EIRB Protocol Template (Version 1.5)

1.0 General Information

***Please enter the full title of your protocol:**

Investigating Medical Massage Therapy for Patients with Sub-Acute Lower Back Pain

***Please enter the Protocol Number you would like to use to reference the protocol:**

MIRROR Project 52: Zeel
* This field allows you to enter an abbreviated version of the Protocol Title to quickly identify this protocol.

Is this a multi-site protocol (i.e. Each site has their own Principal Investigator)?

Yes

Does this protocol involve the use of animals?

○ Yes ◉ No

2.0 Add sites

2.1 List sites associated with this study:

Is Primary?	Site Name
◉	**P and R** - Madigan Army Medical Center (MAMC)

3.0 ▪ Assign project personnel access to the project

3.1 * Please add a Principal Investigator for the study:

Name	Role	Training Record
Grinshpun, German GHENA, DO	**Principal Investigator**	**View Training Record**

Responsibility

☐ Student
☐ Resident
☐ Site Chair
☐ Fellow

3.2 If applicable, please select the Research Staff personnel:

A) Additional Investigators

Name	Role	Training Record
No Additional Investigators have been added		

B) Research Support Staff

Name	Role	Training Record
Abrams, Onika Elise	**Team Member**	**View Training Record**
Lucio, Whitley B, MS	**Non-engaged Administrator**	**View Training Record**
Morris, Victoria Galica	**Team Member**	**View Training Record**
Ory, Rian Lyndzie, MS	**Non-engaged Administrator**	**View Training Record**
Son, Janel Moira Cuevas	**Research Coordinator**	**View Training Record**

3.3 *Please add a Protocol Contact:

Name	Role	Training Record
Grinshpun, German GHENA, DO	**Study Contact**	**View Training Record**
Lucio, Whitley B, MS	**Study Contact**	**View Training Record**
Ory, Rian Lyndzie, MS	**Study Contact**	**View Training Record**
Son, Janel Moira Cuevas	**Study Contact**	**View Training Record**

The Protocol Contact(s) will receive all important system notifications along with the Principal Investigator. (i.e. The protocol contact(s) are typically either the Protocol Coordinator or the Principal Investigator themselves).

3.4 If applicable, please select the Designated Site Approval(s):

Name	Role	Training Record
No Designated Department Approval have been added		

Add the name of the individual authorized to approve and sign off on this protocol from your Site (e.g. the Site Chair).

4.0 Project Information

4.1 * What department(s) will be associated with this protocol?

	Emergency Medicine
	Pain Management

	Physical Therapy
	Physical Medicine & Rehab
	Rheumatology
	Family Medicine

4.2 * Is the IRB of record for this study an IRB/HRPP that does NOT use EIRB? If Yes, complete the application according to the IRB/HRPP Determination.

If your Projects or Protocols are under the oversight of another IRB that does use EIRB, stop this submission and contact the core site and request an invitation as a performing site.

If your Project or Protocol is now being submitted for the first time to an IRB that does use EIRB, continue with this application and answer the questions to be reviewed by the IRB.

Answering yes means the board of record is an IRB that does NOT use EIRB.

○ Yes ◉ No

4.3 * Is this protocol research, expanded access, or humanitarian use device?

◉ Yes ○ No

4.4 * What type of protocol is this?

- ☐ Behavioral Research
- ☑ Biomedical Research
- ☐ Clinical trial (FDA regulated)
- ☐ Educational Research
- ☐ Expanded Access
- ☐ Humanitarian Use Device (HUD)
- ☐ Psychosocial Research
- ☐ Oral History
- ☐ Other

4.5 Are you conducting this project in pursuit of a personal degree?

○ Yes ◉ No

4.7 * Is this human subjects research? (As defined by 32 CFR 219) Human subject means a living individual about whom an investigator (whether professional or student) conducting research:
(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
(ii) Obtains, uses, studies, analyzes or generates identifiable private information or identifiable biospecimens.

◉ Yes ○ No

4.8 * Do you believe this human subjects research is exempt from IRB review?

○ Yes ◉ No

5.0 Personnel Details

5.1 Does the Principal Investigator have a Permanent Change of Station (PCS) Date or Estimated Institutional Departure Date (EIDD)?

○ Yes ◉ No

5.2 List any Research Team members without EIRB access that are not previously entered in the protocol:

No results found

5.3 Are any Contractors or Subcontractors involved in this study? If yes, please list them and describe their role.

◉ Yes ○ No

Name: (Last, First, M.I.)	Phone Number:	Email Address:	Associated Institution:
Lucio, Whitley Role on Protocol: MIRROR Sr. Regulatory Affairs & Data Manager	202-375-8831	whitley.lucio.ctr@usuhs.edu	The Geneva Foundation / USUHS
Name: (Last, First, M.I.) Ory, Rian Role on Protocol: MIRROR Regulatory Affairs Manager	Phone Number: 909-904-5034	Email Address: Rian.ory.ctr@usuhs.edu	Associated Institution: The Geneva Foundation / USUHS
Name: (Last, First, M.I.) Morris, Victoria Role on Protocol: MIRROR Data & Analytics Manager	Phone Number: 860-803-2722	Email Address: victoria.morris.ctr@usuhs.edu	Associated Institution: The Geneva Foundation / USUHS
Name: (Last, First, M.I.)			

Son, Janel Role on Protocol: Research Coordinator	Phone Number: 253-968-3288	Email Address: json@genevausa.org	Associated Institution: The Geneva Foundation / MAMC
Name: (Last, First, M.I.) Abrams, Onika Role on Protocol: MIRROR Data Management Analyst	Phone Number: 205-615-6554	Email Address: onika.abrams.ctr@usuhs.edu	Associated Institution: The Geneva Foundation / USUHS

5.4 Will you have a Research Monitor for this study?

- ○ Yes
- ◉ No
- ○ N/A

6.0 Data/Specimens

6.1 Does the study involve the use of existing data or specimens only (no interaction with human subjects)?

○ Yes ◉ No

7.0 Funding and Disclosures

7.1 Source of Funding:

Funding Source	Funding Type	Amount
: Other Uniformed Services University of the Health Sciences (USUHS)	: Research Development Testing and Evaluation (RDT&E) funds Restoral	1777000

Total amount of funding:

1777000

7.2 Do you or any other Investigator(s) have a disclosure of a personal interest or financial nature significant with sponsor(s), product(s), instrument(s) and/or company(ies) involved in this study?

○ Yes ◉ No

All personnel engaged in research must complete and attach a Conflict of Interest (COI) form.

8.0 Study Locations

8.1 Is this a collaborative or multi-site study? (e.g., are there any other institutions involved?)

◉ Yes ○ No

8.2 Study Facilities and Locations:

Institution	Site Name	Site Role	FWA or DoD Assurance Number	Assurance Expiration Date	Is there an agreement?	IRB Reviewing for Site
Army	MAMC	Lead site	FWA00003277	04/29/2029		: RHC - P IRB
P&R	USU	Coordinating center	FWA00005897	08/22/2028	: IAIR	: RHC - P IRB

Other:

Other Institution Site	Site Role	FWA or DoD Assurance Number	FWA or DoD Expiration Date	Is there an agreement?	IRB Reviewing for Site
No results found					

8.3 Are there international sites?

Attach international approval documents, if applicable, when prompted. Note: Ensure local research context has been considered

○ Yes ◉ No

8.4 Is this an OCONUS (Outside Continental United States) study?

○ Yes ◉ No

Select the area of responsibility:

Have you obtained permission from that area of responsibility? (This is a requirement prior to study approval)

○ Yes ○ No

9.0 Study Details

9.1 Key Words:

Provide up to 5 key words that identify the broad topic(s) of your study

Low back pain, massage therapy, subacute

9.2 Background and Significance:

Include a literature review that describes in detail the rationale for conducting the study. Include descriptions of any preliminary studies and findings that led to the development of the protocol. The background section should clearly support the choice of study variables and explain the basis for the research questions and/or study hypotheses. This section establishes the relevance of the study and explains the applicability of its findings

Musculoskeletal injury (MSKI) affects approximately 800,000 active-duty service members (ADSMs) annually and results in 25 million days of limited duty.[1] These conditions account for 34% of medical evacuations from theatre, and are the primary reasons for medical separation from active duty.[2] Even more concerning is that the disability discharge rate for MSKIs has increased 13x over the past few decades (70 vs. 950 per 100,000 persons),[3] which has a secondary impact on healthcare costs and strains the military health system (MHS). Data indicates that 82% of MSKIs are attributed to overuse injuries,[4] and "it has been estimated that for every injury-related death among Army personnel, there are 17 hospitalizations and over 3,000 outpatient encounters due to MSKIs."[5] In fact, in 2017 alone, more than half of ADSMs sustained at least one injury.[6]

Low back pain is the leading cause for MSKI disability amongst ADSMs,[7-10] and accounts for the second most primary care encounters annually.[11] Young, physically active ADSMs are also exceptionally likely to experience myofascial pain due to greater muscle mass and the prevalence of facet and disc pathology given their age.[12] In fact, a recent four year observational period of military data demonstrated that low back pain (LBP) resulted in six million outpatient visits and 25,000 hospitalizations.[2,3] While every effort is paid towards preventing injury, the reality is that Army soldiers deployed in theatre often wear up to 130 pounds of equipment[13] which adds significant compressive forces to their spine and surrounding musculature, and raises the likelihood for an MSKI. Once LBP manifests clinically, there is a lifetime prevalence rate ranging between 50%-80%, which negatively affects medical restricted duty days (MRDD).[14,15] Nearly 33% of those affected report persistent pain at least one year post injury, and 20% experience substantial impairments long-term.[16] Military personnel with LBP evacuated from theaters of operation have a return to duty (RTD) rate of less than 15%, resulting in challenges for readiness /resilience, thus adding considerable medical cost to our healthcare system.[17-19] The burden of disease for LBP is reaching $100 billion annually in the United States and new methods for prevention and treatment are necessary.[2]

In one of the largest retrospective studies performed to date by investigators of this grant,[20] a total of 52,118 ADSMs were queried from the military data repository in FY2017, and their electronic records were evaluated for cost, care, and utilization. Patients were classified by LBP duration as acute (< 1 month), subacute (1-3 months), or chronic (> 3 months) per standard guidelines.[3] Data demonstrated that the majority of military personnel were chronic as indicated by: Acute [17,916 (34.4%)], Subacute [4,119 (7.9%)], and Chronic [30,083 (57.7%)]. Over the two-year follow-up period, 419,983 outpatient visits were recorded, with the majority occurring at military treatment facilities [363,570 (86.6%)]. The Chronic cohort comprised the highest number of encounters [371,031 (89.2% of total encounters)], including 86% of diagnostic imaging studies (e.g., magnetic resonance imaging) performed for LBP, and cost the private sector $9,986,606 during the observation time. Interventional pain procedures ($2,983,768) and physical therapy ($2,298,779) represented the costliest categories in the private sector for the Chronic cohort, whereas emergency department ($283,307) and physical therapy ($137,036) encounters were the top contributors to private sector costs for the acute and subacute cohorts, respectively. Overall reliance on the private sector was highest for specialty care, including 10,721 interventional pain procedures and 306 spine surgeries. This clinical investigation highlighted the criticality of identifying and treating patients in the acute and subacute phases of LBP to stop the progression to chronic—thereby protecting SMs health/wellness and saving a significant amount for the Department of Defense (DoD) and Department of Veterans Affairs (VA).

