1.0 Title: Home-based approaches for subacute low back pain in Active Duty: Randomized control trial

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e. Medical Monitor: Risk status to be determined by IRB for this study.

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4.0 Research Plan

Abstract

Low back pain is on the increase in the military, and poses a threat to warfighter performance and operational readiness. The number of ambulatory care visits of low back pain (LBP) has shown a striking increase of >62% over the last 5 years in all military services, affecting work performance, limiting activity, and impacting military deployment health. This increase reflects current high operation tempo and frequent deployments of military including demanding training, military operations, and combat injuries. Approximately 80% of acute LBP events will improve within 2-4 weeks, however, a substantial number progress to the persistent, chronic state (LBP >12 weeks) which is resistant to treatment and interferes with military performance. Currently, no evidence-based treatment guidelines exist for the management of subacute LBP (3-12 weeks). Treatments for LBP during the subacute period need further investigation. We have shown that home-based neuromuscular electrical stimulation (NMES) is safe, portable, easy-to-use and improves muscle strength with some pain relief. Evidence suggests that progressive exercise improves patient outcomes in subacute LBP. The use of pain-relieving modalities via primary care management (PCM) combined with muscle strengthening, such as home-based electrotherapy or progressive exercise plan (PEP), could reduce pain, increase strength and improve function more rapidly during the subacute phase of persistent LBP. The proposed study therefore will compare the effects of both NMES and PEP to the standard PCM for service members with subacute LBP. The overall objective of this project is to compare three home-managed treatment regimens for subacute low back pain: Progressive Exercise Plan (PEP), NMES core strength training and standard primary care management (PCM). Our central hypothesis is that the NMES core strength training alone and PEP alone will show significantly greater improvements in muscle strength, pain, mobility/function, daily activity and quality of life (QOL) than PCM alone in military members with low back pain lasting three to twelve weeks. The rationale for this study is that increasing torso muscle strength and decreasing pain
through strength training exercises will significantly improve mobility, physical activity, QOL and reduce disability. Such outcomes will ultimately result in improved deployability, retention of military personnel and decreased economic costs in this population. The specific aims will be to determine whether the two treatment régimes are significantly more efficacious than standard PCM alone in improving lower back muscle strength, daily physical activity, physical function quality of life and symptoms associated with subacute LBP. After consent and baseline testing, we will randomly assign active duty male and female subjects, ages 18 to <45, (n=135) with LBP to one of the three groups. Each of the two treatment arms will be supplemented by PCM and compared to a group receiving standard PCM alone. All groups will receive 9 weeks of home therapy. Using longitudinal mixed regression models, we will examine differences in time trends for the outcome variables among controls and those in the treatment groups. In these regression analyses, the important primary measures will be expressed as a function of time, treatment group, and group-by-time interactions, while controlling for important covariates. Positive results could translate into accelerated rehabilitation, decreased symptoms and lower medical costs with better patient outcomes.

4.1 Objective: The overall objective of this project is to compare three home-managed treatment regimens for subacute low back pain: Progressive Exercise Plan (PEP), NMES core strength training and standard primary care management (PCM). Each of the two treatment arms will be supplemented by PCM.

4.2 Research Questions/Hypotheses to be Tested

The specific aims for this study are:

4.2.1 To determine whether the two treatment régimes are significantly more efficacious than standard PCM alone in improving lower back muscle strength, daily physical activity and physical function. Muscle strength will be measured by isometric flexor and extensor peak torque of the torso; physical activity by steps walked and energy (kcal) expenditure/day; physical function is the number of push-ups in 2-minutes; number of sit-ups in 2-minutes; distance walked in 6-minutes; and time to perform the lumbar trunk muscle test.

4.2.2 To determine whether the two treatments improve QOL and symptoms/disability associated with subacute LBP significantly more than PCM. QOL will be measured by the Medical Outcome Questionnaire and the Centers for Epidemiologic Studies-Depression scale. Symptoms of LBP will be quantified by the Clinical Back Pain Questionnaire, Oswestry Disability Index and Visual Analog scale.

4.3 Significance:
   The number of Active Duty military ambulatory care visits for low back pain (LBP) has increased over the last 5 years in all military services. According to the Defense Medical Surveillance System (DMSS), from 2010 to 2014, the number of low back injury
among active duty service members increased at a striking rate (Table 1). Total of all services showed a >62% increase over this 5-year time span.

The increased number of LBP reflects the physical demands of military service. The upward trend is clearly associated with increases in the number and duration of military deployments by U.S. service members over the past decade. It has been documented that LBP is a significant cause of morbidity during deployment.\(^2\) OIF/OEF medical evacuations consist largely of musculoskeletal injuries (24%) that are non-battle-related, with a low rate of return to duty.\(^3\) With an increase in the number of deployments, there is an increase in prevalence for back problems.\(^6\)

Military members in combat and training settings are required to carry heavy loads of equipment, supplies and protective gear.\(^7\) Troop load carriage is an important aspect of military operations and frequently results in injuries (such as LBP) associated with rucksacks and body armor, loaded road march training, airborne/air assault training, and engaging in combat in austere and suboptimal conditions. Heavier loads cause changes in trunk angle to a more forward inclination that can stress back muscles. Low back injury, pain and limited mobility pose a threat to deployment health and operational readiness.

During a June 2006 DoD conference, Col Francis O’Connor\(^8\) (Command Surgeon, SOCCENT/CFSOCC) detailed the current situation in the theatre of operations among Special Operations Forces (SOF); he noted that MSI pain/injuries are ubiquitous among SOF operators and stated that SOF warriors are currently using NMES in ‘theatre’ to relieve pain and maintain muscle strength/endurance and continue their mission. This use of NMES by SOF warfighters, physically demanding occupational tasks and a high frequency of musculoskeletal pain/injuries point to the need to confront these injuries, which are a major concern with respect to military deployment, force retention, and operational capability.

### Table 1: Numbers of Active Duty Military Ambulatory Visits for LBP*, U.S. Armed Forces, 2010-2014 \(^1\)

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Army</td>
<td>336,003</td>
<td>426,809</td>
<td>490,241</td>
<td>505,900</td>
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<tr>
<td>Navy</td>
<td>74,185</td>
<td>93,773</td>
<td>116,788</td>
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<td>129,581</td>
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<tr>
<td>Air Force</td>
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<td>187,610</td>
<td>216,376</td>
<td>237,671</td>
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<tr>
<td>Marines</td>
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<td>72,192</td>
<td>95,041</td>
<td>102,610</td>
<td>101,784</td>
</tr>
<tr>
<td>Total</td>
<td>612,391</td>
<td>780,384</td>
<td>916,489</td>
<td>974,121</td>
<td>982,260</td>
</tr>
</tbody>
</table>

*LBP based on ICD-9 code 724.2 Lumbago & 724.5 backache.

Summary

Low back pain is on the increase in the military, and poses a threat to warfighter performance and operational readiness. A portable treatment that improves back function, muscle strength, pain, disability and QOL is timely. We plan to evaluate the extent to which Primary Care Management supplemented with NMES or PEP improve health and ability to perform typical work and home activities. Evidence suggests that PCM alone may yield positive benefits in acute LBP, and the addition of PEP or NMES may be more than additive for subacute LBP. The potential benefits to military persons with LBP are substantial, given rising numbers, disability and economic issues of low back pain.

4.4 Military Relevance:

Physical training errors, overtraining, trauma, and changes in training programs are some of the main reasons for low back pain (LBP) onset in military populations. Military members in combat and training settings are required to carry heavy loads of equipment, supplies and protective gear on their person. Troop load carriage is an important aspect of military operations and frequently results in load-carriage-related injuries associated with rucksacks and body armor, loaded road march training, airborne/air assault training, and engaging in combat in austere and suboptimal conditions. Heavier loads cause changes in trunk angle to a more forward inclination that can stress back muscles. Low back injury, pain and limited mobility pose a threat to military deployment health and operational readiness of our warfighters. Rehabilitation is emerging as having a pivotal role in preserving unit readiness, requiring a multidisciplinary team to provide comprehensive care to sustain our fighting force.

When LBP progresses from acute to chronic, it becomes resistant to treatment leading to progressive loss of torso strength, endurance and flexibility, as pain intensifies during routine activities. The resulting muscle weakness and pain affects work performance, limiting mobility and impacting deployment health. Ultimately this condition leads to disability and early discharge of otherwise healthy service members. To mitigate this progression, the subacute phase (3-12 weeks) is seen as an ideal window of opportunity for interventions to stop this progression and prevent reinjury. Thus, the use of NMES devices by Special Ops Forces (SOF), coupled with physically demanding occupational
tasks and a high frequency of back pain with typical military training activities, point to the need to confront subacute LBP, which is a major concern with respect to military deployment, force retention, and operational capability. To address this research gap, we propose to study a home-based, portable program of NMES alone, Progressive Exercise Plan (PEP) alone and compare to primary care management (usual care) in service members with LBP lasting 3 to 12 weeks.

The significance of this research to military-relevant science is that NMES or PEP combined with primary care management could produce marked improvements in torso strength, enhance functional performance, readiness and fitness, decrease physical symptoms and possibly prevent future occurrence. These interventions, NMES and PEP, are safe and easy to use in austere conditions such as in the theatre of operations. We propose that NMES and PEP are novel and military-relevant and will narrow the research gap in self-managed approaches that will translate into treatment options in the theatre of operation. The use of NMES and PEP, non-pharmacological therapies, has been under-studied. The results of this project could improve self-management options for this military population. Such outcomes will ultimately result in accelerated rehabilitation, return to world-wide duty status, decreased symptoms and lower medical costs with better patient outcomes. This study will contribute to force health protection and military deployment with positive implications for the military health care system.

4.5 Background/Review of Literature

The number of ambulatory care visits for low back pain (LBP) has shown a striking increase of >62% over the last 5 years in all military services, affecting work performance, limiting activity, and impacting military deployment. The overall incidence rate of LBP in active duty military is 40.5/1000 person-years, with women having a higher rate (58.3/1000 person-yrs.) than men (37.6/1000 person-yrs)\(^9\). These high rates reflect current high optempo and frequent deployments of our military including demanding training, military operations, and combat injuries.

For many, episodes of back pain are self-limited; however, if the pain persists beyond the acute period (<4 weeks), interventions at the subacute phase of healing (4-12 weeks) could play a critical role in prevention of recidivism and chronicity (≥12 weeks). With progression from acute to chronic, LBP becomes resistant to treatment, leading to inactivity with progressive loss of muscle strength, endurance and flexibility, as pain is intensified during routine activities. The resulting muscle weakness and pain affects work performance, limiting mobility and impacting deployment health. Ultimately this condition leads to disability and early discharge of otherwise healthy service members. To mitigate this progression, the subacute phase is seen as an ideal window for interventions.\(^10\)

Although there are conservative therapies for acute and chronic LBP, there are no evidence-based guidelines/treatments for the management of LBP in the subacute phase. Those in the subacute phase are often treated with primary care management (PCM). However, no treatments have been shown to reduce back pain, improve back function, and prevent re-injury in subacute LBP or prevent progression to the chronic state.\(^11\)
Approaches to Improve Core Muscle Strength and Clinical Symptoms in LBP

Traditional Primary Care Management (PCM): Non-specific LBP, where the cause for the pain cannot be determined\textsuperscript{12}, accounts for ninety percent of LBP cases.\textsuperscript{13} Reducing pain and continuing daily activity to prevent deconditioning are the primary therapy goals of PCM. Traditional PCM treatment of LBP includes advice/information on self-care options, over-the-counter analgesics, heat application, and remaining active.\textsuperscript{11,14} Most individuals with LBP will improve within 2 weeks of onset. If LBP persists into the subacute phase (>4 weeks), recommendations are to continue with the first-line treatment and consider interdisciplinary rehabilitation.\textsuperscript{15,16} Yet despite evidence that physical activity is effective, limiting activity remains common; individuals cite pain or re-injury fear as a limiting factor.\textsuperscript{17-19}

Neuromuscular Electrical Stimulation (NMES) Strength Training Programs:
Acute and chronic LBP results in muscle atrophy to the core torso muscles.\textsuperscript{20,21,22} Rehabilitation approaches for LBP often include strength training to address these muscle changes; however current evidence from multiple studies support a low to moderate benefit from exercise therapy.\textsuperscript{23,24,25} One alternative or adjunct to traditional strength training programs for LBP is neuromuscular electrical stimulation (NMES). LBP has been associated with altered muscle recruitment in the lumbopelvic region.\textsuperscript{26} Rehabilitation requires activation of deep stabilizing muscle groups yet traditional exercises specific for deep lumbar stabilizing muscles are difficult to teach with poor compliance. NMES has been shown to be effective for specifically stimulating these muscle groups,\textsuperscript{27,28,29} resulting in enhanced activation, improved muscle performance and reduced LBP.\textsuperscript{26}

Portable, lightweight NMES devices are programmed to exercise core muscles through a series of stimulated muscle contractions. In patient populations, muscle stimulation of the abdominal wall and lumbar paraspinal area has shown to be the most effective to maximally activate deep lumbar stabilizers if performed concurrently in LBP patients.\textsuperscript{30} Whereas in lumbar degenerative kyphosis (LDK) back pain associated with muscle atrophy, NMES significantly activates the deep lumbar stabilizing muscles of LDK patients as verified by real-time ultrasound imaging,\textsuperscript{31} and in stimulating deep abdominal wall and lumbar paraspinal muscles. These muscle groups can be difficult to activate and strengthen with usual exercises. The greatest increases in muscle strength with NMES occurred in weak and atrophied muscles, non-dominant extremities, and in women.\textsuperscript{32} In athletes, NMES of the abdominal region resulted in significant improvements in the muscular strength and endurance of the abdominal region with a 3.5 cm reduction in waist circumference.\textsuperscript{33} NMES may also be important for pain management, and has been shown to give as much pain relief as TENS in subjects with low back pain.\textsuperscript{34} Given its multiple applications, NMES may play an important role in assisting military members with subacute LBP, increasing strength and back function and decreasing pain. We recently demonstrated that battery-powered NMES units provided a convenient, nonpharmacological home-based treatment.\textsuperscript{35} We found that in adults with OA of the knee, a low-to-moderate intensity NMES training program resulted in increased quadriceps muscle strength, a faster walking pace, and faster chair rise test, without exacerbating symptoms. We propose to use the battery-powered Neurotech
Recovery Back as a home therapy to strengthen the low back and abdominal core muscles and reduce pain associated with subacute LBP. We have found it feasible, safe and easy to use with effortless donning and doffing the garment, with consistent and accurate placement of the electrodes. These features should help to increase patient compliance with our home-use program.

