Manual Therapy and Strengthening for the Hip in Older Adults with Chronic Low Back Pain (MASH Trial)

NCT04009837

02/21/2020

Original Protocol Title:

Evaluating the Effects of Two Different Physical Therapy Interventions for Low Back Pain in Older Adults: A Multi-Site Clinical Trial

HUMAN SUBJECTS PROTOCOL
University of Delaware

Protocol Title: **Evaluating the Effects of Two Different Physical Therapy Interventions for Low Back Pain in Older Adults: A Multi-Site Clinical Trial**

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Investigator Assurance:

By submitting this protocol, I acknowledge that this project will be conducted in strict accordance with the procedures described. I will not make any modifications to this protocol without prior approval by the IRB. Should any unanticipated problems involving risk to subjects occur during this project, including breaches of guaranteed confidentiality or departures from any procedures specified in approved study documents, I will report such events to the Chair, Institutional Review Board immediately.

1. **Is this project externally funded? X** YES NO

If so, please list the funding source: NIH/NIA 2 R01 AG041202-06

2. Research Site(s)

X University of Delaware (Clinical Research Laboratory: DE Spine Studies)

X Other (please list external study sites): University of Pittsburgh PT Clinical and Translational Research Center; Duke Clinical Research Institute

Is UD the study lead? **X** YES ☐ NO (If no, list the institution that is serving as the study lead)

3. **Project Staff**

Please list all personnel, including students, who will be working with human subjects on this protocol (insert additional rows as needed):

NAME	ROLE	HS TRAINING COMPLETE?
Gregory E. Hicks, PhD, PT	UD Principal investigator	YES
J. Megan Sions, PhD, DPT, PT, OCS	UD Investigator	YES
Ryan Pohlig, PhD	UD Biostatistician	YES
Peter Coyle, PhD, DPT, PT	UD Clinical research scientist	YES
Jennifer Pugliese, PT	UD Research physical therapist	YES
Angela Dickerson-Schnatz, PT	UD Research physical therapist	YES
Emma Beisheim, DPT, PT	UD Graduate researcher	YES
Patrick Knox	UD Graduate researcher	YES
Mayank Seth	UD Post-doctoral researcher	YES
Kameelah Slater	UD Undergraduate researcher	YES
Alexandria Sisofo	UD Undergraduate researcher	YES
Justin Brown	UD Undergraduate researcher	YES
Taden Gery	UD Undergraduate researcher	YES
Jocelyn Coholich	UD Undergraduate researcher	YES
Chesca Basilio	UD Undergraduate researcher	YES
Alimah Granieri	UD Undergraduate researcher	YES
Ryan Hogan	UD Undergraduate researcher	YES
Casey Weinstein	UD Undergraduate researcher	YES
Jessica Meek	UD Undergraduate researcher	YES
Andrew Hunt	UD Undergraduate researcher	YES

4. **Special Populations**
Does this project involve any of the following:

Research on Children? **No**

Research with Prisoners? **No**

If yes, complete the Prisoners in Research Form and upload to IRBNet as supporting documentation

Research with Pregnant Women? **No**

Research with any other vulnerable population (e.g. cognitively impaired, economically disadvantaged, etc.)? please describe: **Not applicable**

5. **RESEARCH ABSTRACT Please provide a brief description in LAY language (understandable to an 8th grade student) of the aims of this project.**

Low back pain (LBP) is the most frequently reported musculoskeletal problem and the third most frequently reported symptom of any kind in people over the age of 75.[1-5] In fact, 17.3% of all visits to physicians for LBP involve people over the age of 65.[1,6,7] Between one-quarter and one-third of all older adults have may have LBP.[8] Given LBP occurrence, the related costs to society are substantial. First, the financial burden associated with LBP management is significant; for example, over a period of 10 years, Medicare data indicates a 132% increase in LBP patients and a 387% increase in related charges for LBP.[9] In addition to the financial cost for LBP management, there are also the downstream costs related to progressive disability in this group that must be considered. Several large, longitudinal studies have demonstrated that LBP, among older adults, is associated with a steeper rate of decline of mobility function (i.e. walking speed, chair rise performance, balance).[10-12] In this age group, poor and/or declining mobility function is predictive of increased future risk for death, institutionalization and overall disability.[13-17] The prevalence, cost and functional consequences demonstrate the public health significance of LBP in the geriatric population; as such, there is a great need for the development of effective treatments to reduce pain, improve function and limit costs.

While there is longstanding expert agreement that LBP patients should be classified into subgroups prior to treatment,[18-20] no classification systems specific to the geriatric LBP population have been developed. There is strong evidence that classification approaches, where treatments are matched to the patient's limitations of that specific sub-group, can improve outcomes for patients undergoing physical therapy treatment for LBP.[21-24] To develop effective treatments, we must develop appropriate classification systems for older adults with chronic LBP.

Our preliminary data from the initial testing of the proposed hip-focused treatment among older adults with LBP suggest that this LBP subgroup may have a more favorable treatment response when the identified hip deficits, i.e. limitations, are also addressed. Therefore, the natural next step is to refine and further explore this hip-focused treatment for this newly identified at-risk subgroup (i.e. those with hip pain and weakness) through a well-controlled clinical trial. We propose a multi-site, single-blinded (i.e. examiners will not know participant treatment group assignment), randomized-controlled (i.e. participants will have an equal chance of getting 1 of 2 treatment plans), trial that advances findings from our previous study. We will recruit a total of 180 older adults with LBP of at least 3 months duration (i.e. chronic LBP) who are classified as members of the at-risk hip-spine subgroup. We will investigate whether a hip-focused treatment plan warrants further investigation as an approach to improve LBP and outcomes among older adults with chronic LBP. Manual therapy techniques will be used to address hip joint pain and progressive strengthening will be used to address hip weakness in one treatment group as compared to a LBP-focused treatment including manual therapy techniques to the low back region and low back muscle stretching. We will measure disability, LBP intensity, physical function (i.e. walking speed, chair rise performance, balance) and clinical hip deficits at baseline and after 8 weeks of intervention. We will also do a follow-up at 6 months (16 weeks post-treatment) to assess whether improvements hold from post-treatment to 4 months post-treatment.