The Search for an Optimal LBP Treatment

Despite the clinical need for LBP treatments, there is presently no "gold standard" for care and strong evidence as to what is most beneficial is lacking.[21] To highlight the wide variation, options include (but are not limited to): acupuncture, analgesics (paracetamol, opioids), physical therapy, rest, facet blocks and radiofrequency ablation, lumbar supports, massage, multidisciplinary treatment programs, muscle relaxants, non-steroidal anti-inflammatory drugs (NSAIDs), spinal manipulation, temperature treatments (short-wave diathermy, ultrasound, cold compress, heat), traction, transcutaneous electrical nerve stimulation, etc.[22] Nevertheless, several of the options above can be harmful and/or addictive, cause gastrointestinal symptoms, and negatively impact psychomotor, cognitive, and neurological side effects.[22] The wide array of medical recommendations is one of the contributing factors as to why patients often have to limit

their activity levels after sustaining LBP, with recurrent episodes ranging from 24-80% one year post-injury.[16,21,23] Furthermore, SMs are more likely to have myofascial pain, and a significant percentage of back pain is likely to be acute pain since muscle injuries heal; however, degenerated discs and facet joints do not, which leads to more debilitating conditions.[11,24-26]

Despite recognizing the significant burden of disease for LBP, the VA/DoD Clinical Practice Guidelines only call out NSAIDs and the limited use of muscle relaxants as potential therapies. There are presently no recommendations on treatments for LBP that should be used in the acute or subacute setting. Even for those with chronic LBP, only counseling, advising patients to remain active, providing information about self-care options, and cognitive behavioral therapy are advised. The lack of clear indications for early onset LBP extends to the civilian literature as well. *Fulan et al.* reported in a meta-analysis on 3,100 patients in 25 randomized control trials (RCTs) that only one study included patients with acute LBP, while all the others focused on other states.[27] With 75% of United States healthcare expenditures related to chronic disease,[28] and 50% of this cohort not following up with their medical providers regularly,[28] the DoD must invest in a low cost, scalable, replicable, high-quality solution for LBP. As noted by *Quil et al.* there is a "longitudinal relationship management opportunity health systems currently are not capturing."[28]

Massage Therapy for LBP

One of the most promising medical treatments for LBP is massage therapy (MT) given that no special equipment is needed, it can be delivered anywhere, it is non-habit forming, and the likelihood for serious harm is low.[29,30] Massage therapy is unique in that it can naturally enhance local blood flow, thereby providing vital oxygen and nutrients to areas damaged by MSKI to promote healing,[31] offers relaxation and normalization of soft tissue which reduces painful contractions and spasms,[32] lessens swelling, decompresses nerves,[32] clears local pain mediators, induces a parasympathetic response to decrease cortisol production,[33] improves cognitive/psychosocial complications (e.g., depression, anxiety, etc.),[39] aids in sleep quality,[35,36] and provides a positive hormone release.[37-39] MT has an extremely high rate of patient compliance, which is often challenging with many other prescribed therapies; in a 10-week study where subjects were solely responsible for scheduling and completing MT, compliance ranged between 85%-93%.[40] These findings have been corroborated by *Zhou et al.*[41] who demonstrated a two-fold improvement in pain management and functionality for MT patients as compared to traditional exercise groups for intervertebral instability.

On the European continent, MT is a routine form of therapy for acute, sub-acute, and chronic LBP, with a recent survey from Vienna highlighting that 87% of patients with LBP had at least one massage for their condition.[37] In another study by *Bervoets et al.*[42] the author reviewed 26 RCTs and showed that MT as a stand-alone treatment reduced pain and improved function compared to no treatment for MSKI. The United States has adopted a similar affinity for MT, with 47.5 million people having a total of 214 million massages in 2018 to restore function and mobility for patients.[43] Anecdotal evidence has highlighted the benefit of MT, but adoption has remained limited in the private and public sectors in the United States given heterogenous study designs, a lack of agreement on which MT type is most beneficial (e.g., Swedish massage, deep tissue massage, sports massage, chair massage), variations in patient reported outcomes, and inadequate sample size used in RCTs.[10,29]

The largest meta-analysis of treatments for MSK pain (including NSAIDs, opioids, surgery, MT, and corticosteroid injections) found massage therapy measurably reduced pain intensity and increased range of motion.[44] A 2014 study in *Scientific World Journal* revealed that a regular program of deep tissue massage was just as effective at reducing LBP as deep tissue massage combined with NSAIDs, calling into question the benefit of anti-inflammatory medications at all.[45] A trial published in *Annals of Family Medicine* also found that two to three 60-minute massages per week significantly decreased neck pain and dysfunction compared to participants who received either shorter massages or no massage at all.[46]

In another well-designed study by the *Kentucky Pain Research and Outcomes* team, the investigators evaluated MT's impact on pain, disability, and health-related quality of life for primary care patients with chronic LBP.[40] Participants were provided 10 massage sessions with community practicing licensed massage therapists and data was collected at baseline and post-intervention (12 and 24 weeks). Of the 104 patients enrolled, 82% completed 12-week follow ups and 73% finished the full study collection period. The cohort for all time periods showed clinically meaningful improvements in physical/mental questionnaires and reduced bodily pain. The authors concluded, that "results provide a meaningful signal of massage effect for primary care patients with chronic LBP and call for further research in practice settings using pragmatic designs with control groups."[40]

Uniqueness of Zeel

One barrier for successful research, testing, and deployment of MT is finding a national provider for the DoD who can effectively span from evaluation to implementation. Too often research studies are performed without a clear connection to care delivery, which limits uptake, and never achieves the cost savings possible for LBP. However, Zeel is a technology-enabled health and wellness platform that allows patients to schedule MT through an expansive nationwide network of 12,000 health and wellness providers. Zeel is also the only national organization which requires all medical personnel to have registered National Provider Identifier (NPI) numbers, thereby ensuring that providers deliver optimal care in a safe and approved manner. This was especially relevant during the pandemic as delays in care have occurred because of fear and apprehension of going to a crowded hospital facility.

Appointments can be booked via Zeel's best-in-class mobile app or online at www.zeel.com, and data from users have resulted in dramatic benefits to their health: (1) a 58% improvement in activity, (2) a 53% increase in sleep, (3) a 42% reduction in stress, (4) a 38% decrease in pain, (5) 96% adherence to treatment protocols, and (6) an average of 45 minutes saved in travel and wait time for a provider, as Zeel providers travel to the patient home.

Since its launch in 2012, Zeel has successfully delivered more than two million in-home appointments to patients across 40 states (and 54% of clients were treated for LBP). The Zeel network is available for appointments seven days a week, 365 days a year, with customer service teams working around the clock to support patients and providers. Zeel's industry-

leading, Health Insurance Portability and Accountability Act (HIPAA)-compliant technology has placed the organization among ***America's Fastest Growing Companies*** by the Financial Times in 2020, **Crains NY's Fast 50** in 2019, and on the Inc. 5000 from **2017 to 2019**. Partnerships with employers and payers include: Walmart, Dolby, Match, Twilio, Comcast, Northwell, Mount Sinai, NYC Health Systems, Optum, Blue Cross Blue Shield, TriWest, etc.

An Established Zeel-VA Partnership
One point worth emphasizing is that Zeel has an established partnership with the VA and has demonstrated experience working with military patients. In fact, as of February 2025, Zeel is delivering over 7,000 massages per month to Veterans (which is important as they understand complicated cognitive factors such as post-traumatic stress disorder). Zeel was also selected by the VA Community Care Network office (under Dr. Clinton Greenstone) as the clinical delivery and technology partner for their centralized booking pilot program. As part of this arrangement, Zeel is affording military patients and providers seamless access to care, a scheduling module via a smartphone, an ability to treat patients in remote and disparate locations, standardized data collection and pain management protocols, and a mechanism to treat for more patients while reducing the administrative burden on the VA. The time required from identifying a new market of need to opening is exceptionally quick and ranges from 6-12 weeks, which would offer the DoD a means to scale nationally.

9.3 Objectives/Specific Aims/Research Questions:

Describe the purpose and objective(s) of the study, specific aims, and/or research questions /hypotheses

Hypothesis
When used as an adjunct to provider-directed care, a consistent program of MMT (***Group #2***) provided by a qualified practitioner, will shorten the duration of MRDD periods, reduce pain, and decrease unnecessary healthcare utilization in patients with subacute LBP compared to provider-directed care alone (***Group #1***).

Study Aims
This clinical investigation has five specific aims as followed:

- ***Aim 1:*** Determine if a weekly regimen of MMT with provider-directed care (***Group #2***) shortens the duration of MRDD periods in patients with subacute LBP compared to provider-directed care alone (***Group #1***).
- ***Aim 2:*** Assess if a weekly regimen of MMT with provider-directed care (***Group #2***) results in lower self-reported pain/disability and improved quality of sleep scores compared to only provider-directed care (***Group #1***).
- ***Aim 3:*** Evaluate if a weekly regimen of MMT with provider-directed care (***Group #2***) decreases prescribed medications as compared to provider-directed care (***Group #1***).
- ***Aim 4:*** Complete an economic evaluation of healthcare utilization to forecast the potential impact of MMT with provider-directed care (***Group #2***) compared to provider-directed care alone (***Group #1***) for widespread DoD adoption.
- ***Aim 5:*** Identify phenotypic characteristics of responders (i.e., personalized care) who use MMT which will increase efficiency, compliance, cost-effectiveness, and the likelihood of clinical improvement.