**Progressive Exercise Plan (PEP):** Although PEP has not been studied in military personnel with subacute LBP, the literature suggests that this intervention may be of benefit.\textsuperscript{11,36} A meta-analysis showed evidence that graded-activity exercise improved patient outcomes in subacute LBP; however, evidence for other exercise programs were inconsistent.\textsuperscript{37} A general overall strengthening program involving the trunk and abdomen strengthening muscles showed clinically important reductions in low back pain and disability with high adherence.\textsuperscript{38} Still, systematic reviews were unable to support any one type of exercise over another. The use of pain-relieving modalities combined with muscle strengthening, such as home-based electrotherapy or progressive exercise, could reduce pain and improve function more rapidly. The proposed study therefore will compare the effects of both NMES and PEP to the standard PCM for service members with subacute LBP.

**Patient self-managed programs** have been shown to promote adherence,\textsuperscript{39} improve pain,\textsuperscript{40-42} lessen disability,\textsuperscript{42,43} and improve patient outcomes,\textsuperscript{44} and quality of life.\textsuperscript{44} Home-based self-managed programs that combine standardized protocols, telephone communication, and clinic or home visits have been successful with multiple patient populations.\textsuperscript{45,46} To our knowledge, there have been no randomized, controlled trial of home-based treatments promoting multidisciplinary rehabilitation of subacute LBP in active duty military. We propose a multidisciplinary approach using a study coordinator who takes an active part in the intervention, providing frequent reeducation, reinforcement, and encouragement, as well as training in LBP self-management and self-monitoring.

**Preliminary Studies/Progress Report**

We have conducted a number of studies that support the proposed study, including studies using home-based NMES and exercise interventions in military members with musculoskeletal injuries.

**c1. Feasibility and Collaborative History.** This team has a great deal of experience with clinical trials. Drs. Talbot and Metter have successfully conducted TSNRP-sponsored clinical studies over the past several years, including the currently funded TSNRP study testing home-based interventions for patellofemoral syndrome. Drs. Talbot and Metter pioneered the home use of NMES devices. Dr. Morrell is a statistician with over 20 years’ experience with linear and nonlinear models, hierarchical models, and generalized estimating equations. He has been the statistician for 2 TSNRP funded projects with Dr. Talbot. Dr. (MAJ) Garcia, a board-certified nurse practitioner at BACH and prior military clinical nurse, has worked with military populations and their families for over 10 years, using similar self-managed approaches as proposed for the current study. He will serve as the alternate on-site PI. Dr. Smoak a board-certified physician’s assistant and Chief, Soldier Primary Care, has extensive experience in military primary care and will oversee the PCM arm of the study. To round out our research team, we have
assembled doctorally-prepared physical therapists from BACH specializing in physiotherapy in military populations. Dr. (MAJ) Ramirez is OIC, Primary Care Physical Therapy at MEDDAC, BACH and will serve as the on-site PI. Dr. Webb is Director of Physical Therapy at Byrd Health Clinic and a co-investigator on another TSNRP-sponsored study with Dr. Talbot. Dr. (1LT) Bulen is a physical therapist at the Lapointe Health Clinic. In summary, the team has the experience and knowledge to successfully conduct the proposed trial.

c2. Home-based self-managed NMES interventions for osteoarthritis (OA) of the knee in older adults. We have completed two studies examining the feasibility of home-based NMES treatments in elderly subjects with painful knee OA. In the first study, we randomly assigned 34 older adults with symptomatic, radiographically confirmed knee OA to either (1) NMES plus arthritis education (NMES Plus: n=18) or (2) arthritis education only (EDU: n=16)\(^35\). The NMES Plus group used a portable electrical muscle stimulator 3 days a week, 15 minutes each session, for unilateral quadriceps femoris training over 12 weeks. Both groups received 12-week arthritis education and were followed an additional 6 weeks. A 9.1% increase in isometric quadriceps torque was noted for the NMES Plus group, whereas the EDU group saw a 7% loss in strength. The chair rise time decreased by 11% in the NMES group, whereas the EDU group saw a 7% reduction. Both groups improved their walk time by 7%.

In a second study,\(^47\) we examined the effects of NMES on pain at the time of treatment. Twenty OA participants were instructed to use the NMES device as above. We measured pain levels 15 minutes before and after each NMES session using a numerical scale with anchored end points of 1(no pain) and 10 (worst pain). NMES led to a significant decline in pain 15 minutes after the NMES session. The mean pain score declined 22% occurring in 74% of the sessions. This is analogous to the pain relief reported with the use of transcutaneous electrical nerve stimulation (TENS).


This TSNRP-funded randomized study compared the effectiveness of the Army National Guard-Fitness for Life Program to increase moderate-to-high intensity physical activity and improve cardiorespiratory fitness in Army National Guard personnel who failed the Army Physical Fitness Test (APFT) 2-mile run to the traditional Army Physical Fitness Program (APFP). The intervention included 12-weeks of intensive conditioning and 12-weeks maintenance. The Fitness for Life Program was a motivational approach using a pedometer along with telephone calls, mailings and monthly meetings to set goals and track adherence. The control group followed the traditional APFP.

One hundred and fifty-six National Guard soldiers were randomly assigned to the two treatment groups. Physical activity improved modestly in the two groups with an increase during the interventions and decline during the maintenance phase. The study demonstrated that a pedometer-based exercise intervention had results similar to a high-intensity program for passing the APFT.

Medicine.\textsuperscript{48,49} was a TSNRP-funded Nurse Managed NMES protocol which was compared to the standard rehabilitation program for transtibial amputees (TTA) with injuries related to OPERATION IRAQI FREEDOM and ENDURING FREEDOM (OIF/OEF). Forty-eight subjects enrolled and were randomly assigned to the two treatment groups. Those in the NMES group received 12 weeks of electrical muscle stimulation 15-20 min/day, 5 days a week for 12 weeks. Both groups received the standard 12-week standard amputee rehabilitation protocol.

The home-based self-managed NMES protocol was well received by the subjects. Outcomes for the two treatment groups were equivalent, but the sample size recruited was not as large as planned and may have been underpowered to demonstrate a true difference in the two groups. Both treatment groups improved muscle strength in their amputated legs to levels similar to their intact legs. However, the NMES group showed better improvement prior to receiving their prosthesis. Similar improvement was seen in functional mobility. Associated with these changes, improvement in self-perception of physical status that was not associated with an improvement in mental health was seen.

\textbf{c5. Summary}: These preliminary studies suggest that a home-based self-managed strength training program of NMES and exercise increases strength, decreases pain and is safe, feasible and well tolerated by military service members with musculoskeletal injury. Based on our preliminary data, we plan to apply home-based treatments to subacute LBP, a common problem in active duty military personnel. We expect that NMES or PEP with standard primary care management will yield greater improvements in muscle strength, efficiency of movement, mobility, and quality of life than standard primary care management. If significantly greater benefits are shown with these interventions, this will be of value in the treatment of subacute low back injuries.

\textbf{4.6 Research Method and Design:}

\textbf{4.6.1 General study design:}

This study is a randomized clinical trial with repeated measures over time to compare the effects of NMES and PEP on strength, mobility, symptoms, and QOL in military members with subacute LBP to the effects of a standard primary care management. All groups will participate in the standard primary care management protocol. All groups will have an intensive 9-week program.

Participants will be randomly assigned to: 1) NMES with the standard PCM protocol; 2) PEP with standard PCM protocol; \textit{and} 3) standard PCM protocol alone (control group). To minimize dropout problems, we will not randomize participants until after the pre-treatment assessment and the activity monitoring has been completed, so that they are more invested in the study. Participants will be familiarized with the test procedures prior to baseline testing, and then assessed again at 3, 6 and 9 weeks. The primary outcome measures are lower back strength, physical activity, and mobility; and the secondary measures are symptoms/pain and QOL.
4.6.2 Specific study plan: Intervention

Conceptual Model: Military operations and intense training put service members at risk for low back injuries especially when carrying loads greater than 25% of body weight. For those with LBP, pain limits usual activities. The service member will unconsciously not engage the back muscles to perform activities and exercises, which worsens the condition and leads to deconditioning and muscle atrophy of the lumbar multifidus muscle. Weak abdominals exaggerate anterior pelvic tilt causing strain on the back extensor muscles. The result is loss of torso strength, flexibility, endurance and aerobic fitness with wasting of the trunk extensors.
A high percentage of individuals with LBP have recurrences which may lead to chronic pain.\textsuperscript{53,54} Psychological sequelae associated with pain, deconditioning and disability include anxiety, helplessness and inappropriate coping strategies, which compromise quality of life. We believe that effective treatment interventions can overcome many of these issues. Our design and methods are based on the social learning model of acquisition and maintenance of health behaviors put forward by Bandura in 1986.\textsuperscript{55} This model involves both cognitive and behavioral strategies to help individuals progress from lower to higher motivational readiness and subsequent behavioral adoption.

**Behavioral Component of Self-Management:** The study coordinator working with primary care and PT will structure the cognitive and behavioral strategies used in the NMES and PEP Programs. The team will establish a training plan, collaborate with the healthcare team and assist with NMES and PEP at home. Motivational strategies include gaining knowledge, setting goals, logging and tracking progress, developing social support, preventing relapse, creating rewards, increasing self-confidence and staying informed. Text messaging, emails and telephone follow-up are cues to NMES/PEP training and written logs will act as a personal fitness tracker, providing cues and reinforcement to keep the individual on track, and motivational cues for the therapies. The cognitive behavioral strategies teach the importance of these ideas and how to implement behavioral changes.

**Intervention Components:** The rationale for the number of weeks of intervention and the number and timing of assessments is based on our previous work and the literature. NMES was found to increase strength after 36 sessions of training\textsuperscript{35} or greater than 8 weeks.\textsuperscript{56} We will test participants at baseline, 3-weeks, 6-weeks, and 9-weeks when all outcome measures will be tested. Subjects in the NMES/PEP groups will have adjustments made to their Phase 2 and 3 training. Information on pain status will be obtained at weekly checks, regardless of group assignment. The intervention weekly logs to determine pain and difficulty during home exercise, NMES and PEP will be reviewed and adjusted as necessary. We will have weekly contact with participants during the 9 weeks of the study (baseline – week 9) either by in-person clinic visits, phone checks, text messaging or email.

**Standard Primary Care Management (PMC):** All participants will receive standard primary care management for subacute LBP. Primary Care Management follows the clinical practice guidelines for low back pain.\textsuperscript{11} Service members are to stay as active as possible and progressively increase their activity. Medications prescribed begin with paracetamol and NSAIDs as first-line drugs. Second-line drugs include antidepressants, benzodiazepines, tramadol, and opioids. All participants will receive an information sheet on LBP advising them to remain active and use self-care options such as heat application. To provide an attention control, the PMC only group will receive weekly communication from the study coordinator regarding pain and medication usage.