The goals, i.e. specific aims, of the proposed research are to:

1. Explore whether a hip-focused treatment leads to reduced disability and improved physical function when compared to a low back-focused treatment in an at-risk hip-spine subgroup (i.e. those with both hip pain and weakness, in addition to low back pain).
2. Determine what contributes to improvements in disability and physical function in this at-risk hip-spine subgroup.

6. **PROCEDURES Describe all procedures involving human subjects for this protocol. Include copies of all surveys and research measures.**

Study Participants.
Participants with moderately intense (LBP rated at least 4/10), chronic LBP (pain of at least 3 months) that impacts daily activities with concurrent hip pain and hip weakness will be recruited from newspaper and online advertisements, as well as from databases of former study participants who have agreed to be contacted for future studies. The sample will be recruited from one of three areas in this multi-site clinical trial: Newark, DE and surrounding communities, Pittsburgh, PA and surrounding communities and Durham, NC and surrounding communities.

Design and Randomization Plan.
In total, 180 participants meeting the inclusion/exclusion criteria will be randomly assigned into one of two intervention groups: (1) spine treatment supplemented with a hip-focused manual therapy and hip-focused exercise intervention, or (2) spine-focused rehabilitation with stationary cycling. We will use statistical software to generate a randomization plan that ensures by the end of the study that an equal number of participants are randomly assigned to each of the two treatment conditions. We will perform randomization separately in men and women given the reported sex differences in pain conditions among older adults[25]; this approach will ensure equal randomization of men and women into both randomization groups. The treatment assignments will uploaded into the web-based data entry application for the study. A participant's study allocation will be revealed to approved study personnel (i.e. not physical therapy testers) once all eligibility criteria have been entered and eligibility is confirmed.

Pre-Entry Phase. Potential exclusions will be examined in two phases, first over the telephone using a structured questionnaire, then on-site with a standardized history and physical examination performed by a licensed physical therapist to validate the inclusion and exclusion criteria obtained by telephone. All of the on-site screening procedures will be performed after individuals have signed informed consent. All persons screened via phone or on-site will be assigned a number. If they are ineligible, a reason will be listed. They will also be asked if they would like to be contacted for future studies. If they verbally consent to future contact, their name, age, and contact information will be kept in a separate password protected folder under an encrypted UD server. All other documents will be shredded.

Assessments. All participants who are included based upon the screening criteria will receive identical pre-treatment assessments. A trained research assistant (masked to the intervention assignment) will administer outcome measures at baseline, prior to randomization. The same assessments will be made at the end of the intervention (i.e. 8 weeks post-enrollment) and 16 weeks post-treatment (i.e. 6 months post-enrollment).

Primary Outcome Measures

Self-Report Measures: These questionnaires evaluate self-perception:

1. Pain-Related Disability: The Quebec Back Pain Disability Scale[26], is reliable and valid questionnaire, which assesses low back pain-related disability. It has an established minimally clinically important change of 30%.[27]

2. Pain Severity: Pain Thermometers (which have excellent reliability in older adults[28,29]) will be used to assess pain severity in both the lumbar spine and hip at baseline, post-treatment, and 6 months.

3. Patient-Reported Outcomes Measurement Information System (PROMIS)-29:[30-34] Developed by

the National Institutes of Health (NIH), the PROMIS-29 is a bank of questions for the clinical research community. It has demonstrated good reliability and construct validity for evaluating health-related quality-of-life. The PROMIS-29 profile includes questions assessing the following domains: physical function, anxiety, depression, fatigue, sleep disturbance, ability to participate in social roles and activities, pain interference, and pain intensity.

Functional Performance Measures: Observed measures of functional performance that focus on mobility-related function will be included because observed measures and self-report measures evaluate distinct constructs. Performance will be assessed with the:

1. 10 Meter Walk Test: This is a reliable[36] and valid[37] test that asks participants to walk along a linear pathway. The test will be conducted at the participants 'usual pace' and 'as quickly as possible, but safely' for three trials per condition. Average gait speed will be determined using the central 6 meters of the course, allowing for 2 meters of acceleration and deceleration at either end. The minimally clinically important change is .07 m/sec.[38]

2. Timed Get-Up-and-Go (TGUG)[39-41]: This test measures the time it takes a person to rise from a standard height chair (seat height 46 cm) with armrests, walk 3 meters, and return to a seated position in the same chair. One practice test is performed followed by three recorded trials. The test has proven to be reliable and valid for quantifying functional mobility in a variety of patient populations.

3. Six-Minute Walk Test: This test measures the distance that a person walks during a six minute timed period. This test has been used extensively to evaluate exercise tolerance in older adults.[42] We will ask patients to report their low back pain intensity (0-10) before walking and at each minute of the test.

Adverse Events: The occurrence of AEs is monitored for each participant on an ongoing basis throughout the study by all study staff who interact with the participant, including during on-site assessment visits, intervention sessions and during monthly phone calls between the immediate post-intervention assessment and the final assessment at 6 months.

An adverse event (AE) will be defined as any unfavorable or untoward medical occurrence in a human study participant, including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participant's involvement in the research, whether or not considered related to participation in the research.

Some examples of adverse events include:

- Any new and pre-existing symptoms or conditions that have become worse either in frequency or severity or both, even if the event was not caused by the study treatment or procedure.
- Any recurrence of previously resolved condition whether or not it is related to the study treatment or procedure.
- Any clinically significant findings from the study-related or non-study related procedures such as vital sign measurements, physical exams and any other procedures.

