control behavioral intervention (score of 5/10 or less on the Short Portable Mental Status Questionnaire)	Primarily due to appropriateness for the AcTIVE-CBT vs. TBSCE
	Severe medical comorbidities posing major functional limitations in ambulation and function or medical prognosis, including vascular, pulmonary or coronary artery disease, metastatic cancer. Exclude patients with MD-diagnosed fibromyalgia or chronic widespread pain	Primarily due to general study participation
		Primarily due to general study participation
Final Screening Criteria		
Must meet all of the above Initial Screening Inclusion Criteria	Must continue to meet all of the above Initial Screening Exclusion Criteria	
'Positive responses' to 2st set of lumbar MBBs, including 1) ≥50% pain improvement		

of typical low back pain, and 2) onset of typical lumbar back pain relief within 30 mins, and relief lasting at least 30 mins after the onset of initial pain relief Depending on the distribution of recruited participants' MBB responses (50-79% vs. ≥80%) after the initial period of recruitment, we may restrict study participation in the participant selection phase in order to oversample participants who have ≥80% relief with MBBs.		

5.5 Study Evaluations

Screening

Pre-screening and screening procedures have been described above in pp. 27-33. See the Screening Checklists (Attachments L, RR, SS).

Study Measures

The primary study outcome is the Roland-Morris Disability Questionnaire (RMDQ). We will also collect several secondary outcomes as described below. All the main study outcomes as described below are patient-reported outcomes (PROs), except for Fitbit Zip-assessed daily step counts. A schedule of when each study measure will be administered is provided below in Table 5. The Study Measures are contained in the study assessments (Attachments, P, Q, R, and S).

- *Roland-Morris Disability Questionnaire (RMDQ):* The RMDQ is a back pain specific functional status questionnaire adapted from the Sickness Impact Profile (SIP).[3] The RMDQ consists of 24 yes/no items, which represent common dysfunctions in daily activities experienced by participants with low back pain. A single unweighted score is derived by summing the 24 items, with higher scores indicating worse function with 0 (no disability) to 24 (maximum disability). The RMDQ was designed for paper administration, and is also well-suited for telephone use.

- *Fitbit Zip-Assessed Daily Step Counts:* Multiple recent studies have demonstrated the reliability and validity of the Fitbit Zip units as compared to actual observed step counts or legacy reference standard activity monitors such as the Modus Health StepWatch.[4-6]

- *Pain Numerical Rating Scale (NRS):* We will measure back pain using a 0-10 pain NRS (0=no pain and 10=worst pain imaginable) assessing average pain over the past week and pain "right now". Numerical rating scales of pain intensity are valid, reliable, and sensitive to detecting change in pain intensity after treatment.[7,8] We will also ask participants to make a second report

of what they expect their NRS rating for back pain would be if they were not currently or recently taking medications for pain (analgesics).

- *PROMIS Short Form 10:* The NIH Task Force on Research Standards for Chronic Low Back Pain[62] recommended using PROMIS Short Form items to assess the constructs of depression, anxiety, physical function, pain interference, fatigue, sleep disturbance, and satisfaction with participation in social roles. We will use the PROMIS Short Form 10, as recently recommended by an expert panel on the optimal core outcome measurement instruments for clinical trials in nonspecific low back pain (Chiarotto et al. *Core outcome measurement instruments for clinical trials in nonspecific low back pain.* Pain. 2018 Mar;159(3):481-495.)

- *Physical Activity*: Self-reported moderate and vigorous physical activities from the Behavioral Risk Factor and Surveillance System studies.

- *Global Perceived Effect:* This is a 7-point Likert scale describing change in disability since baseline and ranges from "much worse" to "much better".[63-65] Participants will also assess their satisfaction with treatments received for LRFA, simulated LRFA, AcTIVE-CBT and TBSCE control.

- *Medications:* Patients will report medications they have taken for pain in the past 3 days.

- *Adverse Events:* Patients will report any adverse events they have experienced since the day of randomization/day of LRFA vs. simulated LRFA procedure.

