TITLE: The Manual Therapy and Strengthening for the Hip (MASH) trial: Protocol for a Multisite Randomized Trial of a Subgroup of Older Adults with Chronic Back and Hip Pain

RUNNING HEAD: Multisite Trial Protocol for Geriatric Hip and Low Back Pain

ARTICLE TYPE: Protocol

SECTION: Geriatrics

SUBMITTED: April 15, 2021

REVISED: August 14, 2021

ACCEPTED: October 11, 2021

AUTHORS: Jenifer M. Pugliese, PT, DPT[1]; Peter C. Coyle, PT, DPT, PhD[1]; Patrick J. Knox, PT, DPT[1]; J. Megan Sions, PT, DPT, PhD[1]; Charity G. Patterson, MSPH, PhD[2]; Ryan T. Pohlig, PhD[3]; Corey B. Simon, PT, DPT[5], PhD; Debra K. Weiner, MD[6-9]; Steven Z. George PT, PhD, FAPTA[4] ; Sara Piva, PT, PhD, FAPTA[10]; Gregory E. Hicks, PT, PhD, FAPTA[1]

[1] Department of Physical Therapy, University of Delaware, Newark, DE.

[2] Clinical and Translational Sciences Institute, University of Pittsburgh School of Medicine, Pittsburgh, PA.

[3] Department of Epidemiology, University of Delaware, PT

[4]Duke School of Medicine, Department of Orthopedic Surgery, Durham, NC

[5]Duke Clinical Research Institute, Duke University, Durham, NC

[6] Geriatric Research Education and Clinical Center, Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA.

[7] Department 15 of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA.

[8] Department of Anesthesiology, University of Pittsburgh School of Medicine, Pittsburgh, PA.

[9] Division of Geriatric Medicine, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA.

[10]Department of Physical Therapy, University of Pittsburgh, Pittsburgh, PA.

CORRESPONDING AUTHOR: Gregory E. Hicks, PT, PhD, FAPTA; Department of Physical Therapy, University of Delaware; 540 S. College Ave, Suite 210E, Newark, DE 19713; Email: ghicks@udel.edu; ORCID iD: 0000-0001-8611-994X

ABSTRACT

Objective: Chronic low back pain (CLBP) is a disabling and costly condition for older adults that is difficult to properly classify and treat. In a cohort study, a subgroup of older adults with CLBP who had elevated hip pain and hip muscle weakness was identified; this subgroup differentiated itself by being at higher risk for future mobility decline. The primary purpose of this clinical trial is to evaluate whether a hip-focused low back pain (LBP) treatment provides better disability and physical performance outcomes for this at-risk group when compared to a spine-focused LBP treatment.

Methods: This study is a multisite, single-blinded, randomized controlled, parallel arm, Phase II trial conducted across 3 clinical research sites. A total of 180 people between 60 and 85 years of age with CLBP and hip pain are being recruited. Participants undergo a comprehensive baseline assessment and are randomized into 1 of 2 intervention arms: hip-focused or spine-focused. They are treated twice weekly by a licensed physical therapist for 8 weeks and undergo follow-up assessments at 8 weeks and 6 months after randomization. Primary outcome measures include the Quebec Low Back Disability Scale and the 10-Meter Walk Test, which are measures of self-report and performance-based physical function, respectively.

Impact. This multicenter, randomized clinical trial will determine whether a hip-focused or spine-focused physical therapist intervention results in improved disability and physical performance for a subgroup of older adults with CLBP and hip pain who are at increased risk of mobility decline. This trial will help further the development of effective interventions for this subgroup of older adults with CLBP.

Introduction

Chronic low back pain (CLBP) is a prevalent, costly, and disabling problem in the older adult population; the rising prevalence suggests that current treatment approaches are not effective.[1-8] Several large, longitudinal studies have demonstrated that CLBP among older adults is independently associated with a steeper rate of decline in performance-based mobility function (ie, gait speed, chair rise performance, balance) compared to older adults without low back pain (LBP).[9-11] As poor and/or declining mobility function in this population is predictive of increased future risk for mortality, institutionalization and overall disability,[12-16] effective interventions are needed in order to improve function.