**Self-Managed Progressive Exercise Program (PEP):** The primary goal of PEP is to reduce back pain, disability, and improve trunk flexibility, strength and endurance through controlled, gradual, progressive back exercises. PEP teaches muscle strengthening exercises and self-management strategies to promote back fitness. The PEP sessions provide the participant with a standardized self-management framework for
performing the exercises at home. PEP is performed every other day/week for about ~1 hour over a period of 9 weeks. PEP consists of 3 sequential phases with each phase lasting 3 weeks. As the participant progresses through each phase, the exercises become progressively more difficult and intense, focusing on back stretching and strengthening that progressively load and unload the lumbar spine by means of flexion/extension exercises. During the baseline visit, participants will be provided a handout and given a demonstration of the Phase 1 exercises to be performed at home for 3 weeks. The participant will perform a return demonstration to be sure of proper form and performance of the exercises. At each return 3-week visit, the same parameters (described above) will be used to teach Phase 2 and 3. The PEP group will perform 31 exercise sessions for 60 minutes on alternating days. Pain status will be assessed at each visit.

**Self-Managed Neuromuscular Electrostimulation (NMES) Program:** The NMES treatment group will receive a portable battery-operated device, Recovery Back™ (Neurotech®, Minnetonka, MN) with a 2-garment site-specific system: back & abdomen. NMES muscle contractions will be elicited by an electrical impulse generated by the Recovery Back™ system. The device delivers a pre-set program of NMES using a symmetrical biphasic square pulse waveform. The garments are light-weight, breathable fabric that wraps around the waist with precise placements for the reusable electrodes. The controller uses a rechargeable battery with charger supplied. The NMES protocol consists of 30-minutes of NMES stimulation alternating between the abdominal and lumbar site over 9-weeks (one day Back training, next day Abdominal training).

**The Recovery Back Abdominal garment:** The garment delivery of abdominal stimulation causes involuntary contractions of the abdominal muscles (obliques, transverse abdominus and rectus abdominus). Parameters for the work cycle of the NMES abdominal garment will be pulse duration of 250 µs; a ramp time of 2:2 seconds; frequency of 55Hz; intermittent cycling and a duty cycle of 3 seconds on/5 seconds off. The Abdominal garment has 3 conductive gel electrodes (one large square pad and 2 smaller oval pads) specifically designed for the abdominal garment (Neurotech®, Minnetonka, MN). The Abdomen garment is placed with the center square electrode over the navel.

**The Recovery Back Lumbar garment:** The Lumbar garment (see Figure 1) stimulates involuntary contractions to the lumbar paraspinal muscles. The Lumbar garment training program consists of 3 sequential phases with each phase lasting 3 weeks. Phase 1 will use a 1:3 duty cycle specific for early stage of muscle rehabilitation training (atrophy rehabilitation). Parameters for the Phase 1 work cycle of the NMES Lumbar garment will be pulse duration of 300 µs; a ramp time of 1:0.5 seconds; frequency of 50Hz; intermittent cycling and a duty cycle of 5 seconds on/15 seconds off. Phase 2 will use a 1:2 duty cycle specific for intermediate stage of muscle rehabilitation (strengthening). Parameters for the Phase 2 work cycle of the NMES Lumbar garment will be pulse duration of 300 µs; a ramp time of 1:0.5 seconds; frequency of 50Hz; intermittent cycling and a duty cycle of 5 seconds on/10 seconds off. Phase 3 will use a 1:1 duty cycle specific for advanced stage of muscle rehabilitation.
rehabilitation (strengthening). Parameters for the Phase 3 work cycle of the NMES Lumbar garment will be pulse duration of 300 μs; a ramp time of 1:0.5 seconds; frequency of 50Hz; intermittent cycling and a duty cycle of 5 seconds on/5 seconds off. The Back garment has 4 oval-shaped electrodes, designed specifically for the lumbar garment (Neurotech®, Minnetonka, MN). Placement of the Back garment will be over the lower back area between the last rib and iliac crest centered and aligned with the spine. The training time for all 3 phases is 30 minutes.

**Training Intensity:** Participant will increase the intensity of the stimulation to the point of muscle contraction then to tolerance. Incremental increases of intensity and Lumbar garment parameter changes (Phase 2 & 3) will be made at the 3- and 6-week clinic visits. Individualized instructions for adjusting the amplitude dial settings, with a return demonstration, will be used to maintain the appropriate usage. The first 5 minutes of each study visit will be used to review training logs, determine if NMES goals were achieved and troubleshoot any problems.

**Balanced NMES and PEP Training:** The goal is to balance the number of treatment sessions for the PEP and NMES groups. PEP will perform 31 hourly sessions alternating days, NMES will perform 62 half-hour sessions daily (31 abdominal NMES and 31 back NMES).
4.6.3 Specific study plan:
Table 3 gives a list of study variables, measurement instruments, measurement points and time commitment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Instrument</th>
<th>Estimate time</th>
<th>Entry</th>
<th>Daily</th>
<th>3</th>
<th>6</th>
<th>9</th>
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<tbody>
<tr>
<td>Inclusion/Exclusion Criteria</td>
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<td>Consent Form</td>
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<tr>
<td>Muscle Strength</td>
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<td>X</td>
<td>X</td>
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<td></td>
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<tr>
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<td>Steps walked</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Energy (kcal) expenditure</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Mobility</td>
<td>Push-ups (2-minutes)</td>
<td>5</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sit-ups (2-minutes)</td>
<td>5</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Lumbar trunk muscle test</td>
<td>5</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6-minute timed walk</td>
<td>10</td>
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<td>X</td>
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<td>X</td>
<td>X</td>
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<td>X</td>
<td>X</td>
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<td></td>
</tr>
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<td></td>
<td>Clinical Back Pain Questionnaire</td>
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<td>X</td>
<td>X</td>
<td></td>
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<td>Quality of Life</td>
<td>CES-D, SF12</td>
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<td>X</td>
<td>X</td>
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<td></td>
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<td>Clinical Factors</td>
<td>Clinical demographic form</td>
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<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Composition</td>
<td>Height, weight (BMI), BP, HR, Abdomen Skinfold, Waist circumference</td>
<td>15</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td></td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PEP Groups log</td>
<td>5</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Weekly Totals (minutes) 105 5 70 70 70
Study Visit Total 320 minutes

4.6.4 Collection of the Human Biological Specimens: N/A

4.6.5 Data collection:
Variables and Their Measurement
Clinical and Demographic Variables: Information will be collected on age, sex, co-morbidities, medication use, use of assistive aids, symptom duration, history of...
injuries/trauma, changes in frequency, duration and intensity of training, previous surgeries, imaging studies and other self-care methods currently being used to improve pain and/or mobility. Height and weight will be measured without shoes using a calibrated balance beam scale and stadiometer and body mass index (BMI) will be calculated. Resting blood pressure (B/P) will be measured in triplicate in a seated position. The lowest of three blood pressure measurements will be recorded. Resting heart rate will be measured using the radial pulse over 1 minute's duration.

The amount of abdominal fatness dampens the amount of electrical current reaching the muscle, potentially affecting the strength of the contraction. We will measure abdominal fatness by way of skinfold and circumference measurements. The subject will be in a standing position with measurements taken on the right side. Skinfold measurements will be taken at the umbilical site and suprailiac site using calipers (Lange Skinfold Calipers, Country Technology, Gay Mills, WI), with both a low spring tension (measured at 5 g at the opening of the caliper) and a normal spring tension (measured at 26 g at the opening of the caliper). For the **umbilical** measurement, a vertical skinfold will be taken 1 inch to the right of the umbilicus. For the **suprailiac** site, a diagonal skinfold will be taken just above and slightly forward of the iliac crest (superior border of the iliac crest and in-line with the natural angle of the iliac crest). Three measurements will be taken at each site and the closest 2 measurements will be averaged for analysis. To obtain the skinfold, the skin will be grasped between the thumb and index finger above the location. The caliper will then be applied 1 cm below and at right angles to the pinch to obtain a skinfold measure. When the same person performs these measures on different days, the coefficient of variation is less than 5%. We will use one person to perform each measure to ensure reliability and avoid contamination by inter-tester variability. **Abdominal and waist circumference** will be measured using a fiberglass tape (Gulick, Country Technology, Gay Mills, WI). For the **waist** circumference, the smallest horizontal circumference will be measured at the mid-point between the lowest rib and the top of the iliac crest. The **abdominal** circumference will be measured horizontally at the level of the umbilicus.

**Outcome Measures:** The primary measures to be studied are torso muscle strength, physical activity, and mobility; secondary measures are symptoms of LBP and QOL.

**Assessment of Torso Muscle Strength:** The strength of torso flexion and extension muscles will be measured using a modified version of the U of Michigan strength test system\(^5\) (Workability Systems, West Chester, Ohio) and a Chattanooga-Baseline® Hand Dynamometer - Digital LCD Gauge - ER™ 300 lb capacity (DJO Global, Chattanooga, Vista, CA USA). We will use the protocol \(^5\) as described by McNeill et al \(^5\), Nachemson et al. \(^5\) and Chaffin. \(^5\) For **trunk flexion**, the participant will stand upright in the test apparatus with buttocks against the padded board and the superior edge set at the level of the iliac crest. The participant is strapped to the apparatus by a canvas belt placed snugly around the chest and under the arms horizontal to the force-measuring dynamometer secured to the apparatus frame. For measurements of **trunk extension**, the participant stands upright with their lower anterior abdomen against the padded board at the iliac crest level. The belt is placed snugly around the posterior back and runs under the arms horizontal to the dynamometer.
Participants will be instructed to pull against the belt as forcefully as they can without injuring themselves and not to use their arms for support; thus, the force exerted will be by the trunk muscles. For each test, participants will perform two maximal efforts maintaining each voluntary isometric exertion for 5 seconds, separated by 30-second rest; the highest value of the two trials will be accepted in kilograms. All subjects will be given the visual analog scale (VAS) for pain to quantify pain during testing. Reproducibility of maximum exerted forces by repeat testing differed by a mean of 22% extension and 13% flexion. Intra-individual performance ratios differed by a mean of 20% for extension-to-flexion. A reasonable percent variance for strength-testing.

**Assessment of Mobility and Physical Activity:** Mobility will be measured by these procedures: 2-minute push-up test, 2-minute sit-up test, lumbar trunk muscle test and a 6-minute walk test. Additional physical activity measures will be the monitoring of steps walked and energy expenditure. After completing the tests, a VAS for pain will be administered to quantify pain during the effort.

The 2-minute push-up and sit-up tests will be completed in accordance with the Army APFT protocol, and are similar to that described by the ACSM. Test-retest reliability for a timed push-up test has been reported to be 0.93; the sit-up test has been reported to be 0.88-0.94. The 2-minute push-up test evaluates upper body endurance and strength as well as the stabilizing torso muscles of the abdomen and back. Starting in a prone position, the participant is positioned with their hands on the ground (shoulder width apart), toes in contact with the floor, spine parallel to the floor, elbows and hips in extension. The body moves as a single rigid unit and is lowered to the ground until elbows are at 90° angle. The body is then returned to the starting position by pushing the arms up to full extension. A push-up is counted if the elbows were brought to flexion of 90° or greater and then return to full extension, while keeping the body elevated on the toes. The number of push-ups performed in 2-minutes is recorded. The 2-minute sit-up test tests trunk flexion and abdominal endurance. Starting in a supine position, the knee joints are flexed at a 90° angle, with fingers behind the head, soles of the feet and shoulder blades in contact with the floor. With the command to begin, the upper body is raised forward by flexing the abdominal muscles and then lowered. A sit-up is counted if the hands are behind the head, bringing the base of the spine to a vertical position and then returning the shoulder blades to the floor. The number of repetitions performed in 2-minutes is recorded. Correlates to disability and LBP pain (r) range from -0.39 to -0.46; P < 0.001.

The Lumbar Trunk Muscle Test will assess back extension and endurance. Participants will be asked to lie in a prone position while holding the trunk in 15° of extension (sternum off the floor) for as long as they are able. A small pillow will be placed under the lower abdomen and to decrease lumbar lordosis as illustrated by Ito et al. Participants will be asked to maintain maximum flexion of the cervical spine while contracting the gluteal muscles. The time during which the subject keeps the upper body straight and horizontal is recorded. For subjects who experience no difficulty in holding the position, the test is stopped after 300 seconds (5 minute). Test-retest correlations (r) were 0.97 - 0.94 for healthy men and women and 0.93 - 0.95 for patients with chronic LBP with endurance measurements significantly high (p<0.01).
The 6-Minute Walk Test (6-MWT) measures the distance a participant walks at a “fast” pace over a 6-minute period. Participants will “walk as quickly as you can” with the opportunity to stop and rest if required. This test measures functional capacity of walking. Normal reference for healthy adults on the 6-min walk distance has been published. The 6-MWT has demonstrated submaximal exercise at 72.7% +/- 11.6% of \( \dot{V}O_2_{\text{max}} \) with rank order correlation of 0.49 (P = 0.001) between 6-MWT and \( \dot{V}O_2_{\text{max}} \). Test-retest reliability was ICC = 0.917 [0.862-0.951].