- *Ad hoc AE reporting*: Participants will be given instructions at the time of informed consent to contact research staff by phone for AE reporting at any time, after the day of randomization/day of LRFA vs. simulated LRFA procedure.

- *Bang Blinding Index:* To assess success of participant blinding.

A schedule of study assessments is provided in **Table 5**. Over the follow-up period lasting at least 3 months, the following study assessments will be performed at VA Puget Sound, or conducted by telephone, as described below:

VISIT 1 (taking place at the time of the second MBBs) (60-70 mins duration)

Study assessments for Visit 1 will be conducted in person, coordinated to coincide with the timing of the participant's 2nd set of MBBs, *after* the 2nd set of MBBs. Where this is infeasible, some or all of the Visit 1 study assessment will be conducted over the phone, after the 2nd set of MBBs. Either in person or over the telephone, participants will answer questions (Attachment P – Survey Visit 1) including sociodemographic factors, the RMDQ, low back pain NRS, and medication use.

If Visit 1 is conducted in-person after the 2nd set of MBBs, research staff will also make a brief follow-up phone call at least 2-5 days after the 2nd set of MBBs, to ascertain the duration of low back pain relief after the 2nd set of MBBs (Attachment L – Screening Checklist, question 21). This brief phone call will last <5 minutes.

VISIT 2 (taking place on the same day as the LRFA or simulated LRFA with targeted steroid injections procedure, before the procedure) (20-30 mins duration)

Study assessments for Visit 2 will be conducted in person. Participants will answer questions (Attachment Q - Survey Visit 2) including the RMDQ, low back pain NRS, other pain questions, PROMIS SF-10, and medication use.

VISITS 3-4 (taking place 1 month and 2 months after your procedure (10-15 mins duration)

Table 5* Study Phase	Screening & Baseline	Treatment	Optional

Study assessments for Visit 3-4 will be conducted by telephone, unless a participant prefers to have these conducted in person at the Seattle campus. Participants will answer questions (Attachment R – Survey Visit 3_4) including the RMDQ, low back pain NRS, Global Perceived Effect and Satisfaction, medication use, and adverse event reporting.

VISIT 5 (taking place 3 months after your procedure (20-30 mins)

Study assessments for Visit 5 will be conducted by telephone, unless a participant prefers to have these conducted in person at the Seattle campus. Participants will answer questions (Attachment U – Survey Visit 5) including the RMDQ, low back pain NRS, other pain questions, PROMIS SF-10, Global Perceived Effect and Satisfaction, medication use, and adverse event reporting.

Visit Number/Name	1/Final Screen and Consent	2/ Baseline	3/ Month 1	4/ Month 2	5/ Month 3 (1° outcome)	Interim	6-14
Visit Timeline**	-1 to -4 wks.	0	1 mo.	2 mo.	3 mo.	3-6 mo.	Monthly
Length of Visit (min.)	60-70	20-30	10-15	10-15	15-20	10-15	10-15
Informed Consent	✓						
Randomization		✓					
LRFA vs. Simulated LRFA Procedure		✓					
Sociodemographics	✓						
Roland-Morris Disability Questionnaire and Physical Activity	✓	✓	✓	✓	✓	✓	✓
Low Back Pain NRS	✓	✓	✓	✓	✓	✓	✓
Average Opioid Use	✓	✓	✓	✓	✓	✓	✓
Other Pain Questions		✓			✓		
PROMIS SF 10		✓			✓		
Global Perceived Effect and Satisfaction			✓	✓	✓	✓	✓
Self-reported Medications		✓	✓	✓	✓	✓	✓
Adverse Event Reporting		✓	✓	✓	✓	✓	✓
Compensation	$35	$25	$10	$10	$25	$10	$10

* Fitbit activity tracking is not listed, since it occurs continuously during the study period.
**Dates of initial and final screen are approximate, contingent on the dates of potential participant's clinical visits.

Interim Study Visit

If a participant elects a major change to their procedural or behavioral treatments for low back pain in the first 3 months after their procedure, we will offer an additional study visit that could be conducted over the phone, unless a participant prefers to have this assessment conducted in person at the Seattle campus. Participants will complete a questionnaire with several different sections, including the RMDQ, low back pain NRS, Global Perceived Effect and Satisfaction, medication use, and adverse event reporting.