A serious adverse event will be considered one that:

- Results in death
- Is life threatening, or places the participant at immediate risk of death from the event as it occurred

- Requires or prolongs hospitalization
- Causes persistent or significant disability or incapacity
- Is another condition which investigators judge to represent significant hazards

After consent and prior to randomization, only adverse events that are a direct result of study procedures determined by the site principal investigator (PI) or occur while the participant is under study staff supervision will be recorded. Examples of AEs that will be tracked prior to randomization include (but not limited to): falls during the functional testing or emotional distress caused by the questionnaires. Following randomization, all AEs, regardless of relationship to study procedures, will be collected until the end of the study.

Secondary Outcome Measures

Self-Report Measures

1. Research Task Force (LBP) Impact Score[43]: This will be used to assess the personal impact of LBP. Impact is defined as a combination of pain intensity, pain interference with normal activities and function, using 9 items from the 29-item PROMIS short form (score range: 8-50). NOTE: This questionnaire will also be used as part of inclusion/exclusion screening.

2. Low Back Activity Confidence Scale: A relatively new questionnaire that measures a person's confidence in their ability to perform 15 different activities, including carrying, pushing, sitting, walking, and exercising, that may be directly affected by low back pain. Reliability and validity has been previously established.[44]

3. Keele STarT Back Screening Tool (SBT)[45,46]: This tool was developed as a stratified approach to subgrouping patients with low back pain in the primary care setting based on prognostic factors. Using this 9-item screening tool, physical and psychosocial factors help identify subgroups of patients and match them with targeted interventions. The STarT has acceptable test-retest reliability and predictive validity for long-term disability outcomes in patients with chronic low back pain. A total score (0-9) and psychosocial subscore (0-5) are calculated in which subscores (questions 5-9) of >/= 4 constitute patients who are considered "High Risk". Total scores of >3 with subscores (questions 5-9) of <4 constitute "Medium Risk," but both physical and psychosocial prognostic factors are present. Patients scoring 0-3 are considered "Low Risk".

4. Hip Disability and Osteoarthritis Outcome Score (HOOS)[49]: This responsive and valid measure is comprised of 40 items across five domains (pain, symptoms, activity of daily living, sport and recreation function and hip-related quality-of-life), which together yield a hip-related disability and osteoarthritis outcome score. It should be noted that Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[39] scores can be calculated from this questionnaire. NOTE: This questionnaire (HOOS items P4-P8, raw scores) will also be used as part of inclusion/exclusion screening.

5. Pain Catastrophizing Scale: This scale has 13 items assessing how individuals perceive pain, where each item is rated 0 (not at all) to (4) all the time. Items can be scored as three subscales to evaluate the constructs of rumination, magnification, and helplessness. It has established test-retest reliability and validity in patients with chronic low back pain.[52]

6. Patient Health Questionnaire-9 item (PHQ-9)[53-57]: The Patient Health Questionnaire-9 item (PHQ-9) is a reliable, valid, and responsive measure of depression severity, where scores of ≥ 10/27 have a sensitivity of 88% and specificity of 88% for major depression. In brief, we will use a cut-point of ≥10/27 as an indicator of major depression and refer participants back to their primary care providers in these cases, with a written letter. We will also provide these participants with the crisis hotline

number (i.e. Crisis Intervention Services of Northern Delaware: 302-577-2484 or 1-800-652-2929), which is staffed 24 hours/day, 7 days a week, to whom they can reach out if they feel desperate, hopeless, and/or at risk for suicide. The 9th item on the PHQ-9 has been identified as a consistent predictor of suicide attempts and suicide deaths in large primary care and population studies. If the participant endorses 1, 2, or 3 on the 9th item of the PHQ-9, we will offer to put participants in touch with the crisis hotline while the participant is at the facility and provide a letter for the participant to share with their primary care provider. Scores of ≥10/27 and/or endorsement of the 9th item will not render the participant ineligible.

Functional Performance Measures:

1. Functional Reach Test: Participants are asked to reach forward as far as possible 3 times without losing their balance, touching the wall, or taking a step. Three trials are completed using the dominant arm; distance reached is recorded. This test has been used to assess anterior-posterior trunk stability and has established test-retest reliability among older adults.[58,59]

2. 30 Second Chair Stand Test: Participants are seated in a standard chair with their arms crossed over their chest. They are then asked to stand up and sit back down as many times as possible in 30 seconds. They are asked to rate their LBP intensity before performing the test and every 10 seconds of the test using a 0-10 pain rating scale. Test-retest reliability has been established in older adults with hip involvement.[60]

Other Self-Report Measures: The following self-report measures, which will be administered at baseline, 8 weeks, and 6 months, will allow for characterization of the participant sample for future publications and will allow us to evaluate for between-group differences:

(1) Demographics Questionnaire: Includes questions related to sex, age, marital status, surgical history, race, ethnicity, and education level. NOTE: Will only be completed at baseline.

(2) Comorbidity Questionnaire[61]: Asks about current and past health since the age of 55 years and how much each health condition affects daily activities (o=none; 3=quite a bit). Covers the following domains: cardiac, respiratory, musculoskeletal, neurologic, general, cancer, diabetes, and visual. NOTE: Will only be completed at baseline.

(3) Medication Sheet: Participants will be asked to list all medications they have taken in the past 2 weeks and specify medication dose and frequency. This will enable us to document medications used to treat low back pain in this population, including pain medications, anti-spasmodics, and anti-depressants. Completion of these sheets will also allow us to see whether the participant's dose or frequency changes over the course of the intervention. The general Medication Sheet be sent in mailer prior to the onsite evaluation for completion. The Pain Medication sheet will be completed in the electronic system by the evaluating physical therapist using the general medication sheet as a reference.

Screening Measures: The following measures will be administered at the onsite assessment at baseline to determine participant eligibility:

1. Mini Mental State Examination (MMSE)[62,63]: This 30-item questionnaire, which takes <8 minutes to administer, is the most commonly administered cognitive screening. Scores <24 suggests uncertain reliability of participant answers on self-reported outcome measures due to impaired cognition and thus, all participants must score at least a 24 to be included in the study. Participants with scores <24 will be given a letter to share with their primary care provider.