**Mobility: Physical Activity Measures:** Physical activity will be measured using the Fitbit Charge 2 (San Francisco, CA). The Charge 2 is a wrist-worn three-axis accelerometer that measures steps walked, distance traveled, energy expenditure and floors climbed. The unique feature of this device is a wireless function that automatically uploads data to designated mobile phone devices or computers. Batteries are rechargeable and last 5-7 days. Fitbit products use similar accelerometry for all their products. Thus, we assume that each of their products have similar validity and reliability. In our personal experience comparing the Charge to the Jawbone and the well validated Digiwalker, we found very similar accuracy of steps. Fitbit devices have been shown to be reliable and valid when compared to standard research-grade devices for energy expenditure (r=0.89-0.97). Fitbit accuracy estimates report 10% error (90% CI) for energy expenditure compared to a portable metabolic system. In the current study, baseline data will be ascertained by wearing the Charge for 3 days while maintaining a typical activity pattern. Subsequently, the device will be worn daily for 9 weeks.

**Assessment of Symptoms of Low Back Pain:** Pain associated with daily activity (walking, sitting, standing, bending, sport, resting, work) and body functions (pain, sleep, bending, leg weakness, loss of feeling) will be measured by the Clinical Back Pain Questionnaire (CBPS), also known as Aberdeen LBP scale, a 19-item back pain specific self-report questionnaire. Scores range from 0 to 100 with higher scores indicating greater disability. In patients with low back pain, the CBPS demonstrates test-retest reliability correlation of 0.94, Cronbach’s alpha of 0.8 for internal consistency and responsiveness to small change.

LBP-related disability and functional limitation will be measured by the Oswestry Disability Index (ODI), a well standardized outcomes questionnaire that is LBP-specific for activities of daily living and degree of disability. The 10-section instrument assesses pain, personal hygiene, lifting, walking, sitting, standing, sleeping, sex life, social life, and traveling for those with back pain. Each section contains six statements, ranging from 0 to 5, the final score is calculated using a standard scoring method. The ODI has demonstrated reliability and construct validity in comparison to other pain and disability measures.

The Visual Analog Scale (VAS) of pain will be used to assess pain at rest and after activity. Participants will complete this scale following the push-ups, sit-ups, 6-minute walk and the lumbar trunk muscle test. This VAS pain subscale is a 100-mm horizontal line index with descriptive anchors at each end. At the far left (0.0 cm) is “no pain” and at the far right (10 cm) is “worst possible pain”. The participant is instructed to place a vertical line at some point between the anchors to describe his/her level of pain. The VAS pain scale shows high correlations with acute pain levels.
Assessment of Quality of Life (QOL): The SF-12v2 Health Survey\textsuperscript{86} will be used to determine each participant’s overall health-related quality of life. It is a shorter version of the MOS 36-item Short Form Health Survey (SF-36)\textsuperscript{87} demonstrating similar reliability\textsuperscript{88} and maintaining the eight health domains with one or two questions per domain. This widely used multidimensional scale has two summary scores for physical and mental health as well as eight subscale scores. It has been validated in patients with a variety of orthopedic conditions\textsuperscript{89-92} and in athletic patients.\textsuperscript{93} Reliability estimates for individuals in orthopedic settings how internal consistency reliability coefficients ranging from 0.75 to 0.91 for the eight scales, with a median of 0.84,\textsuperscript{94} reliability estimates for LBP range from 0.80-0.92.\textsuperscript{95}

In addition, depressive symptoms will be measured by the Centers for Epidemiologic Studies Depression instrument,\textsuperscript{96,97} a self-administered questionnaire that contains 20 items. The CES-D shows excellent internal consistency (coefficient alpha >0.85) and test-retest correlations (r >0.5).\textsuperscript{97}

Compliance/Adherence to Treatments: Compliance/adherence to the interventions will be measured at multiple levels. Adherence to the standard PCM protocol, PEP and NMES will be computed as the number of home sessions reported on the participant’s log divided by the total number of sessions prescribed (daily). Adherence to NMES back training will be defined as the number of sessions achieved in each phase divided by the number of sessions prescribed. The Recovery Back™ system has a hidden internal compliance timer that records the amount of time the stimulator was used. This time will be compared to the training logs. Individual NMES reliability will be assessed from the total stimulation time recorded in the stimulator compliance monitor and by cross checking with training logs in which participants record their daily stimulation time.

4.6.6 Investigational New Drug / Investigational Device Exemption:

The Recovery Back device is FDA approved for treating muscle atrophy, the objective of this study. It is being sold in the United States for this purpose.

Neurotech Recovery Back System: The Recovery Back System has been designated a 510(k) by the FDA and approved for the specified use in this study. The letter is attached. Information below was retrieved from the FDA website: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmncfm

Specifics are:

<table>
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<tr>
<th>Device Classification Name</th>
<th>electrode, cutaneous</th>
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<tr>
<td>510(k) Number</td>
<td>K112934</td>
</tr>
<tr>
<td>Device Name</td>
<td>NEUROTECH RECOVERY</td>
</tr>
</tbody>
</table>
| Applicant                   | BIO-MEDICAL RESEARCH, LTD. | bmr house
p|armore business park, west galway, IE el |
| Applicant Contact           | anne-marie keenan    |
This study meets the specifications for the use of the Neurotech Recovery Back System for NMES usage in treating muscle atrophy.

4.6.7 Human Biological Specimens/Tissue (HBS/tissue) N/A

4.7 Study population:
To obtain a sample size of 135 adults with subacute LBP, we will draw upon Active Duty members and Reserve/National Guard members on active duty status through the physical therapy clinics, family practice/primary care clinics and satellite clinics at BACH. All racial, ethnic, and gender groups will be recruited for the study.

The number of visits required for participants in all groups is 4 visits, including 1 baseline visit, 2 visits for assessment, intervention adjustments, and testing (weeks 3 and 6) and one 9-week post-test assessment visit, for a total of 4 visits. The 3, 6, and 9-week visits will include training adjustment, review of logs and abbreviated testing. Each standard visit will take 10 minutes, and each assessment (Weeks 3, 6, 9) approximately 1 hour and 10 minutes, with baseline testing 1 hour and 45 minutes; the total time over the 9 weeks will be approximately 5 hours and 20 minutes (Table 3).

4.7.1 Repository Information: N/A

4.7.2 Inclusion Criteria
The study will be open to all active duty personal who are:

4.7.2.1 diagnosed with low back pain, categorized as lumbago or unspecified backache;
4.7.2.2 greater than 3 weeks and less than 12 weeks since the onset of the episode of LBP;
4.7.2.3 active duty military service member at the time of diagnosis;
4.7.2.4 age ≥18 and <45 years;
4.7.2.5 ability to provide freely given informed consent.

4.7.3 Exclusion Criteria
Those who might be at risk of adverse outcomes from the study interventions will be excluded. This includes individuals with
4.7.3.1 recurrence of LBP that is less than 3 months from prior episode;
4.7.3.2 a significant co-morbid medical condition (such as severe hypertension, neurological disorder or pacemaker/defibrillator) in which NMES strength training or unsupervised exercise is contraindicated and would pose a safety threat or impair ability to participate;
4.7.3.3 previous back surgeries;
4.7.3.4 inability or unwillingness to participate in an exercise or strengthening program;
4.7.3.5 clinical evidence of a lumbar radiculopathy;
4.7.3.6 inability to speak and/or read English;
4.7.3.7 pregnancy;
4.7.3.8 vision impairment, where participant is classified as legally blind;
4.7.3.9 unwillingness to accept random assignment; or
4.7.3.10 a score >=23 on Center for Epidemiological Studies-Depression scale.

Neurotech, the manufacturer of the Recovery Back devices states “safety of NMES for use during pregnancy has not been established.” A urine test will be performed to confirm eligibility for participation in the study. Women randomized into the NMES group will perform a urine pregnancy test at baseline, 3 and 6 weeks. If the test is positive, the woman will be ineligible to continue in the study.

4.7.4 Recruitment
4.7.4.1 Subject selection must be equitable. (32 CFR 219.111.a.3)
In the study proposed, there will be no exclusions based on race, ethnicity, or gender. The study will include both females and males. Using the Defense Medical Surveillance System (DMSS), we estimated our targeted enrollment for the study (Table 4). Estimates were based on the 2014 DMSS database of active duty (AD) Army men and women. For diagnosed Lumbago (ICD-9 724.2) and unspecified backache (ICD-9 724.5), the first occurrence was 16.6% in military women and 83.4% in military men98. The proportion of African-Americans with diagnosed LBP pain was 8% in AD women and 17% in AD men. For whites, the proportion with diagnosed low back pain was 50% for AD women and 58% for AD men. The “other” racial category in the DMSS accounted for 2.2% AD women and 8.3% AD men with diagnosed low back pain.
To calculate ethnic enrollment, we used (1) the portion of military men (81.6%) and women (18.4%) with low back pain (above) and (2) the percentage of Hispanic ethnicity (11.6%) in the DoD Active Duty force. Table 4 depicts the targeted planned enrollment. Our minority recruitment goal will be 33.7% (N=45), with most of these expected to be African-Americans (23.2%) (n=31), with representation from Hispanics (11%) (n=15) and Asian-Americans (10.5%) (n=14). The targeted sex/gender enrollment was based on the number of cases reported for 2014 in the DMSS of LBP (for military men (83.4%) and military women (16.6%) and the 2014 military demographics.

The outreach effort to enhance the recruitment of women and minorities to this intervention study is limited to Ft. Campbell and surrounding areas of Kentucky and Tennessee. Our methods for recruitment follow: Military installations - newspapers, media advertising, online central information boards, and flyers to military physicians and other health professionals. We will also advertise in local military newsletters. Eligible potential participants will be given a brochure about the study with attempts to recruit them into the study. We will actively recruit African-American participants, and personal contacts (with an African-American team member whenever possible) will be made with all African-American participants who meet eligibility criteria. There will be no monetary compensation. As part of our retention plan, we will hold orientation sessions and testing before and after work to aid in participant retention.

Table 4: TARGETED/PLANNED ENROLLMENT TABLE (N=135)

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</tr>
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<td></td>
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<td>18</td>
<td>102</td>
<td>3</td>
</tr>
</tbody>
</table>

We will schedule appointments at the participants’ convenience, including at lunch, as well as before and after work. We will also telephone and send emails/texts to participants to remind them of scheduled appointments. The research team will monitor the process and outcome of our minority and gender recruitment and retention plan each quarter. An important part of our retention plan will be to hold orientation sessions and testing before and after work to aid in participant retention.

**Inclusion of Children**

There are regulations concerning age of enlistment into the military service or selective services. By federal law (10 U.S.C., 505), the minimum age for enlistment in the United States Military is 18 years without parental consent (17 years with parental consent). The limited number of children available for study (if any) would not be representative of the group and could skew the results. Therefore, children are not eligible for this study.

**4.7.4.2 Describe from where, when, and how the study subjects will be recruited.**

**Recruitment** will be thru participant self-referral or provider referral. Informational brochures will be placed in outpatient clinics frequented by active duty soldiers. The brochure will explain the study and provide contact information to call if the soldier desires more information and is interested in possible enrollment. An in-person orientation to the study will be given to military physicians, nurse practitioners and other health professionals at these locations, with flyers and brochures distributed. Recruitment efforts will also come through a cooperative effort with the research team and management at the satellite clinics; announcements of the study will be made at provider meetings, special functions and online bulletin boards. Providers will be informed of this research project, the study aims, and inclusion/exclusion criteria that will be used for participation.

Study team members, who have approved access to CHCS and AHLTA and the primary care and physical therapy clinic schedule, will conduct a pre-screening of the schedule. We will use CHCS and ALTA to identify possible participants who are on the schedule and/or referred to primary care/physical therapy with low back pain. The pre-screening process will involve searching for potential eligible patients by analyzing the “reason for appointment” in the clinic schedule. For patients that have descriptions that meet eligibility criteria, the study team member will contact the appointed provider and verify eligibility. If the provider confirms eligibility, the patient will be approached by the provider/study team member during the patient’s future appointment at the clinic. For those that do not have a reason for appointment, the provider will be approached to determine the “reason for the appointment” and if it fits the study eligibility criteria. If the provider confirms eligibility, the patient will be approached by the provider/study team member during the patient’s future appointment at the clinic.

Additionally, participants will be recruited from Blanchfield Army Community Hospital and associated clinics using advertisements in the BACH newspaper, on the BACH intranet and internet website, BACH Facebook, electronic bulletin, and posting flyers on BACH bulletin boards, and distributing tri-fold brochures. All eligible participants will be contacted by the study investigators or trained designee and asked if they are interested in learning more about the project and participating in the study.
4.7.4.3 Compensation for participation. There will be no monetary compensation.

4.7.5 Consent Process: (32 CFR 219.116 and 117)

Initial contact will be by a trained member of the research team, who will provide a brochure and information on the study (Personnel designated to obtain informed consent are listed in section 14.0). The research team member will read a standardized script that describes the study, the nature of the participant’s involvement, and risk and benefits, assures confidentiality, and provides contact information. If the potential participant voices interest in the study, then the interviewer will then go through a list of questions to determine eligibility. After the initial screening, an appointment will be made for informed consent and in-person screening.