9.4 Study Design:

Describe study design in one to two sentences (e.g., prospective, use of existing records/data /specimens, observational, cross-sectional, interventional, randomized, placebo-controlled, cohort, etc.). Specify the phase – Phase I, II, III, or IV – for FDA-regulated investigational drug research

The study is a randomized interventional prospective trial in which patients receive either provider-directed care or medical massage therapy and provider-directed care to assist with subacute low back pain.

9.5 Target Population:

Describe the population to whom the study findings will be generalized

ADSMs

9.6 Benefit to the DoD:

State how this study will impact or be of benefit to the Department of Defense

Low back pain is the most common MSKI and is a threat to military health and safety. For ADSMs impacted by this debilitating condition, there can be significant social, physiological, and economic impact.[10] Most concerning is that there is high underreporting in the medical literature ranging from 16-62% at 6–12 months post injury.[10] Service members who are injured during basic training and combat are often hesitant to share that they are in pain as this will result in MRDD. One of the most popular complementary and alternative medicine options is MMT since it can be deployed in any setting, has been shown to help with pain management and functionality, and is affordable for the military. Heterogeneity in studies, however, have thwarted widespread usage in the DoD and a RCT is required to highlight the benefit for medical providers and patients.

This study developed herein has high impact and low cost for the military. Successful demonstration with a proven provider (Zeel) will offer a solution to immediately scale and help ADSMs nationwide. Data will be rigorously collected by a team with 20+ years of collective experience together, who have published collectively 500+ peer-reviewed publications and abstracts, and who are supported by an expansive research infrastructure in the Musculoskeletal Injury Rehabilitation Research for Operational Readiness (MIRROR) organization sponsored by DHA.

10.0 Study Procedures, Data Management, and Privacy

10.1 Study Procedures:

Describe step-by-step how the study will be conducted from beginning to end

Recruitment, Pre-Screening, Informed Consent:
Potential participants will be identified by the following methods:

1. Under the provisions of an approved HIPAA Waiver, local study team members will review medical records of patients coming into the local clinics for suspected/confirmed LBP in order to identify prospective research participants to approach and offer study participation.
2. Patients may be referred to the study team directly from healthcare providers in the local clinics.
3. Patients may self-refer to participate in the study. Interested individuals will be able to contact a member of the study team via phone or email.
4. Study advertisements will be provided to clinic staff and will be posted within the following locations:
    - Internal Medicine
    - Aviation Medicine
    - H2F (Holistic Health and Fitness)
    - McChord Clinic
    - Winder Clinic
    - Okubo Soldier-Centered Medical Home
    - Allen Soldier-Centered Medical Home
    - Soldier Recovery Unit
    - Puyallup Community Medical Home
    - South Sound Community Medical Home
    - Armed Forces Wellness Center
    - Intrepid Spirit Center
    - Madigan Medical Mall
    - Pharmacy waiting areas, if possible
    - Physical Therapy
    - Podiatry
    - Sports Medicine
    - Tactical Human Optimization, Rapid Rehabilitation and Reconditioning (THOR3)
    - Physical Medicine and Rehabilitation
    - Coffee bar
    - Dining Facility entrance
    - Intranet screensaver page
    - 2/75 Ranger Clinic
    - Pain Management

If a potential participant expresses interest in learning more about the research study, a member of the research staff will briefly introduce the study, express the voluntary nature of participation, assess interest, and screen the potential participant for eligibility. Eligibility will be determined in person using the Inclusion/Exclusion Case Report Form (CRF) (Appendix A).

If the potential participant meets eligibility criteria and expresses interest in participating, an authorized study team member will initiate the formal consent discussion and, if applicable, obtain informed consent.

Individuals who consent to participate will be added to a Master List (Appendix J) that will match the participant's unique study ID with their name and other direct identifiers. The Master List will be stored in a password-protected electronic document on a common access card (CAC)-enabled server; only on-site study team members will have access to this file. This coded study ID will be used on all research data collection forms in place of the participant's name, DoD ID, or other protected identifier.

The local research team will maintain a separate electronic Screening Log (Appendix I) containing DoD ID number, eligibility status, and date screened. This log will be password protected and stored in a secure folder on a secure drive accessible only by authorized local research staff. This log is needed to avoid duplicative screening of individuals. This reduces burden on potential participants, providers, and study team, and ensures the study team will not screen the same person twice or examine records for eligibility criteria when screen status is already established.

Contact Information:
Immediately following consent, the participant will complete an Intake CRF (Appendix B). The Intake CRF will collect participant contact information (full name, DoD ID number, preferred mobile phone number, email address, etc.).

With the exception of the Consent Form, the Intake CRF is the only paper research form that will contain PII. It will be stored with the signed consent forms (in a locked cabinet inside of a locked room) and separately from all other paper research forms. All remaining paper research forms will be identified using a unique study ID. The Intake CRF will not be entered into REDCap (data storage system described more below).

Demographics and Baseline Data Collection:
Prior to receiving study treatment, participants will complete a Demographics CRF (Appendix C) to collect relevant demographics including personal and military and employment demography.

Additionally, participants will complete a Baseline Data Collection CRF (Appendix D) that collects military & work status, validated self-report measures, and study-specific measures.

Randomization:
After consenting, participants will be randomized to either provider-directed care (***Group #1***) or MMT and provider-directed care (***Group #2***) by the study team. This will occur via the REDCap randomization tool. Participants will be informed immediately after whether they were assigned to **Group #1** or **Group #2**.

Sampling will be checked at interim time points by a biostatistician to ensure age, biological sex, and initial pain presentation match; this is critical to show the true impact of care and ensure translation to the civilian sector afterward. If it appears there is an imbalance, the biostatistician will be consulted to best understand how to collect additional data while preserving integrity and relevance for the general population.

Study Intervention:

Provider-Directed Treatment:
All participants will receive provider-directed care treatment modalities at the discretion of their healthcare provider to address their LBP. Provider-directed treatment will not be standardized across study participants and/or dictated by study-specific criteria. Participants will be asked to refrain from any invasive interventions such as interventional spine injections, dry needling, acupuncture, cupping, and trigger point injection for the duration of the study. If a participant reports receiving any invasive treatment during their participation in the study, it will be documented.

MMT Standardized Delivery:
Participant information will not be shared with Zeel if a subject is assigned to **Group #1**; however, **Group #2** participant names and contact information will be shared with Zeel via telephonics and/or through an encrypted and safe manner (e.g., DoD SAFE) in order for Zeel to facilitate and schedule MMT appointments.

Participants in **Group #2** will also sign a standard notice of privacy practice and consent for treatment from Zeel prior to care. Participants will receive one massage and educational session (approximately 60 minutes) a week for 12 weeks (up to 16 weeks to accommodate temporary changes in participant's schedule or location). This will ensure high compliance and minimize potential loss of follow up data. Licensed massage therapists who have been trained in MMT in schools accredited by the Commission on Massage Therapy Accreditation will perform the intervention. Trained practitioners that routinely perform home massages are located in the proposed service areas by Zeel using standardized protocols.

Participants will be asked to have a 6' x 10' space cleared for the massage table. The providers will bring all equipment required, such as the massage table, bolsters, and hypoallergenic lotion. During the first visit, the Zeel provider will ask questions to better understand the participant's health profile. The provider will then explain to the participant the treatment process and ask permission to touch their lower back. The provider will complete the MMT treatment plan.

During the treatment, the participants will remain clothed. They will be asked to wear loose-fitting clothing that allows for access to the treatment area and enables a full range of motion. If clinically appropriate, the medical massage therapist may choose to access areas underneath clothing – including shoulders, lower back, and thighs – as part of the pain management protocol. The rendering massage therapist will tailor treatment and education based on the patient's individual needs, with each treatment to include both Swedish and deep tissue massage modalities as part of the MMT as deemed appropriate by the therapist based on the patient's soft tissue, clinical presentation. There will be 5-10 minutes of targeted patient education during the massage session. The topics for education and content that will be shared includes the following: anatomy and physiology, breathing and relaxation techniques, hydration, posture, passive stretching, active mobility, core stability exercises, and ergonomic adjustments.

Following the session, the provider may instruct the patient in ways to improve recovery such as stretching and modalities between treatments to support care. Future appointments will be scheduled following the evaluation with the appropriate weekly cadence for 12 weeks per the study design. All documentation, including treatment and any reactions to treatment for the visit, will be completed contemporaneously and recorded in Zeel's system for future use. Medical massage will follow state and federal guidelines.

The process used for providing at-home massages for this investigation will be:

- Medical massage therapy is identified as a necessity by a referring provider or through patient self-referral and the patient is randomly assigned to **Group #2**.
- Participant name, address, days/times of availability and mobile phone number will be provided to Zeel via a secure method (DoD SAFE or telephonic transmission).
- All participants will be treated at their residence or other pre-designated, preferred location. The corporate NPI for Zeel will be used to identify Zeel in HealthShare Referral Manager (HSRM) prompting the referral to be sent to Zeel.
- The participant will be contacted by Zeel's scheduling team to schedule the initial appointment day/time. The participant will receive a confirmation text confirming their appointment date/time. Future appointments will be scheduled directly with the massage therapist assigned to the participant.
- Zeel will facilitate care per study protocol

Follow-Up Data Collection:
Regardless of study arm assignment, all participants will be asked to complete weekly (+/- 2 days) self-report assessments. Follow-up data will be recorded on Follow-up Data Collection CRF (Appendix E).

Data may be captured in-person or remotely (e.g., entered directly into REDCap using a personalized coded link with no log-in required, verbally over the phone with a study team member, etc.), as applicable. In cases when a participant enters their data directly into REDCap, an authorized research team member will email the study participant a personalized survey link that does not require a login. Upon accessing the link, participants can enter their data directly into REDCap. The project dashboard in REDCap enables authorized research team members to verify survey completion. The lead research coordinator (or another authorized team member)

will be responsible for printing the completed forms and filing them in the participant's hardcopy research record to serve as source documentation.