2. Blood Pressure Assessment: To maximize participant safety, blood pressure screening in both arms will occur at the start of each evaluation/re-evaluation (at a minimum). The average of the two pressures will be used to make a determination as to whether or not the participant is safe to enroll in the study, which includes exercise (regardless of group assignment). Participants with systolic readings of ≥180 mmHg and/or diastolic readings of ≥110mmHg will be excluded; these participants will receive a letter with their results and will be encouraged to share these letters with their primary care provider. Examiners will follow established study guidelines when interpreting blood pressure at re-evaluation visits.

Other Clinical Measures: The following additional tests and measures will also be performed:

(1) Anthropometric Measurements: These will include height and weight for determination of body mass index (BMI). Hip strength will also be normalized to body weight.[64]

(2) Lower-Limb Landmark Measurements[64,65]: Hip strength outputs are impacted by the lever arm (amongst other variables), therefore, we will take lower-limb landmark measurements to allow consideration of lever arms when interpreting hip strength data.

(3) Quantitative Sensory Testing: Pressure pain sensitivity will be assessed using a digital force gauge with a 1-cm^2 flat rubber tip to four different sites on the right and left side of the body: upper trapezius, posterior superior iliac spines, greater trochanters, and tibialis anterior. Pressure will be applied to each region, incrementally, until the participant perceives the first onset of pain, at which time they will verbalize 'pain' and testing will cease. Each site will be assessed 3 separate times, alternating between sides for each trial.[66-69]

(4) Hip Strength: We will assess hip internal rotation (used to help determine participant eligibility), hip external rotation, hip extension, and hip abduction strength using a hand-held dynamometer with standardized methods that have demonstrated good-to-excellent reliability.[70,71] The highest measurement of three, 3-second trials with a 5-second pause between trials will be used in data analyses.

(5) Hip Special Tests: We will perform the following hip special tests:
a) *Scour's Test*[72]: This test is a pain-provocation test used in evaluating adults with hip osteoarthritis. While the participant is supine, the hip is passively flexed and then hip adduction is introduced. The examiner compresses the femur into the acetabulum and then passively internally rotates and adducts the hip looking for provocation of symptoms in the lateral hip or groin region. Symptom reproduction is considered a positive test.
b) *Modified Thomas Test*: This test is used to assess tightness of the 1-joint hip flexors. Using an inclinometer, examiners will measure hip position with the contralateral knee flexed and the ipsilateral leg lowered to the table via gravity.[73] Reliability and validity has been previously established.[74]

(6) Hip Range-of-Motion (ROM): ROM of the hip joint, i.e. flexion, internal and external rotation, will be assessed by using a standard goniometer or inclinometer. We will use standardized methodology that has been demonstrated to be reliable.[75] Hip pain with active movements will be recorded for hip flexion and extension and passive hip flexion, as well as internal and external rotation.

Additional Participant Communication:
(1) Follow-Up Phone Calls: To assist with retaining participants over the course of the study, we will conduct monthly phone calls at 3, 4, and 5 months post-enrollment in the study. Each telephone call will be <20 minutes and will ask questions related to falls, hospitalizations, emergency room visits, pain (including low back and hip pain], co-interventions, and exercise compliance, as outlined in the Health Status Update Form. In some cases (e.g. falls, hospitalizations, endorsement of 'moderately

worse' low back or hip pain, the study staff member will need to complete the Possible Adverse Event Reporting and/or Adverse Event Reporting Forms.

(2) Face Sheets for Mailing Packet: Includes pertinent information for our participants and will serve as a written notification of their appointment date and time. This will also review information provided over the phone.

Interventions

Licensed physical therapists (PTs) will be trained to ensure competence and reliability in delivery of the interventions. All participants will be seen twice weekly for 65 minutes by a licensed PT for a total of 16 visits. Both groups will receive trunk muscle training exercises targeting the abdominal and low back muscles as well as moist heat to the low back region.

Home Exercise Program: Both groups will have home programs with exercise logs that they will be asked to complete at least twice weekly, in addition to their physical therapy appointments. It is estimated that their home programs will take <30 minutes/session. Prescribed exercises will be nearly identical to the ones done during treatment, but will not include exercises that require close supervision by a licensed PT, i.e. functional hip exercises. Home programs will be initiated during the first treatment session. Participants will be given a pictorial exercise handout.

GROUP 1: Hip-Focused Intervention. The hip-focused intervention will consist of: (1) moist heat to the low back [10 min]; (2) hip manual therapy [20 min]; (3) hip strengthening exercises [20 min]; and (4) trunk muscle training [15 min].

The manual therapy intervention is based on the protocols used by Hoeksma and colleagues[76,77] which have demonstrated efficacy in the treatment of primary hip osteoarthritis. Treatment will be delivered to both hips. The following techniques will be applied: (a) supine long-axis distraction manipulation in flexion, abduction and internal rotation; (b) supine anteroposterior hip mobilization with hip and knee flexed; (c) prone posteroanterior hip mobilization, and (d) lateral femoral glide with internal rotation using belt. For technique (a), the PT performs 3 sets of sustained stretches for 30 seconds followed by traction manipulations. For techniques (b-d), the PT performs 3 sets of grade III-IV joint mobilizations for a duration of 30 seconds/set. Mobilizations will be followed with manual stretching of the hamstrings and hip flexors by the physical therapist.

The hip strengthening intervention will include a progressive protocol focused on isolated strengthening of the hip abductor, extensor internal andexternal rotator muscles, as well as a functional hip training component. The progressive strengthening component will use elastic tubing and is based on the work of Khayambashi et al,[78] which resulted in hip strength gains from 32-56%. In our preliminary evaluation of the hip intervention in a UD clinical pilot trial, we saw a signal for improvement in gait speed (+.07m/s), but it was not as strong as the changes in pain. Therefore, we added a functional hip progression, including mobility-focused hip exercises, which we anticipate will transfer into greater performance-based mobility gains. See Table 2 for an overview of the hip exercise program.