At this first visit, participants will be oriented to the study and given an opportunity for questions, and will provide written informed consent as well as HIPAA authorization. The in-person screening for eligibility will include collection of demographic data and health status, and evaluation of the lower back. In addition, the interviewer will administer the Center for Epidemiological Studies Depression Scale (CES-D) to measure depressive symptomatology. If the score is over 23, the potential participant will be excluded and treatment providers will be notified. In populations with higher depression prevalence such as back injury, a score of 23 is frequently used to reduce false positives.

Neurotech, the manufacturer of the Recovery Back states “safety of NMES for use during pregnancy has not been established.” A urine test will be performed to confirm eligibility for participation in the study. Women randomized into the NMES group will perform a urine pregnancy test at baseline, 3 and 6 weeks. If the test is positive, the woman will be ineligible to continue in the study.

Written consent, approved by the Dwight D. Eisenhower Army Medical Center Human Use Committee, University of Tennessee Health Science Center Institutional Review Board, and Uniformed Services University Institutional Review Board will be obtained from all participants. During the consent process, participants will be informed that they may withdraw at any time with no effect on their medical care, and that they may refuse to answer any specific questions. Following a discussion of the study and a verbal review of all content on the consent form, comprehension of consent information will be assessed by asking participants to repeat back what they are being asked to do if they choose to participate and what will happen if they do not participate. They will also be given the opportunity to ask any questions about the study or their participation in the study. Written informed consent will then be obtained.

Following screening and informed consent, participants will be baseline tested to include familiarization with the test procedures, followed by baseline assessments of muscle strength, physical activity, mobility, and completion of questionnaires to document low back symptoms and QOL. After completion of baseline testing, participants will be randomly assigned to one of the three groups.

Full informed consent will be obtained from each participant by the principal investigator and/or a trained designee (Trained designee are listed in section 14.0 below). The purpose of the study and requirements for participation will be appropriately
outlined. There will be full disclosure of all risks of the protocol. Participants will be
told participation is voluntary and that they may leave the study at any time. The
Principal Investigator and/or a trained designee will review the consent form with the
participant at the time of the baseline visit. Subjects are informed that they may
withdraw at any time with no effect on their military or medical treatment status, and that
they may refuse to answer any specific questions. Consent will be documented by having
the stamped IRB-approved consent form signed by the participants (prior to enrollment).
A copy will be given to the participant. The signed forms will be maintained in a
notebook and stored in a locked file cabinet in the principal investigator’s office.

5.0 Privacy/Confidentiality: (32 CFR 219.111.a.7)

To protect participants' privacy, no names will be attached to test results. Test
results of individuals will be identified by a unique code number to enable data
matching. Data will be analyzed and reported according to age and gender groups, not
singly. Hard copies and computer files will be stored in a locked testing room.
Personal participant information will be scanned into a computer database using
Teleform® and/or entered using REDcap. All participant research records will be kept
confidential with only subject ID numbers used. Only the PI, clinical research
coordinator and data manager will have access to the database that links individual
names to the individual code numbers. The database will be protected via the use of
passwords and coded numbers. No data will be published or presented in a manner
that would allow the identification of any individual from which the data were
collected. All electronic and hard copy documents related to this protocol that contain
Protected Health Information (PHI) are secured in accordance with the HITECH Act
of 2009.

5.0.1 HIPAA Authorization If your research will collect Protected Health Information
(PHI) such as, physical, clinical, psychological well-being, behavioral and genetic data (e.g.,
blood pressure, type of cancer, disease stage, ADL, PSA, urine protein, use of alcohol,
depression, etc.) along with any of the following 18 personal identifiers, a HIPAA
authorization is required. The research data collected in such format are referred to as
“Identifiable Protected Health Information”

5.0.1.1 Check any of the following 18 personal identifiers that will be
collected during the course of this study. If none of the following will be
collected, proceed to section 5.0.1.4

_X_ 1. Names
_X_ 2. Street address, city, county, 5-digit zip code
_X_ 3. Birth Months and dates (years are OK) and ages >89 (unless all
    persons over 89 years are aggregated into a single category)
_X_ 4. Telephone numbers
    ___ 5. Fax numbers
_X_ 6. E-mail addresses
    ___ 7. Social security number
_X 8. Medical record number
    ___ 9. Health plan beneficiary number
5.0.1.2 Can you limit your collection of personal identifiers to just dates, city/state/zip, and/or “other unique identifier” (#18 of the above)?
___ Yes – then your dataset may qualify as a Limited Data Set – please complete a Data Use Agreement and attach to your protocol. Then go to section 5.0.1.4.
_X_ No – Go to section 5.0.1.3

5.0.1.3 Is obtaining patient HIPAA Authorization “impracticable”? 
___ Yes – Authorization may qualify to be waived by the IRB. Go to Section 5.0.2 HIPAA Authorization Waiver for the application.
_X_ No – Research subjects will need to sign a HIPAA Authorization. Complete the HIPAA Authorization template and submit with this protocol.

5.0.1.4 What precautions will you take to protect the confidentiality of research source documents (Case Report Forms, questionnaires, etc.), the research data file, and the master code (if any)?

To protect participants' privacy, no names will be attached to test results. Test results of individuals will be identified by a unique code number to enable data matching. Data will be analyzed and reported according to age, gender and intervention groups, not singly. Hard copies and computer files will be stored in a locked testing room. Personal participant information will be scanned into a computer database using Teleform® and/or REDcap. All participant research records will be kept confidential with only subject ID numbers used only the study PIs and data manager will have access to the database that links individual names to individual code numbers. The database will be protected via the use of passwords, password-protected participant documents firewall for network computers, and coded numbers. No data will be published or presented in a manner that would allow the identification of any individual from which data were collected.

Consent forms and original research records will be stored within a locked file cabinet in the clinical research coordinator’s locked office within the Physical Therapy Department. Research records sent electronically to the University of Tennessee using the ARMDEC SAFE file sharing system will be kept in the data manager’s office which is in the research lab at the University of Tennessee’s Health Science Center. The lab is locked and can only be opened by key cards cleared by campus police. The data
manager’s office (in the lab) is locked and only the data manager, Dr. Talbot and the campus police possess the necessary keys to open it. The files will be kept in a locked cabinet within this office, and only the data manager will have keys to this file cabinet. PHI and de-identified data will be kept separate at both locations, BACH and UTHSC, respectively, and all original consent forms will remain at BACH. The address of the UTHSC lab is 920 Madison Avenue, Rm WC058, Memphis, TN 38163.

5.0.1.5 When will you destroy the research source documents, data file, and the master code? HIPAA authorization forms need to be saved for 6 years all other research documentation needs to be maintained locally for three years after completion of the study. At that point the investigator should contact the Department of Clinical Investigation to determine final disposition of study documentation/data.

HIPAA authorization forms will be saved for 6 years all other research documentation (hard copy) will be maintained locally (BACH) for three years after completion of the study. At that point, the investigator should contact the Department of Clinical Investigation to determine final disposition of study documentation/data.

The proposed research will contain data from 135 active duty military service members with subacute LBP treated at BACH and its associated clinics. The final dataset will include the following: clinical demographic details, body composition, muscle strength, mobility, functional performance, LBP symptoms, and quality of life. Because this study is an intervention study, we will be collecting identifying information to contact participants during the trial. The final dataset will be free of identifiers that would permit linkages to individual participants. At the completion of the study all links to individual names and individual code numbers will be deleted. The database will be protected via the use of passwords, password-protected PD, firewall for network computers, and coded numbers. Research records (hard copies) will be maintained three years after the research is completed and the study closed with the IRB.

5.0.1.6 Will research data including Identifiable Protected Health Information be sent outside of your/the facility?

_X Yes – Please explain assurances you have received from the outside party that they will appropriately follow confidentiality protections, follow the HIPAA requirements, and abide by the provisions of your Authorization.

___ No

Data will be sent via the ARMDEC SAFE (Safe Access File Exchange) file transfer system, a secure file sharing program that is approved for use by the Department of Defense. Consent forms will remain at BACH along with the original research records, and will be stored within the Physical Therapy Department in a locked file cabinet, within the clinical research coordinator’s locked office.

Research information which includes participant name and DOB will be sent to the PI, and data manager for data confirmation and analysis. These individuals are
employed by UTSHC which is a covered entity. Federal HIPAA requirements will be complied with at UTHSC.

The principal investigators or their designees and member of the University of Tennessee Health Sciences Center will have access to PHI. This information will only be used for this study. The study sponsor (TriService Nursing Research) may need to do an audit of the research records.

Data Center Physical Security:

The datacenter is located on the seventh floor of the Lamar Alexander Building on the University of Tennessee Health Science Campus in Memphis. The floor is accessible to the public only during normal working hours (8:00am to 5:00pm M-F). Elevator access to the floor and datacenter is restricted after hours, weekends, and holidays to approved personnel only. Access is provided by a card reader access control system monitored by Campus Police. In addition to access control, all entrances/exits (doors, stairwells, and elevators) to the 7th floor are monitored by security cameras that record all activity, 24x7 days/week and video is retained for 14 days. Access to the machine room is also controlled by the card reader system at all times. All entry attempts (successful and failed) are logged and kept in the access control application’s database. Inside of the machine room a series of cameras record all activity, also stored for 14 days. In addition to the physical security measures listed above, the HSC has its own University Police force. Security guards patrol the campus and buildings on a 24x7 day schedule.

Fire protection is provided by an automated fire detection system. It is monitored, maintained, and inspected by the Physical Plant and automatically notifies the fire department when activated. The machine room is protected by a Clean Agent (Sapphire) non-halon fire suppression system.

Electrical power to the Data Center is provide through a 160kva UPS. It provides power for short term outages and is backed up with a generator for outages of a longer duration. In addition to providing backup power to servers, it also provides power to all environmental devices to control temperature, humidity, lights, etc. in the Data Center.

Data Security and Provisioning:

Information security is provided by assigning all faculty, staff, students, and other authorized users a unique, directory based netid (username) and password. A netid is assigned when faculty/staff are hired, a student is enrolled, or when a person not directly affiliated with the university, is sponsored (good for one calendar year unless revoked), by authorized university personnel. The netid is valid until termination of an employee, graduation or departure of a student, and expiration or revocation of sponsorships. Network access and provisioning is then based on successful authentication of a user against the directory. With directory based authentication we can enforce access control, group policies, and password policies for password length, complexity and expiration
(based on ‘password best practices’ policy). It can also be used to manage Windows, UNIX, Linux and Mac environments.

Data provisioning is the process of making data available in an orderly and secure way to users, application developers, and applications—is a significant challenge for the university. With many widely varying demands for data, geographically distributed users and data sources, production systems that must be insulated from uncontrolled access, and concerns about intellectual property and confidential data, careful data provisioning is more important and more difficult than ever before. For most ITS managed servers, provisioning is controlled by data owners, either directly or by providing ITS personnel with a request to grant an individual access to their application and/or data.

**Data Backup and Disaster Recovery:**

Three levels of data backups are performed and content is stored in multiple locations for up to thirty days to minimize data loss in the event that information gets deleted or the system goes down for any reason. For Disaster Recovery, Computing Systems provides for full business resumption for server applications in the event of a major and prolonged outage of service. Disaster recovery storage services are contracted through a bonded - offsite third party, and arranged specific to a server application.

**Network Security:**

The University of Tennessee Health Science Center (UTHSC) has a risk-based security management system. All systems and components are managed by employees of and owned by UTHSC.

Network security responsibility is assigned to the Taylor Strickland, Chief Information Officer, Jason Holden, Director of Network Services and Joseph Morrison, Security Officer.

I. **Network Technical Controls**

A. No device may have network connectivity until it is registered with the network access control system by its owner, using a valid University netid and password authenticated against LDAP. Remote access is controlled by a VPN device.

B. Network traffic, both incoming and outgoing, crossing the UTHSC network boundary is examined by a Cisco firewall against its Access Control Lists. Cisco intrusion prevention systems have been deployed to further examine traffic for known exploits, and the traffic shunned or trapped as appropriate. Also deployed are Snort intrusion detection systems that alert on different traffic and vulnerabilities.
C. UTHSC actively monitors the status of network infrastructure devices and traffic. A MARS security information management system which integrates and analyzes various alerts is deployed.

D. UTHSC has deployed a Nessus vulnerability scanning system to detect known vulnerabilities in systems connected its network.

E. Dual network cores consisting of the core switches, network access control systems, and firewalls provide redundancy of critical infrastructure. Dual connections to the internet insure connectivity.

F. Network architecture provides for ‘DMZs’ for systems with public IP addresses while other systems are assigned private IP addresses and to separate VLANS.