Optional Study Assessments

After completing Visit 5, we will offer patients two choices about continued study participation and the manner of continued participation (blinded vs. unblinded). Participants may decide 'yes' or 'no' to either, neither, or both of these two choices listed:

1) Participants can decide to be told which two of the 4 possible treatments they received (LRFA *or* targeted steroid injections to the facet nerves, and extended CBT *or* brief CBT) i.e. 'unblinding', or they may continue on *without* finding out which treatments they received (remaining blinded). If a participant decides to continue on in the study blinded, but wishes to

learn this information at a later date, research staff will provide that participant with their treatment allocation information at any time until the conclusion of this study.

2) Participants may decide to continue on as part of this study (which would involve completing monthly telephone questionnaire by phone, for a period of 3-9 months longer after Visit 5), or decide to end participation in this study. If a participant were to continue as part of this study, the monthly questionnaires would be the same as what the participant completed by telephone during phone Visits 3-4, and would take between 10-15 minutes to complete. These optional assessments (Attachment S – Survey Visits 6-14) are completely voluntary. If a participant initially decides to complete the optional assessments, but later opts to stop completing them, we will not offer the optional assessments again. Participants will be compensated for completing each optional assessment.
3) If a participant spontaneously offers expresses that they are ambivalent about the options discussed in #1 and #2 immediately above (unprompted by study staff), and requests more information, study staff will inform participants that remaining blinded to the treatments received for a longer period of time is more beneficial to meeting the study's goals, as is participants' continuing to complete the optional monthly assessments. Therefore, if a participant is truly ambivalent about the options discussed in #1 and #2 immediately above, remaining blinded and continuing with monthly assessments for as long as participants wish is the most useful course in terms of meeting the study's goals.
4) We will clarify that optional study visits will not take place after the formal end of the study, so some participants recruited late during the study will have fewer "optional" study visits that they can complete.

Participants will be informed that in this study, research staff will need to periodically look up participants' information in the electronic health record. This will be so for the duration of this study, a period that may last up to several years. This includes looking up such information from participants' health records after the 3-month follow-up period, irrespective of whether participants have decided to complete the optional telephone questionnaires. If a participant decides to withdraw from this study, however, and informs the research team not to access his/her health record after that time, we will not access that participant's health record after that time.

5.6 Data Analysis

This is a pilot study, and is not powered to detect specific magnitude effects at the level of statistical significance. Instead, the purpose of this study is to ascertain the magnitude of effects and relevant variability, so that a definitive large-scale future RCT can be conducted.

Since the vast majority of CLBP patients at VAPSHCS have not received prior CBT, the number of patients receiving LRFA will be the limiting factor in recruitment. We intend to pre-screen all MBB procedures that are performed in the VAPSHCS Pain Clinic during the study period, to identify potential LRFA candidates in advance. Based on current procedural volume, we estimate that the VAPSHCS pain clinic will perform 800 LRFA procedures in 2019 and annually during the study period, and ≥40% of these procedures done annually (n~320) will be for individuals with ≥50% pain relief concordant with the expected duration of anesthetic effect from 2 sets of (comparative) MBBs. Based on past experience in the LESS RCT of epidural injections, we estimate that at least 18% of eligible participants (n=58) will meet other study criteria and be willing to be randomized annually during the study period. Of these, we aim to recruit up to for 30 Veterans for this study, and expect to lose up to 10 Veterans during the run-in period prior to randomization, or during follow-up; our target goal is to have n=20 Veterans who will complete the run-in period, be randomized, and contribute 3-month follow-up data for the primary outcome (the RMDQ), with a minimum of 4 Veterans within each of the 4 cells of the 4x4 table (see

Figure 2). If the number of Veterans failing the run-in period, or lost to follow-up, is lower than expected, we may recruit fewer than 30 Veterans total during the course of this study. If the number of Veterans failing the run-in period, or lost to follow-up, is higher than expected, we will request permission from the VAPSHCS IRB to recruit more than 30 Veterans total during the course of this study.