Reminder phone calls, texts, and/or emails will be sent to participants at their preferred contact method indicated. In-person follow-ups will be scheduled for missed appointments to ensure data completeness.

Study participation will end for both groups after the completion of the week 16 (+/- 2 week) follow up.

Additional Information - MIRROR/USU:
This research study is being conducted as part of Musculoskeletal Injury Rehabilitation Research for Operational Readiness (MIRROR), which is based out of the Department of Physical Medicine & Rehabilitation (PM&R) at the Uniformed Services University (USU). MIRROR is focused on advancing MSKI rehabilitative care within the military healthcare system in order to reduce the burden MSIs have on military readiness and to ultimately enhance the operational capabilities of the armed forces. MSIKs affect approximately 800,000 service members annually and result in 25 million days of limited duty. These conditions are the primary reasons for medical discharge /downgrade and result in 34% of medical evacuations from theatre. MIRROR was developed as a means to study risk factors of common MSIKs, generate prevention strategies, optimize treatments, and establish return-to-duty criteria that is based on scientific evidence rather than case-specific clinical judgment alone. MIRROR involves interdisciplinary and inter-service partnerships, the DoD, and several major academic medical centers. To ensure military mission focus and scientific relevance, MIRROR is guided by a steering committee composed of members from the Joint Program Committees (JPCs) at the U.S. Army Medical Research and Development Command (USAMRDC), military operational leaders, and experts in musculoskeletal medicine from the military and civilian communities. MIRROR aims to be the world's leader in military relevant musculoskeletal injury care research. Currently, 40+ research projects are being deployed at more than 20 military and civilian treatment facilities nationwide.

MIRROR/USU is serving as a Coordinating Center for this study and will also be providing remote regulatory support. Staff from MIRROR/USU will not interact with human subjects and will not have access to the Master List during the conduct of this study. Deidentified research data will be shared with MIRROR/USU and maintained indefinitely for possible use in future research.

10.2 Data Collection:

Describe all the data variables, information to be collected, the source of the data, and how the data will be operationally measured.

Please see Appendix H Data Collection Schedule.

The local study team will obtain the information necessary to complete the study CRFs directly from the participant.

Data may be captured in-person or remotely (e.g., entered directly into REDCap using a personalized coded link with no log-in required, verbally over the phone with a study team member, etc.), as applicable. In cases when a participant enters their data directly into REDCap, an authorized research team member will email the study participant a personalized survey link that does not require a login. Upon accessing the link, participants can enter their data directly into REDCap. The project dashboard in REDCap enables authorized research team members to verify survey completion. The lead research coordinator (or another authorized team member) will be responsible for printing the completed forms and filing them in the participant's hardcopy research record to serve as source documentation.

Appendix A - Inclusion Exclusion CRF:
Verifies that the potential participant meets eligibility criteria for study participation.

- Inclusions/exclusion criteria
- Documentation of informed consent

Appendix B - Intake CRF:
Obtains sufficient contact and scheduling information in order to locate and track the participant during study participation, including the contact's address where treatment will occur and days /times the contact is generally available for treatment.

Appendix C -Demographics CRF:
Characterizes the participant's demographics and relevant medical and work history to include personal and military/employment demography

Appendix D - Baseline Data Collection CRF:
Collects relevant baseline research data.

- Military Specific Duty Status
- WPAI-LBP
- DVPRS
- M-ODI
- GPS
- PROMIS-29
- Randomization documentation

Appendix E Follow-Up Data Collection CRF:
Collects relevant follow-up research data.

- Weeks: 2-5 & 7-11
    - Satisfaction & treatment history
    - Military specific duty status
    - WPAI-LBP
    - DVPRS
    - Physical Therapy appointment history
        - How many PT appointments since last study visit
        - Which body part(s) treated
        - What treatment modalities were performed
- Weeks 1, 6, 12, & 16:
    - Satisfaction & treatment history
    - Military specific duty status
    - WPAI-LBP
    - DVPRS
    - M-ODI
    - GPS
    - GROC
    - PROMIS-29
    - Physical Therapy appointment history
        - How many PT appointments since last study visit
        - Which body part(s) treated
        - What treatment modalities were performed
- Weeks 1-16: Adverse Event (AE) assessment
    - An authorized staff member will ask participants whether they have experienced any complications or adverse events since their last visit.

Appendix F Study Completion CRF:
Documents participant study completion status.

- Study completion status
- AE assessment
- Protocol Deviation (PD) assessment

Appendix G Protocol Adherence CRF:
Documents protocol adherence for each study visit.

- AE assessment
- PD assessment

Each survey tool is described in more detail as follows:

- **M-ODI** – The M-ODI is the most commonly used aid for evaluating disability due to LBP.[48,49] This free instrument delivers medical providers information related to functional limitation and pain management. As noted by Nishant et al., "the modified ODI is time saving and accurate, and it avoids the need to measure other scores and has stronger correlation with visual analogue scores."[50]

- **Satisfaction & Treatment History Self-Reported Data** – Participants will self-report differences in healthcare utilization and prescription medication fulfillment, as well as satisfaction with care
- **Work Productivity and Activity Impairment Questionnaire (WPAI-LBP)** - The Work Productivity and Activity Impairment (WPAI) Low Back Pain (LBP) questionnaire is an instrument used to assess the impact of low back pain on a person's ability to work and perform daily activities. The questionnaire focuses on absenteeism (missing work), presenteeism (reduced productivity at work), and limitations in non-work activities due to low back pain
- **Defense and Veterans Pain Rating Scale (DVPRS)** - The Defense and Veterans Pain Rating Scale (DVPRS 2.0) is a pain assessment tool that utilizes a numerical rating scale enhanced by functional word descriptors, color coding, and pictorial facial expressions matched to pain levels.
- **Global Pain Scale (GPS)** - The GPS is a comprehensive assessment of pain evaluating pain, emotions, clinical outcomes, and daily activities. This may be a valuable tool for evaluation and treatment planning for interventional pain management physicians.
- **Global Rating of Change Score (GRoC)**- The GRoC is a frequently used outcome measure that has been used to independently score self-perceived improvement in a patient and has been used as an anchor method to determine minimal clinically important change scores[54]. The GRoC is a single-item, recall-based questionnaire of well-being that is based on progress (or lack of progress) since an initial treatment encounter.
- **Patient-Reported Outcomes Measurement Information System (PROMIS-29)-** The PROMIS-29 v2.0 profile assesses pain intensity using a single 0–10 numeric rating item and seven health domains (physical function, fatigue, pain interference, depressive symptoms, anxiety, ability to participate in social roles and activities, and sleep disturbance) using four items per domain[55].

10.3 At any point in the study, will you request, use, or access health information in any form, including verbal, hard copy and electronic?

(•) Yes ( ) No

10.4 Review the definitions below and respond to the following two questions. If you are not sure of the answers, email DHA.PrivacyBoard@mail.mil for assistance. The *Military Health System (MHS)* is defined as all DoD health plans and DoD health care providers that are organized under the management authority of, or in the case of covered individual providers, assigned to or employed by, the Defense Health Agency (DHA), the Army, the Navy, or the Air Force *MHS workforce members* are employees, volunteers, trainees, and other persons whose conduct, in the performance of work for the MHS, is under the direct control of the MHS, whether or not they are paid by the MHS. *MHS business associates* are persons or entities that provide a service to the MHS and require protected health information (PHI) to provide the service.

Are you an MHS workforce member?

(•) Yes, I am an MHS workforce member
( ) No, I am not an MHS workforce member

10.5 Have you consulted with an MHS data expert to determine the data elements required for your study?

Consulting with a data expert often saves time later in the compliance process because the data expert can advise on the data available in the numerous MHS information systems, the quality of that data and the methods for encrypting and collapsing data. To schedule a consult with an MHS data expert, send an email to: (**DHA.PrivacyBoard@mail.mil**)

( ) Yes, then complete the questions below according to the data consult
(•) No, then complete the questions below according to the best of your knowledge

10.6 Indicate how you will request data from the MHS. Select all that apply.

☐ Talking with MHS health care providers or MHS health plans about specific research participants

☐ Obtaining MHS hard copy records specific to research participants
☑ Obtaining data from an MHS information system(s)

10.7 If you are obtaining data from an MHS information system(s), indicate whether you plan to receive a data extract or whether you plan to access an MHS information system directly to create a data set.

A data extract is when the MHS or a contractor provides the data set directly to the researcher. When receiving a data set through data extract, the researcher may indicate whether the data elements should be provided as is, encrypted or collapsed. In contrast to a data extract, access to an information system means that the researcher may directly access an MHS information system and create a data set for the research study

☐ Data Extract
☑ Access

10.8 Do you intend to request de-identified data from the MHS in your research study?

There are different two methods for de-identifying data pursuant to HIPAA:
1) Safe Harbor Method: Removing all of the identifiers listed in Table 1 below, provided that the researcher does not have actual knowledge that the remaining data can be used alone or in combination with other information to identify the individual who is the subject of the information
2) Statistical Method: An expert, with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable, determines that the data is not individually identifiable

○ Yes ◉ No

10.9 Indicate the MHS information system(s) from which you will seek to obtain data

If you do not know which system(s) contains the data elements you need, refer to the Guide for DoD Researchers on Using MHS Data or request guidance from an MHS data expert at: **DHA.PrivacyBoard@mail.mil**.

Below is a list of commonly used MHS systems. If the system from which you seek to obtain data is not listed below, list the name of the system in the "Other MHS Systems" category below
PHI Systems:

MHS Information System	Requesting Data
: MHS Genesis	: Yes

PII-Only Systems:

MHS Information System	Requesting Data
No results found	

De-Identified Data & Other Systems:

Information System	Requesting Data
No results found	

10.10 Do you intend to merge or otherwise associate the requested data with data from any sources outside of the MHS, including other DoD systems that are not part of the MHS?