Experts in LBP have speculated that older adults with LBP do not belong to one homogeneous group, but rather belong in subgroups that share similar clinical characteristics.[17, 18] In younger cohorts, evidence exists that matching treatments to the limitations of an individual patient can improve physical therapy outcomes.[19-22] It stands to reason that older adults would similarly benefit from matching treatments to impairments; however, older adults are often excluded from clinical trials.[23] The National Institutes of Health (NIH) has recently highlighted the importance of including participants across the lifespan.[24] Tailored interventions, which align with recent

calls for precision medicine initiatives,[25] may be particularly important in older adults with painful conditions, where heterogeneity is particularly prevalent.[26, 27] Thus, specific classification systems must be developed for this population.

In a previous cohort study involving older adults with CLBP,[28] we identified a subgroup with a combination of elevated hip pain and global hip muscle weakness. This subgroup was at risk for markedly worse CLBP, functional outcomes, and self-efficacy over the course of 12 months, putting them at risk for future mobility decline and institutionalization. When compared to older adults without pain, those with CLBP had a greater prevalence of clinical hip symptoms associated with hip osteoarthritis, which were associated with worse health related quality of life.[29] The totality of these results prompted us to develop the current trial, which focuses on evaluating whether a hip-focused LBP treatment will lead to reduced disability and improved physical function, when compared to a spine-focused LBP treatment. Our primary hypothesis is that members of the at-risk subgroup who receive hip-focused LBP treatment will have decreased pain and better functional outcomes than those who receive spine-focused LBP **treatment**.

METHODS

Design

The Manual therapy And Strengthening for the Hip in older adults with chronic low back pain trial (MASH) is a multi-site, single-blind, parallel arms, randomized controlled, Phase II trial, and adheres to the SPIRIT guidelines (Figure 1).[30]

Setting

Assessment and treatment sessions take place within clinical laboratories at the University of Delaware, the University of Pittsburgh, and Duke University. The home exercise program (HEP) portion is completed without supervision at each participant's residence.

Participants

A total of 180 older adults aged 60-85 are being recruited across the aforementioned three sites. We are utilizing newspaper advertisements, on-site visits to local senior centers, research registries, referrals from nearby rheumatology and geriatrics clinics, and electronic medical record invitations to recruit participants meeting specific inclusion criteria (Tab. 1). Two of the inclusion criteria are used to classify participants into the at-risk subgroup: hip internal rotation (IR) strength <0.26 (taken isometrically with a handheld dynamometer and normalized to body weight), and Hip Disability Osteoarthritis Outcome Score (HOOS) >5 on items P4-P8. These five items from the HOOS pain subscale ascertain the amount of hip pain a person has experienced in the last week during a specified activity; individual items are scored from 0=no hip pain to 4=extreme hip pain, with greater summed scores indicating greater severity. Using data from previous work,[28] we developed a simple decision tree using regression and receiver operating characteristic curve analyses and found that if individuals met the criteria for hip IR strength and HOOS item scores, they were placed accurately into the group with elevated hip pain and global muscle weakness (ie, our study population of focus) 81% of the time. In order to maximize safety, we adhere to specific exclusion criteria as well (Tab. 1).

Enrollment and Assessments

All potential participants complete an initial phone screen. If they are deemed preliminarily eligible, they are invited on-site to participate in **an** in-person screening. During the in-person

screening, they complete the informed consent and answer questionnaires related to demographics. They have their height and weight taken, and undergo hip IR strength testing; this information is used to determine final eligibility.