The analysis will examine treatment groups for baseline imbalances in covariates, understanding that our small sample size will limit the ability to adjust analyses in subsequent steps. We will then conduct an intent-to-treat analysis. Given that this is a preliminary study, the analysis will focus on effect sizes rather than statistical significance. Analyses will be conducted by research staff members biostatistician Dr. Ania Korpak and biostatistician Andrew Timmons at the Seattle ERIC. We will examine for 'interactions' between the effect of LRFA (vs. control) and that of AcTIVE-CBT (vs. TBSCE control) on 3-month RMDQ scores, using a 2-way ANOVA. We will contrast the size of this estimate with that of the *individual* ('main effects') of LRFA vs. simulated LRFA (**Figure 2**; groups A+C vs. B+D) and AcTIVE-CBT vs. TBSCE control (groups A+B vs. C+D). If the size of interaction effect is small relative to the main effects, the main effects will inform estimation of the sample sizes needed for a future adequately powered RCT of LRFA vs. simulated LRFA or AcTIVE-CBT vs. control. Secondary comparisons of cell D vs. cell C, and cell D vs. cell B, would inform sample size estimation for a future RCT of combined treatment with LRFA + AcTIVE-CBT, compared to each of these treatments alone. If the size of interaction effect is large relative to the size of the main effects (making it inappropriate to study 'main effects'), power calculations for the future RCT will be based on the effect sizes yielded from comparisons of cell D vs. cell C, cell D vs. cell B, and cell D vs. cell A. We will follow the same approach for other study outcomes.

5.7 Withdrawal of Subjects

Participant withdrawals

We will record termination/withdrawal information for participants who decide to leave the study prior to completing the 3-month follow-up. Participants may leave the study at their own discretion, by contacting the research team and notifying them of the decision to leave the study. If participants wish to become unblinded, research staff will inform them of their treatment allocations at the time participants give notification of their decision to leave the study. Withdrawal from the study will not affect care participants receive at VA facilities. Participants will continue to receive any VA care for back pain that they elect to pursue, in coordination with their providers and VA clinical care processes.

Participants may be withdrawn from the study without their consent if they become incarcerated during the study, or if the researchers feel that the study is in some way negatively affecting the participant's health or wellbeing. Participants may also be withdrawn from the study if they demonstrate threatening behaviors or potentially harmful behaviors towards research study staff. Participants will be withdrawn from the study if they are unable to be contacted and/or unable to complete study assessments for 3 consecutive monthly study assessments. In this case, it is assumed that they do not wish to continue in the study, and further contacts would be intrusive.

Although not considered 'withdrawal' per se, participants who are consented may be subsequently excluded prior to randomization, if they 1) are found to not meet inclusion/exclusion criteria, or 2) fail the run-in period between Visits 1 and 2 (i.e. they cannot be reached by researchers during the run-in period. These exclusions cannot take place after randomization. For the purposes of the Informed Consent form, to simplify understanding for potential participants, we do not distinguish between

withdrawals and these pre-randomization exclusions.

5.0 Reporting

Collection of safety information (monitoring) will be performed by the research staff that administer the assessment questionnaires and facilitate data collection, during data collection. Collection of safety information will also include any ad hoc participant-initiated contacts with the study team, and follow-ups by study staff if tracking the course of any potential complications. We will establish a Data Monitoring Committee (DMC) to oversee study safety data. The DMC is described further below.

We will record any potential complications as adverse events (AEs), defined as any untoward medical occurrence that may present during treatment, but which does not necessarily have a causal relationship with this treatment. We will also record serious adverse events (SAEs). We will complete an AE adverse events form for any AEs that occur during the course of this trial. We will record each event as it happens (or as soon as it becomes known to study research team) and we will follow the AE in subsequent scheduled/completed monthly assessments until resolution, the end of the patient's participation or study completion (whichever occurs first). Study staff will report all AEs to the study PI within 1 business day of learning of the AE. Study staff will also report AEs to the appropriate clinical treating provider (the interventional spine physician for AEs possibly related to medical issues or procedural issues, and the treating psychologist for AEs possibly related to mental health). Study staff will complete and send the AE CRF to the Study PI within 5 business days of learning of the AE. The study staff will be responsible for entering the AE data into the study database within 5 business days of learning of the AE. Study staff will review the completeness of the entered data and will report the AE to the IRB. AEs will be reported to the IRB at the time of continuing reviews. If appropriate, AEs will be reported to the DMC (as described further below).