Functional Hip Exercises

Table 2.	Standardized Hip Strengthening Progression			Functional Hip Exercises
Weeks	Set 1* (12)	Set 2* (12)	Set 3* (12)	[Done with appropriate guarding by licensed PT.]
1-2	Yellow	Yellow	Red	High Step Marching (2 minutes), Side Stepping in both directions (2 minutes), Forward Step-Ups (3 sets, 12 repetitions)
3-4	Red	Red	Green	
5-6	Green	Green	Blue	Forward Band Walking (2 minutes), Side Band Walking(2 minutes), Lateral Step-Ups (3 sets, 12 repetitions)
7-8	Blue	Blue	Black	
*Values are band color, indicating resistance level. Yellow offers the lowest resistance (3 pounds) and Black is the highest resistance in this sequence (7.3 pounds). The number of repetitions is given in parentheses for each set.				

The trunk muscle training (TMT) program, which was recently used by the principal investigator in a randomized clinical trial[79] among older adults with chronic LBP, is based on evidence from the biomechanical and electromyography studies done by McGill et al[80]. The following muscle groups have been identified in the literature as primary active stabilizers of the trunk: rectus abdominus, transversus abdominus, oblique abdominals, multifidus and erector spinae (see Table 3). The goal of this stabilization program is to increase muscle stiffness and thereby create sufficient stability in the spine through motor control system re-education. The treating PT progresses each patient through the same criterion-based program as each individual patient achieves the specific goals. For each exercise, the goal is that the participant will perform at least 30 repetitions before they can progress to the next exercise in the group. Once achieved, he or she is allowed to progress to the next exercise. With this criterion-based program, if the patient immediately could meet a specific requirement, then he or she could advance to the next exercise. At each exercise session, the participant will perform at least one exercise from each of the targeted muscle groups.

Table 3. Overview of Trunk Muscle Training Program		
Muscle	**Importance of Muscle**	**Examples of Exercise Progression**
Transversus Abdominus (TrA)	• Draws in abdominal wall • TrA may activate in a feed-forward mechanism to stabilize the trunk for extremity motions	Abdominal Bracing in supine>> Bracing in hook-lying with arm movements>> Abdominal Bracing in standing Possible Substitutions: holding breath
Erector Spinae/ Multifidus	• Extend the spine • Segmental extensors co-contract with anterolateral abdominals to stabilize trunk	Single arm lifts-standing while leaning with elbows resting on countertop>> Single arm lifts-prone over bolster>> Progress to quadruped with arm lift
Rectus Abdominus	• Primary flexor of the trunk	Curl ups as described by McGill-- maintain neutral spine & avoid excessive trunk flexion
Oblique Abdominals	• Co-contracts with multifidus for trunk stabilization, generates side-bending and rotation forces in	Same as above for transversus abdominus

GROUP 2: Spine-Focused Intervention. This intervention will consist of: (1) moist heat to the low back [15 min]; (2) manual therapy to the lumbar spine [15 min]; (3) trunk muscle training [20 min]; (4) lumbar flexibility exercises [5 min]; and (5) stationary cycling without resistance [10 min]. The intervention was developed from the synthesis of clinical practice guidelines for younger populations, which consistently recommend exercise-based therapy and advice to remain active,[81,82] balanced with our team's clinical and research experiences with the geriatric LBP population. While guidelines suggest minimization of passive modalities, our experience in a previous randomized trial clearly demonstrates increased compliance to exercise when moist heat is a component of the

intervention.[79] Manual therapy will include grade I-II posteroanterior (PA) joint mobilizations to the lumbar spine followed by light effleurage massage to the thoracolumbar paraspinal muscles. The TMT program will be the same as discussed previously above, except exercises targeting the lateral trunk (i.e. oblique abdominals), will not be performed as these exercises may concurrently address hip weakness.

7. **STUDY POPULATION AND RECRUITMENT**
Describe who and how many subjects will be invited to participate. Include age, gender and other pertinent information.

For this study, a total of 180 community-dwelling older adults (aged 60-85) with chronic low back pain (LBP) will participate. In addition to having a primary complaint of chronic LBP, participants must also have co-existing hip weakness and hip pain.

Participants will be recruited from one of three regions: Newark, DE and surrounding communities, Pittsburgh, PA and surrounding communities and Durham, NC and surrounding communities.

Inclusion Criteria

(a) Low Back Pain for at least 3 months with LBP being an ongoing problem for at least half the days in the past 6 months. The NIH Research Task Force on Chronic LBP (RTF) established this as the definition of chronic LBP for future trials.[43,83] A patient with pain on at least half the days in the past 6 months would have accumulated at least 3 months' worth of pain days, and the Task Force concluded that this would be the recommended definition for 'chronic' pain.

(b) At least moderate pain intensity (> 3 on a scale of 0 (no pain) to 10 (worst pain imaginable), which has been shown to be significant in the pain literature, is required to ensure our ability to detect treatment effects.

(c) Classified into the "weak+painful" hip-spine subgroup: Participants must have hip internal rotation strength (normalized to body weight) that is less than .26 and a HOOS raw score on pain items P4-P8 less than 15. In our previous sample of 250 older adults with low back pain, we found that 41% met these criteria.

(d) Age: Age range (60-85) was selected to permit study of the effect of the intervention on a representative sample of community-dwelling older adults. While individuals < age 60 often suffer from chronic LBP, little is known about how to intervene for those ≥ age 60. Thus, we will focus on older adults in the proposed study.

(e) Fluent in speaking and reading English: Community-dwelling older adults who are only fluent in other languages will not be included because of the lack of feasibility of employing reliable instruments and interviewers fluent in other languages.

Attach all recruitment fliers, letters, or other recruitment materials to be used. If verbal recruitment will be used, please attach a script.

Participants will be recruited through print advertisements posted in local newspapers, newsletters, senior centers, and online. We will also recruit participants with low back pain who have participated in prior research and signed a 'consent-to-be-recontacted' form.

Recruitment materials, including the verbal script, have been uploaded with the package.