Eligible participants that provide informed consent undergo three assessments: (1) Baseline (completed at the time of the in-person screening), (2) 8 weeks post-randomization (post-intervention), and (3) 6 months post-randomization. Each comprehensive assessment is performed by a licensed physical therapist and includes self-report questionnaires, range of motion and strength measurements, and physical performance tests. Gerontological evidence indicates self-report and performance-based measures of function offer complementary information; therefore, both types should be used in the comprehensive assessment of physical function.[13, 31-34] For this trial, primary outcome measures are the Quebec Low Back Pain-Related Disability Scale (QBPD)[35] and the 10-Meter Walk Test (10MWT).[36, 37] The QBPD is a disease-specific self-reported measure of physical function that has excellent reliability and good construct validity in comparison to other pain and disability measures among older adults.[35] The 10MWT is a reliable and valid measure of gait speed, which is predictive of disability and mortality in older adults.[12-16] Secondary outcome measures were selected to capture constructs such as self-efficacy and pain perception (Tab. 2).

Modifications related to COVID-19: Early in study recruitment, the COVID-19 pandemic forced changes to our assessment protocol. Modifying trials to reduce in-person exposure is consistent with current clinical trial recommendations.[38, 39] We sought to reduce the on-site time and accomplished this by having participants fill out questionnaires remotely.

Randomization and Blinding

The study biostatistician uses statistical software to generate a randomization plan using permuted block with random block sizes to ensure a roughly equal number of participants is assigned to each arm by the end of the study in a 1:1 allocation. Randomization is stratified by site, as well as by sex, due to the reported sex differences in pain conditions among older adults.[20] Assignments generated by the statistician are uploaded into the electronic data capture (EDC) system. The site study coordinator retrieves the assignment once a participant is deemed fully eligible and provides this information to the treating therapists (interventionists), thereby concealing allocation. Therapists performing the assessments (assessors) are masked to group assignment. Interventionists are masked to participants' outcome data. Since treatment assignment cannot be withheld from the participants, both assessors and interventionists ask the participants to avoid discussion of any aspects of treatment with the assessors and other research participants. Interventionists are not assigned to a particular intervention arm and may treat participants in both groups.

Interventions

Eligible participants are randomized into one of two intervention arms: hip-focused or spine-focused treatment. Participants receive treatment from a licensed physical therapist twice weekly for eight weeks. All interventionists participate in at least 4 hours of one-on-one training, during which they practice hands-on techniques under the supervision of a therapist trained in the MASH trial treatments; assessments of treatment fidelity occur regularly. Interventionists give participants an HEP that includes a pictorial exercise handout and an exercise log, and ask them to perform it twice weekly on non-therapy days. Although education related to the HEP is primarily focused on correct performance, interventionists also discuss several principles: the promotion and understanding of the anatomical and structural strength of the human spine; the

use of active coping strategies, such as exercise; early resumption of daily, vocational, and social activities, even when pain is present; and the importance of improved activity levels, not just pain relief.[40] All exercises are progressed based on meeting a quota criterion (eg, 3 sets of 10 repetitions). Interventions are displayed in Table 3. Full manual therapy protocols, exercise protocols, and HEP pictorial handouts for both groups are included in Supplementary Appendix. Our intervention development was informed by both our pilot work and current evidence.

Hip-Focused: The hip-focused LBP treatment consists of two parts: an on-site session and an HEP. During the on-site session, participants receive manual therapy to both hips and participate in supervised functional hip exercises. Manual therapy to the hip includes joint mobilizations and stretching. Joint mobilizations include long-axis distraction (with a manipulation at the end of the 30 seconds) as well as oscillatory grade III-IV (3x30 seconds) joint mobilizations in three other directions: anterior-posterior, lateral glide with internal rotation, and posterior-anterior. Hip joint mobilizations were adapted from prior work, where they were shown to be effective in improving various clinical outcomes among individuals with a primary diagnosis of hip osteoarthritis.[41, 42] Stretches include supine hamstring stretching and either side-lying or supine hip flexor stretching. Functional hip exercises focus on strength, endurance, and control of the hip muscles while completing functional tasks (ie, squatting and stepping). They are performed with therapist supervision for safety. The last fifteen minutes of each on-site treatment session are dedicated to moist heat pack application and education regarding the delivery of the HEP: therapists demonstrate all exercises, ensure that participants use proper form, and increase the dosage on HEP logs according to each participant's progress.