- The study team will notify the study PI about any SAEs that occur within 1 business day of learning of the SAE. The study PI will notify the IRB within 5 business days of learning about the SAE. The DMC will review SAEs at their scheduled meetings. All SAEs will be reviewed and clinically evaluated by the treating physician. Subsequent clinical evaluation and any further assessment, that may include laboratory or imaging testing as well as treatment, will be done per clinical standards of care.
- Any death that occurs to a subject during their participation in the study is reportable to the IRB and the DMC. The notification to the DMC and the IRB will include a determination from the study PI as to the likelihood of a relationship to the study procedure.

A. Definition of an Adverse Event, Anticipated Adverse Event and Serious Adverse Event

An **adverse event (AE)** is any untoward medical occurrence that may present during treatment, but which does not necessarily have a causal relationship with this treatment. It can therefore be any unfavorable and unintended event (such as an abnormal laboratory finding), symptom, or disease temporally associated with research participation, whether or not related to research participation.

Anticipated AEs/potential AEs are those which might reasonably be expected to occur from LRFA or simulated LRFA with targeted steroid injections. These might include, but are not necessarily limited to:

- *Pain treatment-related:* pain at the procedure site, increased pain in low back pain or nerve pain

- *Neurological:* paralysis, temporary weakness or numbness in legs, dysesthesias or allodynia
- *Hypersensitivity reactions to the medications used during the procedure (e.g. anesthetic, or sedative)*: respiratory or cardiac reactions, seizures, allergic reaction, serious and occasional fatal hypersensitivity (anaphylactic) reactions
- *Endocrine:* short-term increases in blood glucose levels may occur with one-time administration of corticosteroid, in patients with diabetes
- *Infection*
- *Cardiovascular:* bleeding at the incision site, injury to blood vessels, clotting of veins
- Vasovagal reaction, hypotension (low blood pressure) (these occur only intra-procedure or immediately after the procedure)
- *Miscellaneous:* Swelling and bruising at the incision site

Anticipated AEs following prolonged fluoroscopy (X-ray) might include: hair loss, skin redness, and skin damage.

A **serious adverse event** (SAE) is defined as any untoward medical occurrence that:

- Results in death
- Is life-threatening (Note: the term life-threatening in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe).
- Requires inpatient hospitalization or prolongation of existing hospitalization.
- Results in persistent or significant disability/incapacity.
- Results in congenital anomaly/birth defect (if exposure to a medical product prior to conception or during pregnancy may have resulted in an adverse outcome in the child).
- Requires intervention to prevent permanent impairment or damage.
- Important medical events that may not result in death, be life-threatening or require hospitalization may be considered a SAE when, based on appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

In the proposed trial, the following events are **considered SAEs:**

- Neurologic: paralysis, stroke, central nervous system infection
- Serious hypersensitivity: anaphylactic reactions
- Death
- An event that is life threatening, is permanently disabling, or requires inpatient hospitalization

Severity of adverse event grading scale:

- Mild: an experience that is usually transient, and requires no special treatment or intervention
- Moderate: an experience that is alleviated with simple therapeutic treatments
- Severe: an experience that requires more than simple therapeutic interventions

Relationship to research participation AEs:

- Unrelated - This causal relationship is assigned when the AE is definitely not associated with the research participation/treatment
- Unlikely - This causal relationship is assigned when there is no temporal relationship to the administration of the investigational material or other factors are more likely to have caused the

event.