G. UTHSC has developed and implemented an Emergency Response Plan for its core information systems assets.

H. Systems at UTHSC are required to run current anti-virus software. The university-provided anti-virus software has a management agent that reports host system events such as attempts to uninstall the antivirus or malicious software that is not cleaned.

I. The IPS and IDS systems, above, both respond if they detect malicious code.

II. Physical Security

A. Networking equipment in the buildings is housed in a locked wiring closet. Keys to the wiring closet are limited to network services personnel. Power conditioning and UPS is utilized.

B. Core networking equipment is housed in a climate controlled room with power conditioning/UPS and automatic fire suppression. Access is by card-key.

C. After hours building access is controlled by door locks and key-card entry.

D. A CCTV camera network has been deployed across the campus.

E. UTHSC has its own University Police force in addition to local law enforcement. Security guards are also used to patrol the campus and buildings.

III. Additional Security Programs
A. UTHSC has an incident response program in effect to direct mitigation activities for compromised systems. This program documents security incidents and collects basic forensics about the systems to determine root cause.

B. UTHSC has a comprehensive set of security policies for information systems in effect. These policies address topics including data classification, mission critical information and disposal and re-use of electronic media.

C. UTHSC requires all users to complete security training modules.

**Software Applications:**

We host both purchased and in-house developed software applications. Purchased applications usually come with a software support package. They are hosted on servers maintained by the Systems group. As revisions and patches are released by the vendor, our staff applies them to a development/test platform for testing and quality assurance. They are then incorporated into the production environment. We will use the Fitabase application to interface with the Fitbit device and merge the activity data into the REDcap data base.

5.02 HIPAA Authorization Waiver. N/A

6.0 Benefits: (32 CFR 219.111.a.2) The benefits from participating in this study far outweigh the risks. Benefits for all participants will include assessments of muscle strength, physical fitness, mobility, height, weight, and body composition at no cost. Participants in either the NMES alone or PEP alone may potentially obtain higher levels of strength, reduced pain and improved movement. Participants in the primary care management group may experience a reduction in pain and diminished disability. Still, there may be no personal benefit from participating in this study; however, some individuals derive altruistic benefit from knowing they are contributing to future knowledge. This study could potentially benefit future individuals with LBP by contributing to the body of knowledge regarding therapies that influence symptoms of LBP.

7.0 Risks: (32 CFR 219.111.a.1 (i and ii))

The consent form will make a full and meaningful disclosure of all tests (Table 5). Increased physical activity or exercise training may cause some post-exercise discomfort such as sore lower back, fatigue and sore muscles. With functional testing, there is a possibility of falling. The risks associated with electrical muscle stimulation are discomfort associated with involuntary muscle contraction. With NMES there may be a slight reddened area under the pad.

<table>
<thead>
<tr>
<th>Table 5: Data Collection Sets and Corresponding Potential Risks to Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Software Applications:</strong></td>
</tr>
<tr>
<td>We host both purchased and in-house developed software applications. Purchased applications usually come with a software support package. They are hosted on servers maintained by the Systems group. As revisions and patches are released by the vendor, our staff applies them to a development/test platform for testing and quality assurance. They are then incorporated into the production environment. We will use the Fitabase application to interface with the Fitbit device and merge the activity data into the REDcap data base.</td>
</tr>
<tr>
<td><strong>5.02 HIPAA Authorization Waiver. N/A</strong></td>
</tr>
<tr>
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</tr>
<tr>
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</tr>
<tr>
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</tr>
</tbody>
</table>
### Data Collection Set

<table>
<thead>
<tr>
<th>Strength testing</th>
<th>Potential Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RARE. The participant may experience muscle soreness or fatigue or back pain. In some cases, dizziness, lightheadedness or fainting may occur during maximal effort.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anthropometrics</th>
<th>Potential Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RARE. The calipers could potentially bruise sensitive skin. The tester will apply pressure to the abdomen briefly to avoid possible bruising.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical Performance Measures of Mobility</th>
<th>Potential Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RARE. There is a potential that the participant may fall during the testing, but most of the procedures are self-paced and should not impose any serious risk. However, after the exercise, the participants may be a bit sore. With exercise testing, there is the possibility that participants might slip, but every precaution will be taken, such as having spotters at their sides. There is also the possibility that a participant might experience chest or back pain and/or a heart attack.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Height, weight, blood pressure</th>
<th>Potential Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RARE. The blood pressure cuff will apply pressure to the arm briefly.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Potential Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1) Post-exercise discomfort such as fatigue, muscle soreness and muscle stiffness may occur with changes in physical activity. (2) The risk associated with the PEP program is the possibility of falling. (3) The risks associated with electrical muscle stimulation are discomfort and unfamiliarity with involuntary muscle contractions. (4) With NMES occasionally a slight reddened area may occur where a pad is placed on skin of the torso. (5) The Recovery Back device for NMES is not recommended during pregnancy. Female participants will be tested for pregnancy.</td>
</tr>
</tbody>
</table>

### Procedures for Protecting Against Risks

Importance will be given to minimizing risk to participants in this study. As a first step, the inclusion and exclusion criteria will be strictly followed for the selection of participants. There will be full disclosure to the participants in regard to risks. During all study strength testing procedures, a physician, registered nurse, or trained physical therapy technician will be available in the clinic area. Procedures for fainting will have been reviewed with the testers. Specifically, participants will be taught not to hold their breath during maximal effort and the trainer will watch for participants performing a Valsalva's maneuver during maximal effort.

**Manual of Operation Procedures.** A manual of operation procedures (MOOP) will be developed for the study and the procedures will be strictly followed. All study personnel will be trained in sessions that will cover all procedures and human subjects’ issues, including recruitment, informed consent, measurements, randomization, participant follow-up, and adverse events. Adherence to the procedures in the MOOP will be assured by periodic assessment and retraining. Manuals, same persons performing measures, training, competency worksheets, and weekly meetings will be part of the study to assure consistency of measurement and
fidelity of training.

**Confidentiality**

To protect participants' privacy, no names will be attached to test results. Test results of individuals will be identified by a unique code number to enable data matching. Data will be analyzed and reported according to age and gender groups, not singly. Hard copies and computer files will be stored in a locked testing room. Personal participant information will be scanned into a computer database using Teleform®. All participant research records will be kept confidential with only subject ID numbers used. Only the PI and data manager will have access to the database that links individual names to the individual code numbers. The database will be protected via the use of passwords and coded numbers. No data will be published or presented in a manner that would allow the identification of any individual from which the data were collected.

**Safety Analysis Plan.** The proposed interventions have a very low expectation of serious events. The PI along with the medical monitor will be responsible for monitoring the safety and efficacy of the study. Adverse events will be reported to the IRB as required.

After each adverse event, the PI and medical monitor will review the circumstances surrounding the event as described on the AE form. If an excessive number of events are noted, then discussion with the IRB will occur to determine whether the events reflect a higher level of risk that needs to be addressed. The protocol has no plan for interim analysis, since the study is powered based on 135 subjects. If no medical monitor is required by the IRB and the study is determined to be minimal risk or less, the PI will be responsible for monitoring safety and efficacy.

### 8.0 Statistical Analysis:

**Determination of Sample Size:** Sample size was determined using 1) an alpha level of 0.05 and power of 0.80; 2) review of the LBP literature and data from pilot work; and 3) calculation of effect sizes for detecting group differences over time for a specific sample size based on the main outcome of muscle strength. Previous work suggested an effect size of 0.5-0.9 as an expected outcome.\(^{100}\) Sample size was estimated using 1000 simulated datasets with subjects tested at baseline, 3, 6, and 9 weeks assuming a multivariate normal distribution with unit variance and a covariance structure consistent with our previous work.\(^{101-103}\) The simulated data were entered into a linear mixed effect model with random intercept and time using lme4 in R.\(^{104}\) The interaction between time and group was tested with a naïve likelihood ratio test. For the primary outcome variable of strength, a sample size of 39 subjects per groups (117 total subjects) gave an effect size (Cohen d, maximal group difference) ranging

<table>
<thead>
<tr>
<th>Variable</th>
<th>Time-averaged group difference</th>
<th>Difference in change over time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steps per day</td>
<td>2000 steps</td>
<td>220 steps/wk</td>
</tr>
<tr>
<td>Push-up in 2 min</td>
<td>9.5 rises</td>
<td>1.0 rise/wk</td>
</tr>
<tr>
<td>Sit-ups in 2 min</td>
<td>8.2 rises</td>
<td>0.91 rise/wk</td>
</tr>
<tr>
<td>Walk fast pace</td>
<td>370 feet</td>
<td>41 feet/wk</td>
</tr>
<tr>
<td>Lumbar test</td>
<td>42 sec</td>
<td>4.7 sec/wk</td>
</tr>
<tr>
<td>Pain rating scale</td>
<td>7.5 points</td>
<td>0.83 points/wk</td>
</tr>
</tbody>
</table>

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Table 4: Expected Mean Change for Outcome Variables with power 0.8, alpha 0.05, effect size 0.7

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DDEAMC Human Research Protocol  Protocol Version Date: 4 October 2017  Page 35 of 56
from 0.5-0.9 based on the projected changes in strength for the three groups during the study. Based on the published data for back extension strength, the effect size would represent approximately a 7.6% increased difference for an effect size of 0.8 between two of the groups over 9 weeks, an increase difference of 9 pounds of isometric strength between two groups for an average starting strength of 119 pounds.

For the outcomes measures of function, mobility and pain, if we assume that standard errors will be like those observed in our previous work, the sample size of 39 per group is sufficient to detect the expected mean change shown in Table 4. Because we need to account for dropouts, we will inflate the sample size by 16%, for a total of 45 subjects per group and a total sample size of 135.

**Data analysis**

**Data Management:** Data storage has been detailed above. Data analysis will be conducted on a desktop computer. The computer storing these data will be backed up daily, and only the PI and the data manager will have access to the secured hard drive. A copy of the data will also be stored on the UTHSC server, using a secure site that is backed up daily. The data files will be converted to standard statistical datasets for processing and merging with other participant research data. For contact information forms, the project will use a computer data management and analysis system composed of digital scanning with Teleform® which minimizes data entry errors and cleans data files on an on-going basis. REDCap will be the electronic database for the study.

**Data Analysis:** The study will use a repeated measure design with measures at 4 time points. The primary goal of the analysis is to compare changes over time in the two treatment groups and a usual care control group. Potential covariates may include BMI, body weight, age, and other variables deemed to potentially confound the data.

**Statistical Assumptions** will be examined. For these analyses, we will use simple measures of central tendency (means, medians, and mode) and variability (standard deviations). Means and standard deviations will be calculated for continuous variables and percents for categorical variables. Coefficient will be used to examine correlations between variables. **Baseline Group Differences**, ANOVA and chi-square will be used to test for differences in baseline characteristics by groups and groups will be compared for equivalence of potentially confounding variables (such as age, marital status, and gender). Group inequities will be controlled in the analyses by using covariates or other appropriate statistical methods. **Time Differences.** Since data collected over time tend to be correlated within an individual, a linear mixed effects model will be used to deal with individual subject differences at baseline and, if appropriate, over the course of the study. Longitudinal mixed regression models will examine differences in time trends for the outcome variables among controls and those in the treatment groups. In these regression analyses, the important primary measures will be expressed as a function of time, treatment group, and group-by-time interactions, while controlling for important covariates.

**Specific Aim 1: To determine whether the treatment regimens are significantly more efficacious than standard PCM,** using the linear mixed effect method, as described above, we will estimate separate models for each of the following dependent variables: back strength for flexion and extension, energy expenditure, steps walked per day, number of push-ups in 2-minutes, number of push-ups in 2-minutes, distance
walked in 6 minutes, and time to perform the lumbar trunk muscle test. We will construct linear contrasts to compare the rate of change in each treatment group with the rate of change in the usual care group.

**Specific Aim II:** To determine whether the treatments improve QOL, disability and symptoms of LBP significantly more than PCM, using the same linear mixed effect method as with Specific Aim 1, we will estimate separate equations for QOL, disability and LBP symptom dependent variables. Primary independent variables will be treatment group, time, and group-by-time interaction. We will adjust for pain medication.

**Missing Data.** Missing data rates and patterns will be assessed; in particular, missing data rates by treatment group will be examined. For the primary analysis, we will adjust for missing data by using an intent-to-treat analysis. All of the subjects in the study will be included in the analysis. The mixed effects model deals with missingness by weighting subjects based on the data actually collected. Treatment effects will be compared on the basis of the subject’s original group assignment. In addition to the traditional intention-to-treat analyses, we will assess patterns of change both within and between groups using a mixed effects regression model for repeated measures data.

9.0 Adverse Events, Unanticipated problems, and deviations:

**Adverse Events** will be reported immediately to the principal investigator at the time of the visit. Adverse events will be reviewed, treated as appropriate, classified for severity and attribution and recorded in the participant file and adverse event database. Dr. Talbot and the study coordinator will review the participant records monthly at a minimum. Any adverse events in the severe or unexpected category will be recorded on the appropriate IRB form and reported to the IRB as required. These events will be cause for stopping and re-review of the study. All adverse events will be followed until resolution.