The hip-focused HEP consists of three parts: hip stretching, hip strengthening exercises, and trunk muscle training (TMT) exercises. The strengthening exercises, which were adapted from

prior work,[43] focus on the strengthening of various hip muscles using resistance bands. The TMT exercises, which target muscles in the anterior, posterior, and lateral trunk, are used to help improve neuromuscular control and dynamic spinal stability. TMT exercises were adapted from prior work, in which they were shown to improve various clinical outcome among older adults with CLBP.[44]

Spine-Focused: The spine-focused LBP treatment consists of two parts: an on-site session, and an HEP. During the on-site session, participants receive manual therapy to the lumbar spine and participate in TMT exercises and stationary cycling without resistance. Manual therapy includes oscillatory grade I-II central posterior-anterior joint mobilizations to lumbar levels L1-L5 for pain relief, as well as light soft tissue effleurage massage to the thoracolumbar paraspinal muscles. The TMT exercises performed in this group target muscles in the anterior and posterior trunk; lateral trunk exercises are omitted in order to avoid inadvertently targeting the hip abductor muscles. Participants perform stationary cycling without resistance, as clinical practice guidelines highlight strong evidence supporting the effectiveness of low-intensity submaximal fitness and endurance exercises for adults with CLBP.[40] As in the hip-focused group, the last 15 minutes of each session are dedicated to education regarding the delivery of the HEP. Once the HEP education is completed for each session, if there is time remaining, therapists may provide participants with moist heat to the lumbar spine to equalize face-to-face time between intervention groups.

The spine-focused HEP consists of lumbar flexibility exercises and the same TMT performed during the on-site visit. The lumbar flexibility exercises are matched to each participant's preference, and are varied throughout the treatment sessions.

Modifications related to COVID-19: Due to COVID-19, aspects of the interventions were modified to reduce the overall time on-site. We moved the hip strengthening and TMT exercises (hip-focused group) and lumbar flexibility exercises (spine-focused group) from the on-site sessions to the HEP format.

Adherence

Participants are encouraged to adhere to the intervention arm to which they have been assigned; we define intervention adherence based on the number of in-person and HEP completed sessions (Suppl. Appendix). During the last 15 minutes of each treatment session for all participants, interventionists discuss updates to HEPs while the participants are receiving their moist hot pack application. Participants receive positive feedback and reinforcement if they adhere to their HEP and return their exercise logs. Participants receive treatment free of charge, and receive monetary compensation for follow-up assessments. Participants receive follow up phone calls at the 3-, 4-, and 5-month post-randomization time points to promote retention and to monitor for adverse events.

Adverse Events

All study staff are responsible for monitoring for the occurrence of adverse events (AE); AEs are operationalized as any unfavorable or untoward occurrence to participants during their involvement in the clinical trial, including any abnormal sign, symptom or disease that may or may not be related to research participation. Study staff catalogue new signs, symptoms or diseases within Possible Adverse Event Report (PAER) forms. Site investigators adjudicate PAERs, and report any serious adverse events or unanticipated problems to site and sponsor

regulatory officials. We utilize the Common Terminology Criteria for Adverse Events (CTCAE) classification and NIH common data elements (eg, severity) in recording AE classifications.[45]

Process Evaluation

Employing a multisite trial design allows for exploration of the generalizability of the approach and findings, but requires a focused approach to ensure that internal validity is maximized. We employ a rigorous assessment and treatment fidelity approach across sites to promote uniform and high-quality data acquisition: we have implemented a quality control program that includes the use of detailed operations manuals, therapist training, and periodic data review by the principal investigator. Protocols describe each testing or treatment procedure, and contain an exemplar script. We have regular training workshops for all study staff, and have monthly meetings for both assessors and interventionists. The study investigators meet once monthly to discuss AEs and address any issues that have arisen over the prior month.