- Possibly related - This causal relationship is assigned when the AE starts at a reasonable time after study participation but could have been produced by the subject's clinical state or other modes of therapy administered to the subject.
- Probably related - This causal relationship is assigned when the adverse event starts at a reasonable time after study participation, stops/improves when study participation/treatment has been stopped, and cannot be reasonably explained by known characteristics of the clinical state.
- Definitely related - This causal relationship is assigned when the adverse event starts at a reasonable time after study participation/treatment, stops/improves when study participation/treatment has been stopped, can reasonably be explained by known characteristics of the study participation/treatment.

B. Determination of an Adverse Event

AE identification

We will monitor for adverse events during the entire duration of each patient's participation, including all scheduled/completed monthly assessments and reporting offered by participants during unplanned contacts. In the proposed trial, there are two methods for AE identification: active and passive.

Active identification

Patient Reported: At scheduled study assessments, research staff will inquire about medical/adverse events including surgery, ED visits, hospitalizations and ICU admissions, and allergic reactions. When a patient reports any of the medical events listed above, study research staff will complete an Adverse Event form (Attachment V – Adverse Event Form) and ask the patient details about the event. Such information will include, at a minimum, the date of the event, event seriousness, event treatment and event outcome. Assessments of AEs will include an open-ended question: "Did you experience any other complications?" We will treat any response to these questions as if it is an AE until the study PI can further review and discuss it with the study team if needed.

Passive identification

Medical records review: We will monitor medical records for SAEs at the time of scheduled assessments (monthly) until the end of the 3-month data collection, or longer if a participant elects to continue with optional study assessments after 3 months. If we identify an SAE, the study coordinator will complete an AE CRF and inform the study PI. The list of SAEs to be checked for monthly include: a major neurologic event (paralysis, stroke, central nervous system infection), serious hypersensitivity/ anaphylactic reactions, death, a life-threatening or permanently disabling event, or one that requires inpatient hospitalization.

AE attribution and outcome

The study PI will review all AEs to determine study relatedness and outcome of the event. If the PI is not available, AEs that are more pertinent to medical issues or procedures will be reviewed by Dr. Nishio or Soares, and AEs that are more pertinent to mental health will be reviewed by Dr. Williams.

C. **Other reporting**

We will complete an AE CRF for any AEs that occur during the main 3-month follow-up period of data collection. We will record each event as it happens (or as soon as it becomes known to study research team) and we will follow the AE at subsequent scheduled/completed monthly assessments, the end of the patient's participation in the study or study completion, or until directed by the participant's treating provider (treating interventional spine provider or treating psychologist) that the AE has resolved or further tracking is not needed (whichever of these occurrences happens first). Study staff will report all AEs to the study PI within 24 hours of learning of the AE. Study staff will complete and send the AE CRF to the Study PI within 5 business days of learning of the AE. The study staff will be responsible for entering the AE data into the study database within 5 business days of learning of the AE. Study staff will review the completeness of the entered data and based on the type of AE and requirements for the reporting AE (see below including UAPs), will report the AE to the DMC and/or IRB.

Unanticipated problems (UAPs) are any problem that is 1) unexpected given the research procedures and subject population, 2) related or possible related to participation in the research, and 3) that may have placed participants at a greater risk of harm than was previously recognized. Harm can be further classified as potential harm or actual harm. The study team and/or PI will report any UAPs to the IRB within 5 business days of learning about the AE that was later classified as a UAP. If serious, we will report this using the form " Report of Unanticipated AND Related Serious Adverse Event (SAE), Unanticipated AND Related Adverse Device Effect (ADE), and/or Unanticipated AND Related Problem Involving Risk to Subjects or Others (UPIRTSO)" (Attachment W – Serious Adverse Event Form). UAPs encompass 'unexpected AEs' and are reported similarly. The DMC will review UAPs that are serious at their meetings.

All AEs, UAPs, and SAEs will be clinically reviewed by a study physician (Drs. Suri, Nishio, Soares, or Williams as described above) and clinically evaluated and treated as needed, depending on the problem at hand.

The study team will notify the study PI about any expected or unexpected SAEs that occur within 24 hours of learning of the SAE. The study PI will notify the IRB within 5 business days of learning about the SAE. The DMC will review SAEs at their meetings. All SAEs will be reviewed and clinically evaluated by the treating physician.