Describe what exclusionary criteria, if any will be applied.

Exclusion Criteria

Participants will not be eligible for participation if he/she has:

a. Significant pain in the legs greater than the back or acute LBP: Since we will be specifically evaluating chronic LBP and its impact on function, we do not want to confound the outcome data with prominent pain from the legs; it is unlikely that pain in the shoulder, neck, or upper body will affect functional testing, therefore, there is no need to exclude these individuals with pain in these areas. Thus, only individuals with LBP severity greater than pain severity in the lower extremity will be included.

b. Known spinal pathology other than osteoarthritis: (e.g., a history of back surgery or recent trauma within the past 6 months, vertebral fractures within the past year, ankylosing spondylitis, carcinoma metastatic to the spine). In these other cases, LBP may be of non-mechanical origin and non-responsive to the proposed interventions.

c. Previous hip fracture repair, hip fracture without repair in last 15 years, or total hip replacement: These are confounding variables that may impact patient prognosis.

d. Non-ambulatory, or severely impaired mobility (i.e., require the use of an assistive device greater than a cane): Since functional performance measures in the proposed study includes gait speed and standing balance, conditions other than LBP that could negatively impact these measures may confound our study results.

e. Severe visual or hearing impairment: Since this study will involve questionnaires, telephone evaluations, and onsite evaluations, severe visual and/or hearing impairments may interfere with data collections

f. Current infection/illnesses that would affect participation, recent hospitalization in past 3 months, or abnormal blood pressure: To insure weekly participation and a six month follow-up, potential participants with an acute infection/illness or who are recovering from a recent hospitalization will be excluded from the study. Those who fail the blood pressure screen due to abnormal readings at the initial evaluation will also be excluded and referred to their primary care practitioner.

g. Received manual therapy or exercise therapy (e.g. physical therapy, chiropractic care) for the low back or hip within in the last 3 months. This is to ensure a "washout" period whereas changes in participant status are likely to occur from the proposed treatment intervention rather than a prior intervention.

h. Inability to participate in the study for the full six months for any known reason (i.e. moving, extended vacation, planned surgery): This is an effort to ensure participants receive the intervention as directed and to retain participants over the course of the study.

i. Folstein Mini-Mental State Examination score of <24[62,63]: Individuals will be excluded because of the uncertain reliability of their answers to the self-reported outcome measures.

j. Red flags indicative of a serious disorder underlying their LBP: Red flags that would require specialized medical attention include fever associated with LBP, significant unintentional weight loss (>10 pounds), trauma that preceded the onset of LBP, night pain that is unrelenting and particularly bothersome, or signs and symptoms of cauda equinae (i.e. loss of sensation over

saddle region, significant disturbances in bowel and bladder function, which are potentially related to low back pain). These individuals will be promptly referred to their primary practitioners.

Describe what (if any) conditions will result in PI termination of subject participation.

Termination of the initial evaluation may occur if after the participant has signed the informed consent form, it is determined during the course of the initial onsite evaluation that he/she does not meet study eligibility criteria (e.g. screening criteria, abnormal blood pressure ≥ 180/110mmHg, <24 on mental screen, insufficient hip internal rotation strength deficit). PI termination of subject participation, otherwise, would only occur under a circumstance in which it became clear that the participant could not participate in a safe manner. At this time, there is no foreseeable risk that we could identify that would lead to termination from study participation, although we acknowledge that certain situations may require modification of treatment approach (e.g. increase in LBP or hip pain) or modification of the re-evaluation (e.g. abnormal blood pressure).

8. **RISKS AND BENEFITS**

List all potential physical, psychological, social, financial or legal risks to subjects (risks listed here should be included on the consent form).

Minimal risks to the subjects are expected. The risks of the physical therapy interventions might include muscular strain/soreness. A small risk of a fall (and concurrent injury) during functional performance testing or functional hip strengthening is present. As with any physical activity, there is the possibility that the participant's typical symptoms in the low back and/or hip might increase, although unlikely. There is also the potential for new musculoskeletal pain to occur secondary to physical activity. With increased or new symptoms, the treating therapist will modify the intervention. Study participants will be free to withdraw from participating in the study at any time if they are uncomfortable with any of the procedures. Although no other risks or changes in the existing minimal risks are anticipated, participants will be informed if any new information arises regarding risks of participation that may affect their decision to continue in the study.

In your opinion, are risks listed above minimal* or more than minimal? If more than minimal, please justify why risks are reasonable in relation to anticipated direct or future benefits.

We consider these risks to be minimal given that proposed functional performance tasks are similar to those performed in daily activities and commonly used during physical therapy evaluations, and that the interventions included in this clinical trial are those typically prescribed by physical therapists to reduce musculoskeletal complaints.

*(*Minimal risk means the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests)*

What steps will be taken to minimize risks?

A licensed physical therapist will be present to appropriately assist the participant for all functional performance testing and functional hip strengthening, where there may be an increased risk of falling. Physical therapists will monitor low back and hip pain (and document any new pain), which will allow for treatment modification, as needed. Overall, the supervision of a licensed physical therapist should minimize potential risk, especially since the testing and treatment offered within the context of this study is used on a daily basis by physical therapists in the clinical setting.

Describe any potential direct benefits to participants.

The benefits of this study include free evaluations by a licensed physical therapist that will provide individuals with detailed information concerning their low back and hip pain. Participants will receive 8 weeks of physical therapy services with no out-of-pocket expenses.

Describe any potential future benefits to this class of participants, others, or society.

The potential benefits of this research include (a) improvement of quality-of-life of community-dwelling older adults with chronic low back pain through improved pain management, physical, and/or psychosocial function; (b) development of an alternative non-pharmacologic treatment for older adults with chronic low back pain, and thus protection of future individuals from exposure to potentially toxic medications; (c) a possible decrease in pain and thus, an increase in independence among older adults with chronic LBP, and (d) generation of data for future studies that may lead to decreased health care utilization costs.