○ Yes, will merge data
◉ No, will not merge data

10.11 Indicate the data elements about research participants or relatives, employers, or household members of the research participants that you will request from MHS hard copies or from MHS information systems.
If you will merge data, also indicate non-MHS data elements about research participants or relatives, employers, or household members of the research participants that you will have access to in any form or medium.

Direct and Indirect Identifiable Data Elements	DHA Hard Copies	DHA Data Elements to be Accessed	DHA Data Elements Verbal	Extracted DHA Digital Data	Downloaded DHA Digital Data	Non-DHA Hard Copies or Digital
1. Names	☐	☑	☐	☐	☐	☐
2. Postal address with only town, city, state, and zip code	☐	☐	☐	☐	☐	☐
3. Postal address with all geographic subdivisions smaller than state, including street address, city, county, precinct, zip code and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of Census: 1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and 2) the initial three digits of a zip code from all such geographic units containing 20,000 or fewer people	☐	☐	☐	☐	☐	☐

is changed to 000						
4. Dates including all elements (except year) directly related to an individual, including birthdate, admission date, discharge date, and date of death	☐	☑	☐	☐	☐	☐
5. Ages over 89 and all elements of dates (including year) indicative of such age, unless you will only request a single category of "age 90 or older"	☐	☐	☐	☐	☐	☐
6. Telephone Numbers	☐	☑	☐	☐	☐	☐
7. Fax Numbers	☐	☐	☐	☐	☐	☐
8. Email Addresses	☐	☑	☐	☐	☐	☐
9. Social Security Numbers	☐	☐	☐	☐	☐	☐
10. Medical Record Numbers (MRN) (including record ID)	☐	☐	☐	☐	☐	☐
11. Health Plan						

Beneficiary Numbers (including DEERS ID, Electronic Data Interchange Personal Identifier (EDIPI) or Number (EDIPN))	☐	☑	☐	☐	☐	☐
12. Account Numbers	☐	☐	☐	☐	☐	☐
13. Certificate /License Numbers	☐	☐	☐	☐	☐	☐
14. Vehicle identifiers and serial numbers, including license plate numbers	☐	☐	☐	☐	☐	☐
15. Device identifiers and serial numbers	☐	☐	☐	☐	☐	☐
16. Web Universal Resource Locators (URLs)	☐	☐	☐	☐	☐	☐
17. Internet Protocol (IP) address numbers	☐	☐	☐	☐	☐	☐
18. Biometric identifiers, including finger and voice prints	☐	☐	☐	☐	☐	☐
19. Full-face photographic images and any comparable images	☐	☐	☐	☐	☐	☐

20. Any other unique identifying number, characteristic, or code (including non-military provider IDs)	☐	☐	☐	☐	☐	☐
21. Free Text Fields	☐	☐	☐	☐	☐	☐

If you are obtaining SSNs, provide a justification as to why and explain why a substitute cannot be used.

Due to guidelines stated within DoDI 1000.30, Reduction of SSN Use within DoD, the reduction or elimination of SSN usage must occur wherever possible. If SSNs are required to complete the project, the PI must provide a justification and explanation as to why a substitution cannot be used.
For example:

- If alternatives to SSN (e.g., EDIPNs or pseudo person IDs) are sufficient in other instances, will those alternatives to SSN usage be sufficient to respond to Congressional inquiries and /or Senior DoD stakeholders inquiries?
- Are alternatives to SSN used first?
- Are those alternatives to SSN insufficient to combine data from multiple data sources? Is the issue that some individuals do not possess alternatives ID numbers and SSN is the only way to identify them?

N/A

a. Will you receive or obtain health information?

> ***Note:*** *If you indicate you are not receiving health information, the answer must be consistent with the DHA data source. For a non-health information data request, if you are a non-MHS employee or non-MHS business associate, you may not access an information system that has PHI or LDS. For both MHS and Non-MHS employees and MHS business associates, you may* ***NOT*** *include data elements in the above table on: 1) lines 10 or 11, 2) line 21 if the free text field comes from a PHI or LDS system, and 3) lines 12, 13, or 18 if the account numbers, certificate and license numbers, biometric data, or any other data elements are health information created or received by an MHS health care provider, health plan, or business associate in relation to the physical or mental health or condition of an individual or payment for health care.*

◉ Yes, I will receive or obtain health information
○ No, I will not receive or obtain health information

b. If no data elements were checked in the above table, is it possible that the requested DHA data is or will be identifiable because of any unique data elements, triangulation, or small cell size?

☑ Data elements were checked in the above table, STOP HERE.

NOTE: *A unique data element includes any unique features that alone are not identifiable but that could be used to identify an individual within the context of other information, such as any type of code (such as diagnosis or procedural), rank of general or admiral, gender, or race. Triangulation means using different data elements that when combined can be used to identify an individual, such as including the above lists of unique data elements in a data set.*

Determining whether an individual is identifiable through triangulation requires consideration of all data elements in combination. Within the military, the use of rank and/or diagnosis code, procedural codes, or any other code that changes on a predictable basis, increases the possibility of identification. Small cell size means that there is only a small number of eligible individuals that satisfy the category description. Department of Defense Manual 6025.13, Medical Quality Assurance and Clinical Quality Management in the Military Health System MHS, provides that the threshold for de-identifying data within the MHS requires a cell size of three, but also states that the de-identification standards must meet the DoD implementation of the HIPAA Privacy Rule. Centers for Medicare and Medicaid also gives guidance on small cell size stating that no data cell less than 11 may be published or displayed. However, the Office for Civil Rights' OCR, which is the official regulatory office for the HIPAA Privacy Rule, provides that OCR does not designate a universal value for small cell size in accordance with the de-identification standard; instead, the cell size should be set at a level that is appropriate to mitigate risk of identification by the anticipated recipient of the data set. This means that a cell size of 3 or 11 may not meet the HIPAA Privacy Rule requirements if the cell size level does not appropriately mitigate risk of identification by the anticipated recipient of the data set.

Note: If dates are altered as a means of de-identifying the data, diagnosis and procedural codes need to be rolled-up or collapsed. If dates are provided "as time between events," the roll-up is not necessary.

- ☐ Yes, the DHA data will become identifiable
- ☐ No, the DHA data will not become identifiable

10.12 Do you believe it is possible for the MHS data to become identifiable because of triangulation, a small cell size, or any unique data element(s)?

Triangulation means using different data elements that are not themselves identifiable but that when combined can be used to identify an individual. For example, triangulation would use rank and race together to determine the identity of an individual with a particular health condition.

Small cell size means that there is only a small number of eligible individuals that satisfy the category description. Guidance for acceptable cell size is available from the Centers for Medicare and Medicaid Services. For example, the rank category of four star generals with a particular diagnosis may be less than 30, so the rank category may need to be expanded to include lower ranks.

A unique data element includes any unique features that are not explicitly enumerated in the categories of data in rows 1 – 20 of the table above (in Section 10.10), but that could be used to identify an individual. Unique data elements include characteristics that are not themselves identifying, such as the rank of general or admiral, or a race or gender, but within the context of other information could be identifiable.

- ○ Yes, I believe there is a reasonable possibility the MHS data will become identifiable
- ◉ No, I believe there is no reasonable possibility the MHS data will become identifiable

10.13 Have you completed and uploaded an appropriate HIPAA document (i.e. HIPAA Authorization will be obtained or Waiver/alteration of HIPAA Authorization is being requested)?

- ◉ Yes
- ○ No
- ○ N/A

If yes, please check which one.

- ☐ HIPAA Authorization
- ☑ HIPAA Waiver (Full or Partial)
- ☐ Other (please provide copies when uploading Other Study Documents)

10.14 Managing Data (Data Management and/or Sharing Plan) and/or Human Biological Specimens for this Study:

Include in this section the plan for acquiring data (both electronic and hard copy), access during the study, data/specimen storage and length of time stored, shipment/transmission, and the plan for storage and final disposition at the conclusion of the study. Describe any data agreements in place for accessing data within and/or outside of your institution (e.g., Data Sharing Agreement, Data Use Agreement, Business Agreements, etc.)

Data Capture Methods:
For both groups, the local study team will obtain the information necessary to complete the study CRFs directly from the participant (including in person, via mail, email, or over the phone). The completed CRFs will serve as source documents for this study.

Participants may also enter their coded data directly into REDCap using a personalized survey link (no log-in required). In these cases, the completed REDCap forms will be printed and added to the participant's research record to serve as a source document.

Electronic Data Entry:
Following each research visit, a local study team member will review any completed paper CRFs for accuracy and completeness and then enter the collected non-personally identifiable data from the paper CRFs into REDCap, an encrypted, access controlled, password protected electronic data capture and management system housed on a Department of Defense (DoD) server and maintained by the Uniformed Services University Information Technology (USU IT).

Please see Appendix K for additional information on REDCap.

Data Storage & Access:
With the exception of the ICF, Intake CRF, and electronic Master List all research data (both paper and electronic) will be identified using a unique study ID only, and not by the participant's name, date of birth, DoD ID, or other protected identifier.

The ICF and Intake CRF will be stored separately from the coded paper research forms. Paper research forms and source documents will be stored in a locked cabinet inside of a locked room within the Pain Medicine Clinic at MAMC.

The electronic Master List will be stored separately in a secure, password protected document on a computer and network that requires common access card clearance; this file will only be accessible to local research staff. Study personnel will not share the Master List with the biostatistician as to ensure that analyses are conducted with the highest integrity and neutrality.

The coded electronic research data for this study will be stored in REDCap, an encrypted, access controlled, password protected electronic data capture and management system housed on a Department of Defense (DoD) server and maintained by the Uniformed Services University Information Technology (USU IT). No PHI/PII will be entered into REDCap.

All research data and forms (both paper and electronic) will only be accessible by authorized study staff, authorized staff from MIRROR/USU (coded data entered into REDCap only, as described below), the IRB of record, the local research office (if applicable), and applicable governmental agencies as part of their duties and in accordance with federal law. These duties include making sure that research participants are protected.

Informed Consent Forms will be maintained for a period of six years following study closure and then securely shredded. Paper research forms will be maintained for a period of five years following study closure and then securely disposed per organizational standards. The Master List connecting unique study identification to participant identifiers will be destroyed at study closure.

Is this a data repository?