**The Anticipated Risks** include these: (1) Post-exercise discomfort such as fatigue, muscle soreness and joint stiffness may occur with changes in physical activity. (2) The risk associated with the home Progressive Exercise Program is the possibility of falling. (3) The risks associated with electrical muscle stimulation are discomfort and unfamiliarity with involuntary muscle contractions; and occasionally with NMES a slight reddened area where a pad is placed on the skin. (4) The Recovery Back device for NMES is not recommended during pregnancy. (5) Strength testing may cause muscle soreness or fatigue or back pain. Additionally, there is the risk of dizziness, lightheadedness or fainting. (6) With physical performance testing, there is the possibility that the participant might fall during the testing, but most of the procedures are self-paced and should not impose any serious risk. There is also the possibility that a participant might experience chest or back pain and/or a heart attack. (7) With anthropometric measurements, the calipers could potentially bruise sensitive skin. There are no other known risks associated with participating in this study. Participants might become tired during the sessions. Frequent rest periods will be provided.
The following definitions and grading scales will be used for adverse event monitoring.

**Mild**: adverse event of little clinical significance. These may include discomfort, pain, agitation, and/or embarrassment.  

**Moderate**: adverse event between mild and severe - causing some limitation of usual activities. In this event the participant will be removed from the study and the event will be reported to the IRB. The study will continue unless the IRB asks for it to be discontinued.  

**Severe/Serious**: adverse event that results in death, is life-threatening, requires or prolongs hospitalization, causes persistent or significant disability/incapacity, represents a significant overdose or breach of protocol, results in congenital anomalies/birth defects or produces cancer, or in the opinion of the investigator, represents other significant hazards or potentially serious harm to the research subject or others. This event will cause a temporary discontinuation of the trial and re-evaluation by the IRB.

The Attribution Scale for rating the relation of the adverse event to the study will be as follows:

- **Not related**: clearly NOT related to the study  
- **Possible**: may be related to the study  
- **Probable**: likely related to the study  
- **Definite**: clearly related to the study  
- **Unable to assess**

The DSMB or IRB (as appropriate) will be the arbiter of the severity and attribution of adverse events. Overall, the investigator and investigative team will serve as the regular data monitors for this study and will provide reports as required to the IRB. The PI will provide an interim report of all adverse events to the IRB at the time of continuing review.

Study participants will be monitored throughout the study for adverse events, both anticipated and unexpected. The participant will have paging access to the data monitor for reporting adverse events. Reported adverse events will be reviewed by Laura A. Talbot, RN, EdD, PhD, in collaboration with the on-site PI (CPT Vanessa Ramirez) and medical monitor and managed according to standard clinical practice. All adverse events will be tracked to resolution.

Any serious or unexpected adverse events will be reported to the IRB within the required timeframe. All serious and unexpected adverse events will be reported to the IRB using the appropriate forms. The frequency of serious adverse events will be monitored bi-annually by the investigative team, medical monitor and PI. The PI will provide an interim report of all adverse events to the IRB at the time of continuing review. **Stopping Rule**: The study will be stopped prior to its completion if the frequency of serious or unexpected adverse events is higher than that anticipated.
Expected adverse events which are not serious are reported on the Continuing Review (CR) Progress Report CR is generally performed on a 12-month cycle. More frequent Progress Reports may be required at the discretion of the IRB.

Serious Adverse Events: The PI, within 24 hours, must report all related or possibly-related AND serious adverse events (SAE) occurring in subjects enrolled at BACH. This is accomplished by submitting an adverse event report to the IRB via IRBNet. Serious adverse events must be reported even if the PI believes that the adverse events are unrelated to the protocol.

Unexpected (but not serious) adverse events occurring in subjects enrolled at BACH which, in the opinion of the PI, are possibly related to participation AND places subjects or others at a greater risk of harm that was previously known or recognized in the protocol must be reported by the PI within 24 hours of discovery by email or phone to the IRB and the Research Monitor. A follow-up written report within 5 business days to the IRB and the Research Monitor through IRBNet is required.

Unanticipated problems involving risks to subjects or others (UPIRTSOs) must be reported to the IRB and Research Monitor via email or telephone within 24 hours of discovery and a written follow up report within 5 business days. If no medical monitor is required by the IRB, events will be reported to the PI.

When a deviation occurs, the investigator shall report the occurrence to the IRB. The investigator is required to make the determination whether the deviation meets the criteria for an unanticipated problem involving risks to subjects or others. The IRB Chair or IRB staff member shall also make the determination if the protocol deviation meets the definition of an unanticipated problem involving risks to participants or others. If the IRB Chair or IRB Staff member determines and documents that the deviation is an unanticipated problem involving risks to subjects or others or the deviation resulted from serious or continuing noncompliance, the IRB staff member shall place the deviation on the agenda of the next available IRB meeting for review. If the IRB Chair or IRB Staff member determines and documents that the deviation is not an unanticipated problem involving risks to subjects or others, the IRB Chair or staff member shall acknowledge the submission and complete the review through an administrative review procedure.

As a reminder, according to DoDI 3216.02 (November 8, 2011), the IRB shall approve an independent research monitor by name for all DoD-conducted research involving human subjects, determined by the IRB to involve more than minimal risk to human subjects. Additionally, the research monitor may be identified by an investigator or appointed by an IRB or Institutional Official (IO) for research involving human subjects determined to involve minimal risk.

The research monitor may perform oversight functions and will report their observations to the IRB or a designated official. The research monitor may discuss the research protocol with the investigators, interview human subjects, and consult with others outside of the study about the research. The research monitor shall have the authority to stop a
research protocol in progress, remove individual subjects from a research protocol, and take whatever steps are necessary to protect the safety and well-being of human subjects until the IRB can assess the monitor’s report. Research monitors shall have the responsibility to promptly report their observations and findings to the IRB or other designated official. The research monitors shall have expertise consonant with the nature of risk(s) identified within the research protocol, and they shall be independent of the team conducting the research involving human subjects. If no medical monitor is required by the IRB, this role will be performed by the PI.

9.2 Reporting Unanticipated Problems Involving Risks to Subjects or Others, Serious Adverse Events and Deaths to the Human Research Protections Office (HRPO). All unanticipated problems involving risk to subjects or others, serious adverse events, and all subject deaths will be promptly reported by phone (706-787-8053), by e-mail (usarmy.gordon.medcom-eamc.mbx.irb@mail.mil), by facsimile (706-787-8123) to the RRCO.

9.3 Medical Monitor. The medical monitor will review all unanticipated problems involving risk to subjects or others, serious adverse events and all subject deaths associated with the protocol and provide an unbiased written report of the event to the HRPO and DDEAMC IRB. The medical monitor will comment on the outcomes of the event or problem and in the case of a serious adverse event or death comment on the relationship to participation in the study. The medical monitor will also indicate whether he/she concurs with the details of the report provided by the study investigator. Reports for events determined by either the investigator or medical monitor to be possibly or definitely related to participation and reports of events resulting in death will be promptly forwarded to the HRPO and DDEAMC IRB. *If no medical monitor is required by the IRB, this role will be performed by the PI.*

10.0 Subject withdrawal from study participation: Subjects are informed that they may withdraw at any time with no effect on their military or medical treatment status, and that they may refuse to answer any specific questions. The anticipated circumstance under which a participant’s participation may be terminated by the investigator or others is (1) health and safety issues where participation would be dangerous or detrimental to the subjects’ health, (2) loss of funding, (3) pregnancy, (4) if military contingency requires it; or (5) if the subject become ineligible for military care as authorized by Army regulation.

11.0 Funding: We is to be awarded $581,966 (total award) by Triservice Nursing Research Program (Grant #N17-B01). The table below details the budget for this study.

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personnel</td>
<td>$148,611</td>
</tr>
<tr>
<td>Consultant</td>
<td>$8,000</td>
</tr>
<tr>
<td>Supplies</td>
<td>$59,183</td>
</tr>
<tr>
<td>Equipment</td>
<td>-</td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>--------------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Travel</td>
<td>$6,457</td>
</tr>
<tr>
<td>Other Direct Costs</td>
<td>$7,212.00</td>
</tr>
<tr>
<td>Consortium/contractual costs (HJF)</td>
<td>Direct: $193,597</td>
</tr>
<tr>
<td></td>
<td>Indirect: $26,523</td>
</tr>
<tr>
<td>Total Direct</td>
<td>$449,583</td>
</tr>
</tbody>
</table>

The University of Tennessee Health Science Center, Memphis does not have a master Cooperative Research and Development Agreement (CRADA) with the US Army. The Henry M. Jackson (HMJ) Foundation has a master CRADA with the Department of the Army. By UTHSC subcontracting with the Foundation, the approval processing time for new protocols at Army facilities is significantly reduced and only a statement of work is needed. A letter of commitment has been established with the HMJ Foundation for study personnel that are to work at Blanchfield Army Community Hospital. We plan to subcontract with HJF for this study.

12.0 Facilities to be Used: (32 CFR 219.114)

Blanchfield Army Community Hospital (BACH)
Primary Care Clinic
Physical Therapy Department
650 Joel Drive
Fort Campbell, KY 42223

Byrd Health Clinic, BACH
Primary Care Clinic
Physical Therapy Clinic
Building 7973, Thunder Boulevard
Fort Campbell, KY 42223

Lapointe Health Clinic, BACH
Primary Care Clinic
Physical Therapy Clinic
5979 Desert Storm Ave
Fort Campbell, KY 42223

Campbell Airfield Soldier Centered Medical Home
Building 7149
Black Sheep Run Rd.
Fort Campbell, KY 42223

University of Tennessee Health Science Center
College of Medicine, Department of Neurology
920 Madison, Room WC058
Memphis TN 38163

12.1 Impact statements:
Primary Care Services
Physical Therapy Services
13.0 Time Required to Complete: The timeline below presents an overview of the milestones by month and year for the subacute low back pain project. The study will be completed in 3 years. We will recruit 135 participants in waves of 15-22 every 3-4 months over a period of 24-26 months. In the last 3-4 months of year 3, the last participants will be completing their 9-week intervention and no new recruitment will take place.

<table>
<thead>
<tr>
<th>Year One</th>
<th>1 - 2</th>
<th>3 - 4</th>
<th>5-6</th>
<th>7-8</th>
<th>9-10</th>
<th>11-12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organize Study; Submit IRB application</td>
<td>S</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hire/train personnel</td>
<td>S</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prepare Manual of Operating Procedures (MOOP)</td>
<td>S</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Order equipment/supplies</td>
<td>S</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Develop database</td>
<td>S</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Recruit/screen/test 44 participants</td>
<td>S</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Year Two</td>
<td>13 - 14</td>
<td>15-16</td>
<td>17-18</td>
<td>19-20</td>
<td>21-22</td>
<td>23-24</td>
</tr>
<tr>
<td>Recruit/screen/test 66 participants</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Intervention</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Monitor: Recruitment, adherence</td>
<td></td>
<td>S</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year Three</td>
<td>25 - 26</td>
<td>27-28</td>
<td>29-30</td>
<td>31-32</td>
<td>33-34</td>
<td>35-36</td>
</tr>
<tr>
<td>Recruit/screen/test 25 participants</td>
<td>S</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintain database</td>
<td>S</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete recruitment of participants</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete participant testing</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Analyze statistical data</td>
<td></td>
<td>S</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prepare final report and manuscripts</td>
<td>S</td>
<td>C</td>
<td></td>
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</tr>
</tbody>
</table>

S = Start; C = Complete

14.0 Personnel to Conduct the Study / Researcher Responsibilities

14.1 Principal Investigator: Give the name of this person, and the specific tasks this person will perform during the course of this study. What access to data will this person have?

Principal Investigator: LAURA A. TALBOT, PHD, EDD, RN
Col (Ret), USAFR
Professor
UTHSC College of Medicine
Department of Neurology
855 Monroe Avenue, Suite 412
Memphis, TTN 38163
Phone Number: 901-448-3630
Mobile Phone: 410-428-6157 (cell)
ltalbot@uthsc.edu

RESPONSIBILITIES: Dr. Laura Talbot is a Professor in the Department of Neurology, UTHSC. She received her PhD degree from Texas Women's University and completed a postdoctoral fellowship at the National Institute on Aging (NIA) sponsored by National Institute of Nursing Research (NINR) at NIH. Dr. Talbot has extensive experience in working in the area of clinical research especially with multicenter trials and intervention studies. She is the Principal Investigator for a TSNRP funded study (Patellofemoral Pain Study). She has worked extensively in developing and testing self-management approaches for military members that would return them to duty faster with better outcomes.