If there is a Data Monitoring Committee (DMC) in place for this project, please describe when and how often it meets.

The Principal Investigator (Dr. Gregory Hicks), along with the site PI's, will be responsible for ensuring participants' safety on a daily basis. The *Data and Safety Monitoring Board (DSMB)* will act in an advisory capacity to the NIA Director to monitor participant safety, evaluate the progress of the study, to review procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses. The DSMB will have a Safety Officer (SO); the SO will not be involved in the study in any other way. The DSMB reviewed and approved the study protocol on 8/19/2019 (i.e. prior to initiation of enrollment). The PI will be informed of serious adverse events as soon as they occur and will notify the NIA and DSMB within 24 hours of notification. The *DSMB* will meet twice annually by teleconference call to review study progress, data quality, and participants' safety.

9. **COMPENSATION**

Will participants be compensated for participation?
Yes

If so, please include details.
Compensation will be provided to all participants for their time and participation in the study. Payment will be in the following increments: $75 after completion of the 8 week re-evaluation and $50 after study completion, i.e. at 6 months. If a potential participant is found ineligible after the on-site screening process, they will receive pro-rated compensation in the amount of $20. Compensation will be provided via mail 3-4 weeks after each of these time points.

10. **DATA**

Will subjects be anonymous to the researcher? No
If subjects are identifiable, will their identities be kept confidential? (If yes, please specify how)

Yes, but their identity will be kept confidential. Participants will be assigned subject identification (ID) numbers. A web-based data management system, developed by the University of Pittsburgh Physical Therapy Data Center (PTDC), which is secure, encrypted, and password-protected, will be used for data entry and management. Electronic versions of all data collection instruments have

been created, so as to create a paperless data entry system. All data entry will be completed on tablets and/or computers. Data will be stored on University of Pittsburgh servers maintained by the Network Operations Center and will be accessible by PTDC staff only. Back-up copies of analysis files and programs used to prepare scientific publications will be maintained and archived indefinitely.

There may be plans to use identifiable data for other research studies outside the scope of this study, as such to recruit participants interested in participating in a separate study, therefore we will ask them on the informed consent. If the participant verbally consents to be contacted in the future for another study or purpose, their name, age, and contact information will be kept in a separate password protected folder under an encrypted UD server.

How will data be stored and kept secure (specify data storage plans for both paper and electronic files. For guidance see http://www.udel.edu/research/preparing/datastorage.html)

Original informed consents will be stored at the clinical site in a locked file cabinet that is accessible only to research personnel. Paper charts for treating therapists that include comorbidity and medication data will be securely stored in a locked file cabinet that is only accessible to research personnel. Electronic data will be stored in the electronic system and only research study personnel will be issued passwords. Recontact information for future studies will be stored in a separate password protected folder on an encrypted UD server.

Each study participant will be assigned a Study Identification Number (SID). The participant names and contact information will be stored in a separate form of the electronic data collection system that is not in the same tables as the research data. Name and contact information will be available to the local site of the participant and to the systems analyst and data manager of the Data Coordinating Center at the University of Pittsburgh. No other persons will have access to names and contact information. Only the research team will be issued passwords to access data.

How long will data be stored?

Data will be securely stored indefinitely for future/additional research purposes. All data collected will be held in locked files in areas accessible only to research personnel.
In the informed consent, participants will have the option to choose 'yes or no' in regards to being contacted for future studies. If the participant chooses to be re-contacted, then we will keep their name, age, and contact information for future use to communicate with the participant.

Will data be destroyed? □ YES X NO (if yes, please specify how the data will be destroyed)

Will the data be shared with anyone outside of the research team? X YES □ NO (if yes, please list the person(s), organization(s) and/or institution(s) and specify plans for secure data transfer)

Research records may be viewed by the University of Delaware Institutional Review Board, which is a committee formally designated to approve, monitor, and review biomedical and behavioral research involving humans and by the National Institutes of Health, the government agency that is sponsoring this research.

Additionally, the following individuals are investigators on this project at the other sites, and will have access to the data:
Dr. Sara Piva – University of Pittsburgh Physical Therapy Clinical and Translational Research Center (PT-CTRC)
Dr. Anthony Delitto – University of Pittsburgh Physical Therapy Clinical and Translational Research Center (PT-CTRC)
Dr. Debra Weiner – University of Pittsburgh School of Medicine
Dr. Steven George – Duke Clinical Research Institute
Dr. Corey Simon– Duke Clinical Research Institute

How will data be analyzed and reported?

Statistical Analysis: Dr. Charity Patterson will supervise the data analyses for this proposal along with Dr. Hicks and all analyses will be performed using SAS software, version 9.4 (SAS Institute, Inc., Cary, NC). The primary analyses will be done using intention-to-treat methods. We will compare the two groups on baseline characteristics to assess the adequacy of the randomization. Baseline characteristics include analgesic use, age, number of comorbidities, body mass index, gender, and race/ethnicity). If statistically or clinically significant between-group differences are noted, we will conduct sensitivity analyses controlling for the unbalanced variables to assess the impact on the inference for the treatment groups. Prior to conducting all of the statistical analyses outlined below, we will evaluate the assumptions of the statistical models and outliers and influential cases will be screened for and removed. All tests will be two sided with type I error of 5%. In order to reduce type I errors, secondary outcomes will be examined using an alpha = .01.

Aim 1: Primary Hypothesis. Following 8 weeks of treatment, a greater improvement in LBP-related disability and physical function (as measured by change in Quebec LBP Disability score and self-selected gait speed, respectively) will be observed for individuals that receive HIP+ compared to spine-focused rehabilitation (SFR).