○ Yes ◉ No

10.15 Managing Data (Data Management and/or Sharing Plan) and/or Human Biological Specimens for Future Research:

If the study involves collecting, storing, or banking human specimens, data, or documents (either by the Investigator or through an established repository) for FUTURE research, address. How the specimens/data will be used, where and how data/specimens will be stored (including shipping procedures, storage plan, etc.), whether and how consent will be obtained, procedures that will fulfill subjects' request as stated in the consent, whether subjects may withdraw their

data/specimens from storage, whether and how subjects may be recontacted for future research and given the option to decline, whether there will be genetic testing on the specimens, who will have access to the data/specimens, and the linkage, the length of time that data/specimens will be stored and conditions under which data/specimens will be destroyed.

Consent for Future Use of Data:
The ICF for this research study states that de-identified research data will be shared with MIRROR /USU and will be maintained indefinitely for possible use in future research. By consenting to participate in this research study, participants agree to allow us to maintain their de-identified research data indefinitely for possible use in future research.
Participants will not be given the option to opt out of us retaining their de-identified research data indefinitely for possible future use. The ICF states, "If you do not want your deidentified data collected as part of this research study to be kept for use in future research studies, you should not sign this consent form."

Long Term Data Storage & Access:
The de-identified electronic dataset will be maintained by MIRROR/USU and the study team indefinitely or as long as it is practicable to maintain.

De-identified electronic research data will be securely transmitted from local study teams to the MIRROR /USU via REDCap or the DoD secure access file exchange (SAFE) application (or other permissible safe data sharing system). REDCap utilizes Secure Sockets Layer (SSL) in addition to other safeguards on its web server to maintain secure communication with end-users (see Appendix K). DoD SAFE uses a TLS (Transport Layer Security) protocol when files are uploaded and downloaded.

Once received, the electronic de-identified research data will be stored within an encrypted, access controlled, password protected electronic data capture and management system housed on a DoD-compliant server.

Access to the de-identified research data will be governed strictly on an individual-by-individual basis within the secure electronic data capture and management system. Individual data access as well as privileges will be clearly delegated, audited, and monitored by MIRROR/USU.

Any future research using retained data will require a research protocol to be approved by an Institutional Review Board or other authorized official responsible for protecting human subjects of research.

Data Withdrawal from Storage:
Participants may request to have their data withdrawn at any time before their personal identifiers have been removed. Once their data has been de-identified (when the study master list is destroyed at study closure), it will be impossible for the researchers to locate their specific study data.

Is this a data repository?

(•) Yes ( ) No

If Yes, provide the name of the Repository

USU OCIO REDCap

Who will have access to the Repository?

MIRROR/USU, study team members, and investigators, as appropriate

What data type will be stored in the Repository?

- [ ] Protected Health Information
- [ ] Limited Data Set
- [x] De-identified Data

11.0 Statistical/Data Analysis Plan

11.1 Data Analysis Plan and Statistical Considerations:

List the statistical methods to be used to address the primary and secondary objectives, specific aims, and/or research hypotheses. Explain how missing data and outliers will be handled in the analysis. The analysis plan should be consistent with the study objectives. Include any subgroup analyses (e.g., gender or age group). Specify statistical methods and variables for each analysis. Describe how confounding variables will be controlled in the data analysis.

At the end of the study, the statistician will be blinded to the study group assignment and information will be shared using the codified fields (e.g., Subject 001, Subject 002, etc.) to understand the impact of MMT vs. provider-directed care.

Descriptive statistics will be used to report mean and standard deviation for normally distributed variables, median and interquartile intervals for ordinal metric variables, and in terms of proportion and size for categorical variables. Values will be reported at baseline by treatment group and overall. Multi-level/hierarchical models will also be used for inferential analyses, specifically, distribution families, effects types, and link functions appropriate for the outcomes of interest; determined using QQ plots analyzed for best model fit. For the five aims, analyses will be conducted as followed:

1. ***Aim #1***, the primary aim, will be addressed by comparing the total sum of MRDD days across the full 16-week study period between treatment arms. A sensitivity analysis under ***Aim #1*** will be used to evaluate the total count of distinct MRDD periods across the 16-week study period instead of total count of days taken.
2. ***Aim #2*** will be compared across weekly data points of self-reported pain/disability and sleep scores; a sensitivity analysis for ***Aim #2*** will consider the fractional change over the full 16-week period for each self-report instead of longitudinal data points.
3. ***Aim #3***, the total sum of prescriptions will be aggregated over the 16-week duration of the study period and will be compared between treatment arms after self-reporting. A sensitivity analysis under ***Aim #3*** will consider the total number of pills prescribed instead of the count of overall prescriptions.
4. ***Aim #4***, the total sum number of each type of healthcare event, will be aggregated over the 16-week study duration and those totals will be compared between treatment arms. Healthcare events compared will include emergency department visits, specialty care visits, prescriptions filled, etc.; we will also estimate the economic impact between provider-directed care (***Group #1***) and MMT and provider-directed care (***Group #2***) cohorts. Estimates of cost by healthcare event will be referenced from reputable and consistent public sources so that data can be extrapolated for the public sector (e.g., the average cost of an emergency department visit in the United States was $1082 for an insured patient and $1220 for an uninsured patient in 2019).[53] A sensitivity analysis for ***Aim #4*** will consider a simulation of varying costs for each healthcare event within a range for each in order to test the variation of the economic comparison between treatment arms given different rates or across-rate ratios present at different institutions.
5. ***Aim #5,*** developing a phenotype for patients that respond to MMT and provider-directed care (***Group #2***) will occur by aggregating important patient information such as psychology history, medical board status, other chronic pain problems, demographics, etc. For continuous variables, a regression will be constructed to understand which variables have the greatest impact and then all data will be cross-checked with binary /qualitative metrics. All requested data will have IRB approval in advance. This will allow the development of personalized medicine in the future.

Our statistical plan will include both between subjects, comparing across groups, and within subjects. We will calculate the distribution of fractional change between baseline and 16-week endpoint in each weekly outcome measure of concern (i.e., self-reports for pain/disability), reporting the distribution of change within each metric and treatment group. Additionally, we will calculate the distribution of fractional change between baseline and six weeks for all measures as well. If a patient drops out prior to 16 weeks but is included at six weeks with valid data, they will be omitted from the 16-week view but included in the six-week view.

Besides the aforementioned calculation of 16 and six week change in which missing endpoint data means removal of a patient's data for the analysis overall, patients will only be removed from analyses if they have completely missing data for a specific analysis. For example, a patient with no data for week 10 with regard to pain self-reports will still be included in ***Aim #2*** analyses. We assume for the sake of simplicity that the absence of any data points for prescriptions, healthcare visits, etc. indicates that they had zero of these events during the 16-week study period. Use of multi-level/hierarchical modeling methods both in longitudinal

analyses and simpler by-group comparison tests allows us to include patients whose data may not be fully complete. Confounding will primarily be counteracted with randomization.

Statistical significance will be considered at the putative threshold (alpha=0.05). Secondary p-values will be subject to a false discovery rate adjustment. Outliers will be removed if determined to be erroneous based on relevant clinical expertise.

11.2 Sample Size:

As noted above, literature evaluating the impact of MMT on LBP is scarce and results are often underreported. Thus, in order to appropriately power this RCT, the investigators used Crawford et al., "The Impact of Massage Therapy on Function in Pain Populations—A Systematic Review and Meta-Analysis of Randomized Controlled Trials: Part I, Patients Experiencing Pain in the General Population".17 Based on this review, there were four quality studies which included 245 patients treated with massage intervention or a wait-listed control to treat musculoskeletal pain. In general, these prior works demonstrate wide ranges of effect sizes in favor of massage for treating pain intensity post-treatment, which spanned 0.26-1.14. While MRDD is a critical method, to the investigator's knowledge, this has not been reported and represents a novelty of the work proposed herein. However, powering the study based on pain change is sufficient to approximate the number of SMs and is better than a One Sample's test. The sample size calculation for this pre-application was computed using a two tailed mean difference between independent samples with an alpha = 0.05 and similar effect of 0.26 noted above to ensure a conservative estimate. For this trial, the investigators would require N=195 total patients (n=98 per group) to demonstrate a statistical difference with 70% power. However, given that our team will also segment individuals based low, medium, high pain levels to determine the optimal group for care in the future, and we will have some patients who are lost to follow up, so we plan to seek permission to recruit up to N=220 patients to make sure we achieve our requested recruitment total (n=100 for Group #1 and n=100 for Group #2).

11.3 Total number of subjects requested (including records and specimens):

220

11.4 If you are recruiting by study arm, please identify the arms of the study and how many subjects will be enrolled in each arm

n=110 for Group #1 and n=110 for Group #2

11.5 Please provide a justification for your sample size

For this trial, the investigators would require N=195 total patients (n=98 per group) to demonstrate a statistical difference with 70% power. However, given that our team will also segment individuals based low, medium, high pain levels to determine the optimal group for care in the future, and we will have some patients who are lost to follow up, so we plan to seek permission to recruit up to N=220 patients to make sure we achieve our requested recruitment total (n=100 for Group #1 and n=100 for Group #2).

Literature evaluating the impact of massage therapy on LBP is scarce and results are often underreported. Thus, in order to appropriately power this RCT, the investigators used Crawford et al., "The Impact of Massage Therapy on Function in Pain Populations—A Systematic Review and Meta-Analysis of Randomized Controlled Trials: Part I, Patients Experiencing Pain in the General Population". Based on this review, there were four quality studies which included 245 patients treated with massage intervention or a wait-listed control to treat musculoskeletal pain. In general, these prior works demonstrate wide ranges of effect sizes in favor of massage for treating pain intensity post-treatment, which spanned 0.26-1.14. To ensure that we appropriately powered our study, we selected an effect size of 0.52 which is double the lower end reported. This is a conservate estimate, and it is better than a One Sample's test which is used when no data exist (and is more hypothetical in nature). The sample size calculation for this application was computed using a two tailed mean difference between independent samples with an alpha = 0.05 and effect of 0.52 as noted above. Data indicates that the investigators would require n=98 subjects per group, which was rounded up to n=100 per group for study logistics; this provides 70% power to find a statistical difference in the metrics captured. However, given that some patients will be lost to follow up (e.g., 10% of enrollees), we plan to include N=220 patients (n=110 for Group #1 and n=110 for Group #2).