We have implemented an internal process review system (Table 4) designed to promote adherence to the study design and provide excellent participant care. Specifically related to treatment fidelity, we utilize processes that increase the likelihood of consistent treatment delivery across sites: automated chart review, manual chart review, and on-site observation of treatment sessions. Compliance issues are mitigated by on-site targeted retraining.

Data analysis plan

All analyses will be performed using intention-to-treat methodology. We will use the QBPD score and gait speed result to test our primary hypotheses regarding changes in disability and physical function both in the short-term (immediately post-treatment) and longer-term (6-months post-randomization). We will use constrained baseline linear mixed models with time (baseline,

8 weeks and 6 months) and the group by time interaction as fixed effects while controlling for repeated measures using an unstructured correlation matrix between time points. We will treat the effect of time as nominal. We will also control for site and sex, since these are stratification factors in the randomization. If the interaction effect is significant, the simple main effect of group will be tested at each follow-up time point. If model normality and homoscedasticity assumptions are violated, we will either consider transformations that can be applied but maintain interpretability or use robust standard errors. We will test the secondary outcome measures using the same statistical models, in order to identify which outcomes should be considered in future trials, with a more conservative alpha.

The sample size for the trial was determined using the GLIMMPSE framework assuming the group by time interactions were significant for disability and physical function.[46] With α=0.05 and 80% power, we will be able to detect a moderate effect, d=.45, for a total sample of 150 or 75 per treatment group. This assumes a correlation of repeated measures of 0.5. This effect size translates to a between-group difference of 6.8 points in QBPD scores and 0.095 m/s in gait speed over time, between groups. For our final sample size of 150, a total of 180 participants will be enrolled, accounting for a dropout rate of 17% based on our previous trial of older adults with CLBP.[44] Sensitivity analyses using logistic regression models will be performed to identify predictors of missed assessment visits using baseline characteristics; if significant predictors are found, they will be included in a secondary analysis of the primary outcomes. If their inclusion results in estimates that differ from the initial analysis, these results will be reported as they would be unbiased if data are missing at random with respect to baseline characteristics.[47] The mixed models yield accurate parameter estimates if data are missing at random and have been shown to perform as well as multiple imputation given the same assumption of the missing data

mechanism.[48] We will conduct several sensitivity analyses assuming non-ignorable missingness with differential imputation of poor change scores and pattern mixture models.[49] We will compare the results from these analyses to our primary analyses with all observed data to assess the robustness of our findings.

Ethics

This study was approved by the Institutional Review Boards at each of the participating study sites; each site provides continuing reviews per their site requirements. Oversight of the entire trial is provided by an independent Data and Safety Monitoring Board. At each site, participants complete the informed consent process and are assigned an identification code. Data is then entered into the EDC, which is password protected and securely stored. Enrollment for the trial began in November 2019 and will continue through 2022; trial recruitment and enrollment were suspended between March 2020 and August 2020 due to site shutdowns related to COVID-19, but were reinitiated as each site re-opened.

DISCUSSION

The development of safe, alternative treatments that lessen the burden of CLBP and promote the independence of community-dwelling older adults is essential. While experts agree that tailored approaches to treatment are necessary, there is a scarcity of evidence relating to older adults. Our study is unique in that by identifying a subgroup with hip impairments, we can determine the effectiveness of a tailored versus standard approach, and address key initiatives set forth by the NIH.