Quebec score and gait speed will be used to test our specific hypotheses about short-term (immediately post-treatment) and longer-term (6-months post-randomization) changes in disability and pain severity. We will use linear mixed models with time (baseline, 8 weeks and 6 months) and the group*time interaction as fixed effects while controlling for repeated measures using an unstructured correlation matrix between time points. The effect of time will be treated as categorical. No main effect for treatment is included as the baseline means are assumed and constrained to be equal due to randomization. We will also control for site and sex as fixed effects since these are stratification factors in the randomization. We will use linear contrasts to test HIP+ versus SFR at 8 weeks and 6 months (Aim 1). GLMM assumptions include homoscedasticity, normality, and linearity using standard graphical methods, the Shapiro-Wilk test, and Box-Cox test respectively. If model assumptions are violated, we will consider transformations (e.g. Box-Cox method) that can be applied but maintain interpretability. We will test the secondary outcome measures related to Aim 1 in the same fashion to identify which outcomes should be considered in future trials.
The rates of individual adverse events and serious adverse events that occur >10% and adverse events classified by organ system and relatedness will be calculated for each group and compared using Chi-square or Fisher's exact tests.

Aim 2: Hypothesis. Reductions in hip joint pain, increases in hip strength and increases in functional self-efficacy will be associated with improvements in LBP-related disability and physical function.

Two sets of regression analyses will be used to determine the degree to which changes in hip pain, hip strength and functional self-efficacy explain changes in LBP-related disability and physical

function, as measured by change in Quebec score and gait speed, respectively. The first set of models will examine the change from baseline to immediately post-treatment (8 weeks) and the second set from immediately post-treatment to 6 month follow up for Quebec scores. The second set will do the same but for changes in gait speed. Sequential Multiple Linear Regression Models will be used to test if predictors of interest are related to the outcomes after adjusting for potential covariates. This can be evaluated by testing the ΔR2 that results from adding subsequent blocks of predictors to each model. If the block is significant, then the tests of the individual predictors will be examined. In the first block will be covariates that are potential confounders (i.e. age and sex) as well as the baseline values of hip pain, hip strength and self-efficacy. [Internal rotation strength relative to body mass, will be chosen as a representative hip strength measure, based on strength of association in our original data]. In the second block of each model will be the treatment group and change values for the predictors of hip pain, hip strength and self-efficacy. All assumptions for models will be tested: multicollinearity by examining the Variance Inflation Factor and Condition Index; normality using Shapiro-Wilk test; Homoscedasticity using the Breusch–Pagan test; and Linearity using the Box-Cox test. If assumptions are violated, transformations suggested by a Box-Cox test will be employed; if that fails Generalized Linear Models will be used.
Additionally, as an exploratory analysis a path analysis will be used to test if the relationship between baseline hip measures (pain, strength, and self-efficacy) and changes in disability and function are mediated by changes in the hip measures. Model fit will be examined using the chi-square model fit test, and standard fit indices (Root Mean Square Error of Approximation (RMSEA), Standardized Root Mean Residual (SRMR), Comparative Fit Index (CFI), and the Tucker-Lewis Index (TLI)) and to address the research question the significance of the indirect effect will be examined. It is likely that this analysis will be underpowered given the number of variables included. However, the analysis will provide a basis for further hypothesis generation and inform the follow-up study.

Reporting: Results will be disseminated through grant applications and written publications in reputable medical journals, as well as through professional presentations.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law.

11. **CONFIDENTIALITY**

Will participants be audiotaped, photographed or videotaped during this study? In some cases for publications, presentations, and/or education purposes, but only with expressed written consent (separate section included on informed consent document). Those participants who willingly identify themselves via the informed consent will be considered for use of their likeness for these purposes.

How will subject identity be protected?

The risk of breaching subject confidentiality will be minimized by identifying all participants by code numbers and by securing all data in locked files accessible only to research personnel. Neither the participant's name or nor any identifying information will be used in any publication or presentation resulting from this study.

Is there a Certificate of Confidentiality in place for this project? (If so, please provide a copy).
No

12. **CONFLICT OF INTEREST**
(For information on disclosure reporting see: http://www.udel.edu/research/preparing/conflict.html)

Do you have a current conflict of interest disclosure form on file through UD Web forms? Yes

Does this project involve a potential conflict of interest*? No

* As defined in the University of Delaware's Policies and Procedures ,a potential conflict of interest (COI) occurs when there is a divergence between an individual's private interests and his or her professional obligations, such that an independent observer might reasonably question whether the individual's professional judgment, commitment, actions, or decisions could be influenced by considerations of personal gain, financial or otherwise.

If yes, please describe the nature of the interest: Not applicable

13. **CONSENT and ASSENT**

_X___ Consent forms will be used and are attached for review (see Consent Template under Forms and Templates in IRBNet)

____ Additionally, child assent forms will be used and are attached.

____ Waiver of Documentation of Consent (attach a consent script/information sheet with the signature block removed).

____ Waiver of Consent (Justify request for waiver)

14. **Other IRB Approval**

Has this protocol been submitted to any other IRBs? Yes

If so, please list along with protocol title, number, and expiration date.

Duke University: Manual Therapy and Strengthening for the Hip in Older Adults with Chronic Low Back Pain: A Randomized Clinical Trial; Pro00100410; expiration date: 8/29/2019

University of Pittsburgh
1. Evaluating the Effects of Two Different Physical Therapy Interventions for Low Back Pain in Older Adults: A Multi-Site Clinical Trial; MOD19050337-001; expiration date: 6/18/2020

2. Evaluating the Effects of Two Different Physical Therapy Interventions for Low Back Pain in Older Adults: A Multi-Site Clinical Trial Data Coordinating Center; PRO18050723; expiration date: 9/16/2019

15. **Supporting Documentation**
Please list all additional documents uploaded to IRBNet in support of this application.

Informed Consent Form

Mailing Packet Site-Specific Documents:

- Cover Letter for Initial/8 week follow-up/16 week follow-up mailing packets
- Directions to Clinical Site (e.g. STAR Campus)

Data Collection Forms
UD Recruitment Materials

- Verbal Recruitment Script
- Print Advertisement
- Flier with Pull Tabs
- Text for Newsletters

New UD Recruitment Materials
Website Materials

UD CITI Training Certificates
UD Good Clinical Practice Training Certificates

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