We plan to recruit up to N=220 subjects knowing we need 200 to remain for our sample size calculation. A 10% drop out rate is standard in research trials.

12.0 Participant Information

12.1 Subject Population:

ADSMs aged 18-64, four to 12 weeks after initial LBP diagnosis will be recruited

12.2 Age Range:

Check all the boxes that apply. if the age range of potential subjects (specimens, records) does not match the range(s) selected, please specify in the text box.

- [ ] 0-17
- [x] 18-24
- [x] 25-34
- [x] 35-44
- [x] 45-54
- [x] 55-64
- [ ] 65-74
- [ ] 75+

12.3 Gender:

- [x] Male
- [x] Female
- [ ] Other

12.4 Special categories, check all that apply

- [ ] Minors /Children
- [ ] Students
- [ ] Employees - Civilian
- [ ] Employees - Contractor
- [ ] Resident/trainee
- [ ] Cadets /Midshipmen
- [x] Active Duty Military Personnel
- [ ] Wounded Warriors
- [ ] Economically Disadvantaged Persons
- [ ] Educationally Disadvantaged Persons
- [ ] Physically Challenged (Physical challenges include visual and/or auditory impairment)
- [ ] Persons with Impaired Decisional Capacity
- [ ] Prisoners
- [ ] Pregnant Women, Fetuses, and Neonates
- [ ] Non-English Speakers
- [ ] International Research involving Foreign Nationals - Headquarters Review is necessary

You must also consider the requirements of DoDI 3216.02, Enclosure 3, paragraph 7.e.

12.5 Inclusion Criteria:

Order Number	Criteria
1	Active-duty service member
2	18-64 (inclusive) years of age
3	Medical evidence of subacute low back pain (as indicated by complications lasting 1-3 months)
4	Willingness to comply with treatment and follow-up schedule
5	Ability and willingness to provide written informed consent

12.6 Exclusion Criteria:

Order Number	Criteria

1	Current dx of any of the following:
	• Presence of significant comorbid pain (e.g., polytrauma)
	• Cancer - active/ongoing treatment for
	• Active Infections, including skin lesions and rashes
	• Flu or other severe cold virus or COVID
	• Severe depression or anxiety
	• Symptomatic Inflammatory/Autoimmune diseases such as Rheumatoid Arthritis and Ankylosing Spondylitis. Acute exacerbation and not in remission
	• High Grade Spondylolisthesis (Grade III and Grade IV)
	• Fibromyalgia
	• Severe Osteoporosis (BMD with T-score of -2.5 or lower, along with the presence of one or more fragility fractures)
	• Neurogenic conditions
	  • Spinal Stenosis with active neurogenic claudication
	  • Cauda Equina Syndrome - acute
	  • Radiating pain below the knee or in the presence of true Neurological signs (numbness/weakness)

2	Historical dx of any of the following: • Spinal Cord injuries with persisting neurogenic sensory or motor loss • Lumbar spine back surgery within the past year
3	Received spinal interventions (e.g., surgery, nerve ablations, steroid injections, etc.) within the past 6 months
4	Current use of blood thinners/anticoagulants
5	Is enrolled or plans to enroll in another clinical trial during this study that would affect the patient's safety or results of this trial
6	[Females only] Currently pregnant (self-reported) or plans to become pregnant during the study intervention period

13.0

Recruitment and Consent

13.1 Please describe the recruitment process, including how subjects will be identified and selected for the study.

In a 12-month period, MAMC providers last year treated 2760 unique cases of low back pain (LBP), which averages to 230 a month. We recognize that not all patients with LBP will qualify for our study based on our exclusion criteria, they may elect to not participate due to person reasons, they may require immediate surgical intervention, etc. However, given that we only need 7% to consent for treatment, we remain confident that we can recruit enough subjects within the appropriate timeline.

Potential participants will be identified by the following methods:

1. Under the provisions of an approved HIPAA Waiver Application for this study, local study team members will review medical records of patients coming in to the Emergency Medicine, Family Medicine, Neurology, Orthopedic, Pain Management, Physical Medicine & Rehabilitation, Physical Therapy, and Rheumatology clinics for suspected/confirmed LBP in order to identify prospective research participants to approach and offer them the opportunity to participate in this research study.
2. Direct referrals from local healthcare providers in the abovementioned clinics.
3. Patients may self-refer to participate in the study. Interested potential participants will be able to contact a member of the study team via phone or email.
4. Study advertisements will be provided to clinic staff and will be posted within the following locations:
    - Internal Medicine
    - Aviation Medicine
    - H2F
    - McChord Clinic
    - Winder Clinic
    - Okubo Soldier-Centered Medical Home
    - Allen Soldier-Centered Medical Home
    - Soldier Recovery Unit
    - Puyallup Community Medical Home
    - South Sound Community Medical Home
    - Armed Forces Wellness Center
    - Intrepid Spirit Center
    - Madigan Medical Mall
    - Pharmacy waiting areas, if possible
    - Physical Therapy
    - Podiatry
    - Sports Medicine
    - Tactical Human Optimization, Rapid Rehabilitation and Reconditioning (THOR3)
    - Physical Medicine and Rehabilitation
    - Coffee bar
    - Dining Facility entrance
    - Intranet screensaver page
    - 2/75 Ranger Clinic

The local research team will keep a separate electronic screening log containing DoD ID number, eligibility status, and date screened. This log will be password protected and stored in a secure folder on a secure drive accessible only by authorized local research staff. This log is needed to avoid any duplicative screening of those that are screen failures. This reduces burden on potential participants, providers, and study team and ensures the study team will not screen the same person twice or examine records for eligibility criteria when screen status is already established.

Recruitment conversations will take place in a private setting (e.g., closed clinic room, investigator's office, etc.) to minimize the potential opportunity to be overheard or inadvertently witnessed.

13.2 Compensation for Participation:

N/A

13.3 Please describe the pre-screening process. If no pre-screening, enter Not Applicable in the text editor

If a potential participant expresses interest in learning more about the research study, a member of the research staff will briefly introduce the study, express the voluntary nature of participation, assess interest in participating, and screen the potential participant for initial eligibility.

Individuals that do not meet inclusion/exclusion criteria will be encouraged to continue to seek care with their primary care provider.

If the potential participant meets eligibility criteria as determined by the Inclusion/Exclusion CRF and expresses interest in participating in the study, an authorized study team member will initiate the formal consent discussion and, if applicable, obtain informed consent. See protocol section 13.4 for additional information on the consent process.

13.4 Consent Process: Revised Common Rule, Section 219.116: General requirements for informed consent, whether written or oral, are set forth in this paragraph and apply to consent obtained in accordance with the requirements set forth in paragraphs (b) through (d) of this section. Broad consent may be obtained in lieu of informed consent obtained in accordance with paragraphs (b) and (c) of this section only with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens.

Are you requesting a waiver or alteration of informed consent?

○ Yes ◉ No

Please explain the consent process:

Consent will be obtained in accordance with principles of Belmont Report and Common Rule guidelines.

The potential participant will be given a copy of the ICF to read before the informed consent discussion with an authorized study team member. Sufficient time will be given to the potential participant to understand the study purpose, study procedures, time commitments, potential risks and benefits, and the types of information that will be collected and used by the research team if they agree to participate in the study.

Questions can be raised by the potential participant at any time. The potential participant will be reminded that their participation is completely voluntary and that they may withdraw from the study at any time without penalty. Their decision to participate, or not, will not affect their access to health care that they are otherwise entitled to and it will not affect their military position.

Formal consent, as represented by the act of signing and dating the IRB-approved ICF for the study, will occur after: confirming eligibility using the Inclusion/Exclusion CRF, thoroughly reviewing what is involved in the study, and answering all questions the participant may have. Informed consent will be obtained in person. A copy of the signed consent form will be given to the participant and the original will be securely stored. No Legally Authorized Representatives will be utilized.

Every effort will be made to eliminate the perception of authority. When applicable, the study investigators will be in civilian clothes instead of uniform and will not utilize or display their military rank when introducing themselves. Some potential participants may be patients of the study PI or AI. In these cases, the consent conversation will be initiated by non-provider study staff to prevent any misconception of coercion or undue influence.

In the event that there are significant new findings that may affect participants' willingness to continue in the study, an information sheet will be provided to all current and past participants, and the ICF will be amended for future participants.

13.5 DoDI 3216.02 requires an ombudsman to be present during recruitment briefings when research involves greater than minimal risk and recruitment of Service members occurs in a group setting. If applicable, you may nominate an individual to serve as the ombudsman.

◉ N/A

Propose ombudsman

13.6 Withdrawal from Study Participation:

Explain the process for withdrawal and specify whether or not the subjects will be given the opportunity to withdraw their data their data/specimens in the event they wish to withdraw from the study

Participant Withdrawal:
Participants may contact a member of the study team in writing to formally withdraw from the study. Participants may withdraw from the study at any time without penalty. Participants will be informed that withdrawal will not affect their access to health care that they are otherwise entitled to and it will not affect their military position.

If a participant withdraws from the study, we may retain and analyze all coded/de-identified data collected up to the time of withdrawal if the data is necessary to maintain the integrity of the study. However, no further data will be collected after the date of withdrawal.

Withdrawal Without Participant Consent:
A participant may be withdrawn from the study without their consent if remaining in the study might be dangerous or harmful to them, the military mission requires it, they lose their right to receive medical care at a military hospital, the study is canceled, they fail to adhere to the protocol and/or therapy plan, or if they display inappropriate behavior towards study personnel.

14.0 Risks and Benefits

14.1 Risks of Harm:

Identify all research-related risks of harm to which the subject will be exposed for each research procedure or intervention as a result of participation in this study. Consider the risks of breach of confidentiality, psychological, legal, social, and economic risks as well as physical risks. Do not describe risks from standard care procedures; only describe risks from procedures done for research purposes

As with all data studies, there is minimal risk of loss of privacy and confidentiality. Further, while MT is considered safe, and well-regarded, there is a chance for discomfort/muscle and joint injury. This may include, but is not limited to: soreness & muscle stiffness, bruising/ecchymosis, fatigue, hypertension/hypotension or blood pressure fluctuations, temporary headaches or dizziness, nerve irritation or pain, inflammation or worsening of pre-existing injuries.