Dr. Talbot will serve as the Principal Investigator of our TSNRP grant and be responsible for all aspects of the project. She will assure that research goals are met in a timely manner, with scientific integrity and completed within budgeted amount. She will ensure that all project activities and expenditures are in compliance with UTHSC and TSNRP policy. She will also be responsible for the scientific integrity of the project and will have the leading role in overseeing the entire project to ensure its success. Dr. Talbot will oversee the study staff, as well as coordination of effort among co-investigators. Dr. Talbot will be involved in the analysis, publication and presentation of the study results and will be responsible for communications with TSNRP project office and for assuring that all reports are submitted on time. Col (ret) Talbot served 30 years in the US Air Force on Reserve and Active Duty status.

DATA ACCESS: As the PI, Dr. Talbot will have access to identifiable data.

CONSENT: As the PI, Dr. Talbot will be authorized to obtain consent. She will have contact with participants.

On-Site Principal Investigator:
VANESSA J. RAMIREZ, PT, DPT, OCS
Major, USA, Army Medical Specialist Corps
OIC, AMH Physical Therapy
Air Assault FMH Physical Therapist
Blanchfield Army Community Hospital
Ft. Campbell, KY 42223
Office: 270-461-2475
vanessa.j.ramirez.mil@mail.mil

RESPONSIBILITIES: Dr. (MAJ) Vanessa Ramirez, DPT, is a board certified physical therapist in orthopedics and the OIC, AMH Physical Therapy at Blanchfield Army Community Hospital, Fort Campbell. She is a licensed physical therapist and has over 14 years’ experience working in military physical therapy clinics. As the on-site PI, MAJ Ramirez will be responsible for the day-to-day supervision of the project at BACH. She will oversee the BACH co-investigators, as well as coordination of effort among BACH co-investigators at the clinics. She will oversee recruitment at BACH. MAJ. Ramirez will be involved in the planning of the interventions, analysis, publication and presentation of the study results.

DATA ACCESS: As the on-site PI, MAJ (Dr.) Ramirez will have access to identifiable data.
CONSENT: As the on-site PI, MAJ (Dr.) Ramirez will be authorized to obtain consent. She will have contact with participants.

14.2 Associate Investigator/s:

Keith L. Garcia
MAJ, AN, DNP, NP-C
BACH, Fort Campbell, KY
Office: 206-321-5273
keithbarry.l.garcia.mil@mail.mil

RESPONSIBILITIES: MAJ Garcia is a licensed family nurse practitioner at Blanchfield Army Community Hospital. He will work with the research team and PI as a military nurse advisor. He will assist in recruitment and referral from the primary care clinics at BACH.

DATA ACCESS: MAJ Garcia will not have access to the data.

CONSENT: MAJ Garcia will not obtain consent. He will have contact with participants.

Tammy M. Smoak, PA-C, MHA
Major, USA
Chief, Soldier Health Services (SHS)
OIC, LaPointe Health Clinic (LHC)
Ft. Campbell, KY 42223
Office: 270-412-8696
BB: 931-217-5838
tammy.m.smoak.mil@mail.mil

RESPONSIBILITIES: Dr. (MAJ) Smoak is a licensed physician assistant at the LaPointe Health Clinic, BACH. She will contribute to the intervention content and deliver, monitor treatment fidelity in the study arms, and assist in oversight of recruitment and retention at the LaPointe Health Clinic (primary care section). As the Chief of Soldier Health Services and physician assistant, MAJ Smoak will provide oversight of the project in MEDDAC’s primary care clinics that offer Soldier health services.

DATA ACCESS: Dr. Smoak will have access to identifiable data.

CONSENT: Dr. Smoak will not obtain consent. She will have contact with participants.

Jennah R. Bulen, PT, DPT
CPT, USA, Army Medical Specialist Corps
Physical Therapist
Ft. Campbell, KY 42223
Office: 270-412-8683
Email: Jennah.r.bulen.mil@mail.mil

RESPONSIBILITIES: Dr. (First Lieutenant) Jennah Bulen, DPT, is a licensed Physical Therapist at the LaPointe Health Clinic, BACH. She will contribute to the intervention content and deliver, monitor treatment fidelity in the study arms, and assist in oversight of recruitment and retention at the LaPointe Health Clinic (physical therapy section).

DATA ACCESS: Dr. Bulen will have access to identifiable data.

CONSENT: Dr. Bulen will not obtain consent. She will have contact with participants.

Lee Webb, DPT
Director of Physical Therapist
Byrd Health Clinic, BACH
RESPONSIBILITIES: Dr. Lee Webb is a licensed physical therapist and the Director of Physical Therapy services at the Byrd Health Clinic. He will provide study oversight at the Byrd Health Clinic. He will monitor treatment fidelity in the study arms, and assist in oversight of successful recruitment and testing at the Byrd Health Clinic.

DATA ACCESS: Dr. Webb will have access to identifiable data.

CONSENT: Dr. Webb will not obtain consent. He will have contact with participants.

Samantha Peterson, PT, DPT
Byrd Health Clinic, BACH
Civilian - Army
Ft. Campbell, KY 42223
Office: 270-461-1135
Email: samantha.l.peterson6.civ@mail.mil

RESPONSIBILITIES: Dr. Peterson is a licensed physical therapist at the Byrd Health Clinic. She will provide study oversight at the Byrd Health Clinic with Dr. Webb. She will monitor treatment fidelity in the study arms, and assist in oversight of successful recruitment and testing at the Byrd Health Clinic.

DATA ACCESS: Dr. Peterson will have access to identifiable data.

CONSENT: Dr. Peterson will not obtain consent. She will have contact with participants.

E. JEFFREY METTER, MD
Col (Ret), USAR
Professor
University of Tennessee Health Science Center, COM, Department of Neurology
415 Link Building 855 Monroe Avenue
Memphis, Tennessee 38163
Phone Number: ( 901) 448-6199
Fax: (901) 448-7440
E-mail: emetter@uthsc.edu

RESPONSIBILITIES: Dr. Jeffrey Metter is a Professor in Neurology, UTHSC. He is a neurologist with a specialty in muscular strength, function and neuromuscular disorders. He was previously an Associate Professor at the Johns Hopkins School of Medicine, Department of Neurology. Dr. Metter’s expertise in directing longitudinal investigations in the area of physical activity, muscle strength and body composition uniquely qualifies him to assist the principal investigator in project design and dissemination. He will assist with the planning of the study, and in the analysis and interpretation of the findings. Dr. Metter will be involved in the publication and presentation of the study results.

DATA ACCESS: Dr. Metter will have access to coded data.

CONSENT: Dr. Metter will not obtain consent. He will not have contact with participants.

BARBARA JENNINGS, M.A., O.D., F.A.A.O.
Senior Research Assistant/ Data Manager (UTHSC)
University of Tennessee Health Sciences Center
College of Medicine, Department of Neurology
920 Madison, Room WC058
Memphis TN 38163
Responsibilities: The responsibilities of the senior research assistants/data managers are to work with all the staff in support of Human Use issues and data management. Under the direction of the PI, she will assist in the maintenance of the database, data entry, securing and maintaining data files, coordinating team meetings, ordering supplies, and assist in the maintenance of subject files for the study.

Data Access: Ms Bryndziar and Dr. Jennings will have access to identifiable data.

Consent: Ms. Bryndziar and Dr. Jennings will not obtain consent. They will have contact with participants.

Responsibilities: The Clinical Research Coordinator will serve as study’s project director and intervention manager, under the direct supervision of the principal investigator (Dr. Talbot), and on-site PI (MAJ Ramirez) as such will be responsible for the day-to-day operations of the project. The Clinical Research Coordinator’s major duties will encompass coordination of all aspects of the study including: (1) directing subject recruitment; (2) coordinating subject screening for eligibility, data entry and scheduling of training sessions and clinic visits (3) assisting in subject testing and data collection; (4) monitoring subject data for completeness and accuracy; (5) performing oversight of staff activities; and (6) coordinating with USARIEM for participant testing. The coordinator’s responsibilities also include all aspects of the implementation of all Self-Managed interventions and teaching the PEP. Specifically: (1) scheduling and conducting subject examinations; (2) training and monitoring participants randomized to the intervention; (3) teaching participants the PEP, teaching the 3 interventions, scheduling the training and testing, and training-the-trainers; (4) teaching the protocols and monitoring participants; (5) collecting, organizing and analyzing data obtained from the subject in the intervention; (6) monitoring for adverse events and consulting with the medical monitor and PI in regard to participant safety issues If no medical monitor is required by the IRB, adverse events will be reported to the PI.; (7) coordinating the screening for eligibility, data entry and scheduling of training sessions and clinic visits; and (8) monitoring adherence for all groups. The Clinical Research Coordinator will train-the-trainers on the intervention and monitor the teaching for consistency. The Clinical Research Coordinator will participate in the weekly research meetings and assist in the
maintenance of subject files for the study. The Clinical Research Coordinator will be certified in either Basic Life Support.

**DATA ACCESS:** The project manager will have access to identifiable data.

**CONSENT:** Clinical Research Coordinator will obtain consent. She will have contact with participants.

Kayla Enochs, B.S.
Rehabilitation Specialist
LaPointe Health Clinic
Fort Campbell, KY 42223
(O) 270-412-3778
(E) Kaya.c.enochs.ctr@mail.mil
Rehabilitation Specialist
Civilian - HJF
Ft. Campbell, KY 42223

**RESPONSIBILITIES:** The Rehabilitation Specialist will work with the clinical research coordinator with the intervention and testing of the participants. Under the direction of the PI, on-site PI and clinical research coordinator, this individual will assist the clinical research coordinator in the recruitment and retention of subjects, screening for eligibility, teaching the interventions, testing of participants, and scheduling & monitoring of participants. The Rehabilitation Specialist will participate in the weekly research meetings and assist in the maintenance of subject files for the study. The Exercise Training Specialist will be certified in either Basic Life Support.

**DATA ACCESS:** The Exercise Training Specialist will have access to identifiable data.

**CONSENT:** Physical Therapy Assistant will obtain consent. S/he will have contact with participants.

14.3 Biostatistician/Consultant:

CHRISTOPHER H. MORRELL, PHD, CIVILIAN
Professor, Statistics
Loyola University Maryland
Baltimore, Maryland

**RESPONSIBILITIES:** Dr. Chris Morrell’s research focus is linear mixed-effects and GEE models. These models can be used to analyze and describe repeated measures data from experimental studies. Dr. Morrell will serve as the biostatistician. He will be responsible for conducting all the statistical analyses, preparing the statistical reports, and performing ad hoc analyses as necessary over the course of the trial to satisfy data safety monitoring requirements. Dr. Morrell will be involved in the analysis, publication, and presentation of the study results.

**DATA ACCESS:** Dr. Morrell will have access to coded data.

**CONSENT:** Dr. Morrell will not obtain consent. He will not have contact with participants.

14.4 Collaborator/consultants:

**Consultant**
Candy Wilson COL, AN
Graduate School of Nursing
Uniformed Services University of the Health Sciences
4301 Jones Bridge Road
RESPONSIBILITIES: COL (Dr.) Wilson is in the U.S. Air Force Nurse Corps and Faculty at the Uniformed Services University of the Health Sciences, Graduate School of Nursing. Her expertise in intervention studies and functional outcomes in wounded military members uniquely qualifies her to assist the PI in project design, implementation, and dissemination. She will also participate in preparation of project reports and manuscripts of the study findings.

DATA ACCESS: Dr. Wilson will not have access to the data.

CONSENT: Dr. Wilson will not obtain consent. She will not have contact with participants.

14.3 Technical Staff: N/A

14.4 Conflict of Interest Disclosure: List the specific conflicts of interest that any person listed above has in being associated with this study. Conflicts of interest include significant financial gain, incurring favor with current or future employers, and any other benefit that could be construed as compromising the judgment and independence of an individual. Conflicts of interest apply to the individual and his/her immediate family members. All personnel associated with this study will additionally have to complete a conflict of interest disclosure form.

15.0 Affirmation of Principal Investigator: (must be updated with each new PI)

15.1 “As the Principal Investigator, I confirm that I have read and will comply with the DDEAMC Human Research Protection Program (HRPP), Chapter 13, Investigator Responsibilities as available at, http://www.ddeamc.amedd.army.mil/clinical/investigation/documents/HRPP.pdf. The protection of research subjects is the shared responsibility of Principal Investigator (PI), Associate Investigators (AIs), Careline/Department Chief, members of the research team, and the DDEAMC Institutional Review Board (IRB). However, the ultimate responsibility for the safety and welfare of research subjects lies with the PI.”

15.2 “I am aware that I am not authorized to accept any funds or other form of compensation for conducting this research.” (DoD personnel)

16.0 Date prepared: 24 July 2017

17.0 References: List all sources of information on a separate page after signature blocks. Make sure all references are numbered in the order that they are presented in this protocol.


98. AFHSC AFHSC. Defense Medical Surveillance System (DMSS). Silver Spring, MD 2014.

PRINCIPAL INVESTIGATOR (overall)
Colonel (retired)
Professor (University of Tennessee Health Science Center)

PRINCIPAL INVESTIGATOR (on-site)
Major
OIC, AMH Physical Therapy