Any death that occurs to a subject during their participation in the study is reportable to the IRB. The study PI will report the event to DMC, and to the study sponsor RR&D according to the timeframes of required reporting. The notification to the DMC and IRB will include a determination from the study PI as to the likelihood of a relationship to the study procedure.

D. **Safety monitoring**

The DMC will review the accruing data to: 1) ensure that study conduct, enrollment, and patient follow-up is adequate; 2) ensure that there are no serious safety concerns; and 3) assess evidence related to the study outcomes. The DMC will convene every 4 months during active recruitment, and in ad hoc meetings as needed. A report will be compiled for each DMC meeting that will outline study progress including recruitment, retention, protocol violations, AEs, SAEs, and unanticipated problems. In addition, the DMC members will be notified of individual SAEs on an on-going, real-time basis. DMC members will also be sent a "complete" safety and efficacy data report after the first 10 subjects have

completed 3-month follow-up, and at the end of data collection for the full expected sample size of 20 participants completing the main 3-month follow-up outcomes. In these "complete" safety and efficacy data reports, we will use a Fisher's exact test to formally compare the event rates between ITT treatment groups and will qualitatively compare to established normative rates. Due to the number of statistical comparisons expected to be made, we do expect to see some differences of $p<0.05$ for some types of events, so we stress the ***qualitative*** nature of these comparisons. Based on the currently published data, we anticipate that AEs in the LRFA arm may be more common than in the simulated RFA arm. If there is a qualitative difference in the proportion of SAEs occurring between the study groups and there are concerns regarding the negative effects of the intervention, then the research team in consultation with both the study statistician and the DMC may recommend protocol changes or discontinue the study.

E. **Withdrawal of subjects due to adverse effects**
We will maintain in the study participants who develop SAEs that are study-related or not, as well as with severe or moderate study-related events (intention-to-treat), unless participants elect to withdraw from the study.

6.0 Privacy and Confidentiality

The study will use participants' Protected Health Information (PHI) for the purposes of participant payment by mailed checks to the participant's current address. Also, PHI will be used to contact participants via telephone (as outlined above). PHI will be contained in the crosswalk file that links participant identifiers with the study-specific StudyID. No PHI will be disclosed as part of this study.

We will take multiple steps to protect participants' privacy, confidentiality, and inappropriate disclosure of data, under strict VA security guidelines. All study staff will maintain current on required VA trainings for privacy and confidentiality. Data will be stored in Participant Data Files that will be de-identified, labeled with a code number that is unique to each patient in the study ('study-specific StudyID'). The study-specific StudyID will be a unique numerical code consecutively numbered in order of approach/screening. We will NOT include any protected health information (PHI) in the Participant Data Files. The Participant Data Files will be stored in a secure password-protected electronic location on the VA servers (expected to be the in the J: drive on the Health Services Research & Development (HSR&D) server), accessible only to study staff members and authorized personnel. Staff will maintain a Master List key code that links participants with the study-specific StudyID. This Master List key code will be stored in a secure password-protected electronic location on the VA servers, separately from all other study data. All hard copy participant data will be stored in locked filing cabinets in the locked/secured offices of the Seattle ERIC, while all electronic data will be stored in password-protected files in a limited access folder (to research staff) on a secure VA network drive. Only IRB-approved study personnel will have access to Participant Data Files or Informed Consent Forms. We will only analyze data that does NOT contain PHI, and will report participant data in aggregate form only- no PHI will be entered into analyses or reports.

7.0 Communication Plan

This section is not applicable since this is a single-site study.

8.0 Information Security and Data Storage/Movement

- Data would only remain within the VA, and would not be moved outside the VA.
- Any hard-copy documents involved will be stored in locked file cabinets in the locked/secured offices of the Seattle ERIC. These will be retained for six years after study closure, until destroyed in accordance with VA procedures, and will not be moved from the ERIC, since there is no need for movement of the documents.
- Similarly, the electronic databases described above in section 7.0 will not be moved. These will be retained for six years after study closure, at which time they will be destroyed in accordance with VA procedures. We will update the above plan as needed if VA procedures and requirements change in the future.

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