14.2 Measures to Minimize Risks of Harm (Precautions, safeguards):

For each research procedure or intervention, describe all measures to minimize and/or eliminate risk of harms to subjects and study personnel

All available measures to minimize risks from MT will be taken in accordance with standard protocols, including utilization of properly licensed, trained, and certified therapists. Lack of contraindications will be confirmed by provider and proper weight-graded equipment and hypoallergenic lotion will be used.

All available measures will be taken by research staff to protect participant confidentiality. See Protocol Section 14.3 for additional information on confidentiality protections.

All participants will be evaluated for AEs at each follow-up visit. All AEs, regardless of severity,

will be reported to the PI and the IRB according to the guidelines stated in Protocol Section 16.0.

14.3 Confidentiality Protections (for research records, data and/or specimens):

Describe in detail the plan to maintain confidentiality of the research data, specimens, and records throughout the study and at its conclusion (e.g., destruction, long term storage, or banking). Explain the plan for securing the data (e.g., use of passwords, encryption, secure servers, firewalls, and other appropriate methods). If data will be shared electronically with other team members/collaborators outside the institution, describe the method of transmission and safeguards to maintain confidentiality. Explain whether this study may collect information that State or Federal law requires to be reported to other officials or ethically requires action, e. g., child or spouse abuse

Upon consenting for the study, participants will be assigned a unique study ID. With the exception of the ICF, Intake Form, and electronic Master List all research data (both paper and electronic) will be identified using this unique study ID only.

Paper research forms and source documents will be stored in a locked cabinet inside of a locked room, accessible only by local research staff designated and authorized by the PI. The paper Intake CRF and ICFs will be stored separately from the coded paper research forms. The electronic Master List will be stored separately from the coded electronic research data in a secure, password-protected electronic document on a computer and network that requires CAC access.

The coded electronic research data for this study will be stored in approved systems to protect confidentiality. All research data and forms (both paper and electronic) will only be accessible by authorized study staff, the IRB of record, the local research office, and applicable governmental agencies as part of their duties and in accordance with federal law. These duties include making sure that research participants are protected.

Any research data shared with an approved agency for review will be linked only to the participant's unique study ID. If the research data is used in scholarly presentations or journal articles, the investigators will protect the anonymity of individual participants and report only aggregate data (e.g., group means) where appropriate. Participants will not be individually identified in any publication or presentation of research results.

14.4 Potential Benefits:

Describe any real and potential benefits of the research to the subject and any potential benefits to a specific community or society

If the individuals in the research are considered experimental subjects (per 10 USC 980), and they cannot provide their own consent, the protocol must describe the intent to directly benefit all subjects

We cannot guarantee that participants will benefit from participation in this research study. The aim of this study is to shorten the duration of MRDD periods, reduce pain, and decrease unnecessary utilization of prescription medications. All participants will still receive treatment modalities at the discretion of their medical provider to address their LBP.

14.5 Privacy for Subjects:

Describe the measures to protect subject's privacy during recruitment, the consent process, and all research activities, etc.

Consent conversations and research activities will take place in a private room, such as a clinic room or a closed office, so as to not be overheard or inadvertently witnessed. No uniformed service members or supervisors will be present during consent discussions. Furthermore, data will be stored in approved systems that are encrypted and protected confidentiality.

14.6 Incidental or Unexpected Findings:

Describe the plan to address incidental findings and unexpected findings about individuals from screening to the end of the subject's participation in the research. In cases where the subject could possibly benefit medically or otherwise from the information, state whether or not the results of screening, research participation, research tests, etc., will be shared with subjects or their primary care provider. State whether the researcher is obligated or mandated to report results to appropriate military or civilian authorities and explain the potential impact on the subject

Incidental findings are not expected to result from this study.

15.0 Study Monitoring

15.1 Your study requires either Data and Safety Monitoring Plan (DSMP) or a Data and Safety Monitoring Board (DSMB).

- (●) DSMP
- ( ) DSMB
- ( ) Both
- ( ) Not Applicable

A DSMP should describe the plan to monitor the data to verify that the data are collected and analyzed as specified in the protocol. Include who will conduct the monitoring, what will be monitored, and the frequency of monitoring. It should also include the plan to ensure the safety of subjects

Participant Safety Monitoring Plan:
To ensure the safety of participants the PI will:

1. Monitor the conduct of the protocol per the approved study plan and ensure protection of human participants. This may involve periodic review of research files of enrolled participants.
2. Review and keep abreast of AEs and protocol deviations (PDs) that occur during the research.
3. Review and sign AE/PD logs and continuing review (CR) progress reports.
4. If there is concern about the welfare of enrolled participants, the PI will stop the research study in progress, remove individual participants from a study, and take whatever steps necessary to protect the safety and well-being of research participants until the IRB can assess the situation.
5. Ensure that all study team members keep current required human subjects research training which require renewal every 3 years.

If an AE or PD occurs, it will be evaluated by the PI and appropriate actions will be taken as outlined in Protocol Section 16.0. In the case of an emergency, first responders will be called. In order to address the challenge of early identification of an increased risk of a known AE, all AE data will be tracked and evaluated.

Participants can elect to withdraw from the study at any time. Participants may also be taken out of the study at any point if it is determined to no longer be safe for them to continue with the study. If a participant elects to drop out of the study or is withdrawn for safety reasons, they will be encouraged to seek care with their healthcare provider.

Data Monitoring Plan:

Data will be collected and stored in both paper CRF and electronic format as described previously in Protocol Section 10.14 Data Management. In addition to data quality and data validation checks done continually by REDCap for electronic format data, authorized MIRROR staff will perform routine checks of the coded electronic data entered into REDCap to ensure that data has been properly input and that data entry is consistent with expected values. The local PI will ensure that paper research forms and the electronic Master List are completed and securely stored in accordance with stated protocol procedures.

Please see Protocol Section. 14.3 Confidentiality Protections and 14.5 Privacy for Subjects for additional information regarding how we will protect participant privacy and confidentiality throughout this study.

16.0 Reportable Events

16.1 Reportable Events: Consult with the research office at your institution to ensure requirements are met. Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event.

Consult with the research office at your institution to ensure requirements are met

• Describe plans for reporting expected adverse events. Identify what the expected adverse events will be for this study, describe the likelihood (frequency, severity, reversibility, short-term management and any long-term implications of each expected event)

• Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the research protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event

AEs & Unanticipated Problems:
All AEs will be recorded by the study team using an AE Log. The PI will promptly review and assess events to determine severity and relatedness to research activities.

All Serious Adverse Events (SAEs) that are at least possibly related to study participation and all Unanticipated Problems Involving Risks to Subjects or Others (UPIRTSOs) will be reported to the IRB via telephone or email within 24 hours of discovery, and a complete written report will be submitted via EIRB within 5 business days.

All expected AEs and all SAEs that are not possibly related to study participation will be reported to the IRB at the time of CR or study closure (as applicable).

Protocol Deviations:
All PDs will be recorded by the study team using a PD log. The PI will promptly review and assess events to determine severity.

All major PDs will be promptly reported to the IRB via telephone or email within 24 hours of discovery, and a complete written report will be submitted via EIRB within 5 working days.

All minor/administrative PDs will be reported to the IRB at the time of CR or study closure (as applicable).

17.0 Equipment/non-FDA Regulated Devices

17.1 Does the study involve the use of any unique non-medical devices/equipment?

○ Yes ◉ No

18.0 FDA-Regulated Products

18.1 Will any drugs, dietary supplements, biologics, or devices be utilized in this study?

- [ ] Drugs
- [ ] Dietary Supplements
- [ ] Biologics
- [ ] Devices
- [x] N/A

18.5 Sponsor (organization/institution/company):

- [x] N/A

If applicable, provide sponsor contact information:

19.0 Research Registration Requirements

19.1 ClinicalTrials.gov Registration:

- ( ) Registration is not required
- (•) Registration pending
- ( ) Registration complete

19.2 Defense Technical Information Center Registration (Optional):

- (•) Registration is not required
- ( ) Registration pending
- ( ) Registration complete

20.0 References and Glossary

20.1 References:

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20.2 Abbreviations and Acronyms:

- ADSM = Active Duty Service Member
- AE = Adverse Event
- BMI = Body Mass Index
- CAC = Common Access Card
- CR = Continuing Review
- CRF = Case Report Forms
- DHA = Defense Health Agency
- DVPRS = Defense and Veterans Pain Rating Scale
- ED = Emergency Department
- EIRB = Electronic institutional review board
- GPS = Global Pain Scale
- H2F = Holistic Health and Fitness
- HIPAA = Health Insurance Portability and Accountability Act
- HSRM = HealthShare Referral Manager
- ID = Identification
- IRB = Institutional Review Board
- JBLM = Joint Base Lewis-McChord
- JPC = Joint Program Committee
- LBP = Low Back Pain
- MAMC = Madigan Army Medical Center
- MHS = Military Health System
- MIRROR = Musculoskeletal Injury Rehabilitation Research for Operational Readiness
- MMT = Medical Massage Therapy
- MRDD = Medical Restricted Duty Days
- M-ODI = Modified Low Back Pain Disability Index
- MSKI = Musculoskeletal Injury
- MT = Massage Therapy
- NPI = National Provider Identification
- NSAID = Non-Steroidal Anti-Inflammatory
- OHRP = Office of Human Research Protections
- PD = Protocol Deviation
- PI = Principal Investigator
- PHI = Protected Health Information
- PII = Personal Identifiable Information
- PM&R = Physical Medicine and Rehabilitation
- PSQI = Pittsburgh Sleep Quality Index
- RCT = Randomized Control Trial
- REDCap = Research Electronic Data Capture
- RTD = Return to Duty
- SAES = Serious Adverse Events
- SM = Service Member
- THOR3 = Tactical Human Optimization, Rapid Rehabilitation and Reconditioning
- UPIRTSO = Unanticipated Problems Involving Risks to Subjects or Others
- USU = Uniformed Services University
- USAMRDC = U.S. Army Medical Research and Development Command
- USHUS = Uniformed Services University of the Health Sciences
- VA = Veterans Affairs
- WPAI-LBP = Work Productivity and Activity Impairment Questionnaire - Low Back Pain