This trial has limitations to consider when results are reported. We specifically exclude people with total hip replacements, as well as certain individuals with a history of hip fracture. This

decision was made with participant safety in mind, as hip mobilization is contraindicated in many of those individuals; however, we recognize that this may exclude participants who would fall into our subgroup of interest. Further, this is a single-blind trial, and there is no way to mask treatment allocation from the interventionists or participants. This leaves open the possibility of a participant inadvertently revealing allocation; we have attempted to mitigate this by consistently reminding participants to discuss treatments with only interventionists and not assessors or other participants. Another potential area of bias may arise if interventionists believe that one treatment arm is more effective than the other; we have attempted to mitigate this by incorporating the concept of equipoise (ie, the understanding that we do not yet know which treatment arm is indeed more effective) into the therapist training modules, as both interventions target impairments commonly experienced in this subgroup. The concept of equipoise is important in this trial due to the potential misperception that one randomly assigned treatment group was favored by the investigator team. Accordingly, we have created a protocol that ensures both treatment groups are receiving similar proportions of active exercise/intervention and both groups received the same type of evidence-informed information regarding exercise and CLBP.[40]

Our trial has several strengths. It is a multisite study involving three sites with access to a broad demographic of older adults. We used specific inclusion criteria to identify members of a subgroup with increased risk of mobility decline. We incorporated tablet technology and an EDC to streamline data collection and reduce operator error. We incorporated internal review processes to promote delivery of standardized interventions and provide treatments with excellence. Importantly, the treatments used in this trial require no specialized equipment or advanced training and should translate well into clinical practice.

Author Contributions

Concept/idea/research design: P.C. Coyle, J.M. Sions, C.G. Patterson, R.T. Pohlig, C.B. Simon, S.Z. George, G.E. Hicks

Writing: J.M. Pugliese, P.C. Coyle, P.J. Knox, J.M. Sions, C.G. Patterson, R.T. Pohlig, C.B. Simon, D.K. Weiner, S.Z. George, S. Piva, G.E. Hicks

Data collection: J.M. Pugliese, P.C. Coyle, P.J. Knox, J.M. Sions, C.B. Simon, G.E. Hicks

Data analysis: C.G. Patterson, R.T. Pohlig, G.E. Hicks

Project management: J.M. Pugliese, P.C. Coyle, P.J. Knox, J.M. Sions, S.Z. George, G.E. Hicks

Fund procurement: G.E. Hicks

Providing participants: C.B. Simon, S.Z. George, G.E. Hicks

Providing facilities / equipment: S. Piva, G.E. Hicks

Providing institutional liaisons: S. Piva, G.E. Hicks

Clerical / secretarial support: J.M. Pugliese, P.C. Coyle, J.M. Sions

Consultation (including review of manuscript before submitting): J.M. Pugliese, P.C. Coyle, P.J. Knox, J.M. Sions, C.B. Simon, D.K. Weiner, S.Z. George, S. Piva, G.E. Hicks

Ethics Approval

This study was approved by the institutional review boards at each of the participating

study sites; each site provides continuing reviews per their site requirements. Oversight of the entire trial is provided by an independent data and safety monitoring board.

Funding

This trial is funded by the National Institutes of Health's National Institute on Aging (grant no: 2 R01 AG041202).

Role of the Funding Source

The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Clinical Trial Registration

This trial is registered at ClinicalTrials.gov NCT04009837.

Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

References

1. Bressler HB, Keyes WJ, Rochon PA, Badley E. The prevalence of low back pain in the elderly. A systematic review of the literature. *Spine (Phila Pa 1976).* Sep 1 1999;24(17):1813-1819.

2. Koch HK, Smith MC. *Office-based ambulatory care for patients 75 years old and over: National Ambulatory Medical Care Survey, 1980 and 1981*: US Department of Health and Human Services, Public Health Service, National …; 1985.

3. Patel KV, Guralnik JM, Dansie EJ, Turk DC. Prevalence and impact of pain among older adults in the United States: findings from the 2011 National Health and Aging Trends Study. *Pain.* Dec 2013;154(12):2649-2657.

4. Cypress BK. Characteristics of physician visits for back symptoms: a national perspective. *American journal of public health.* 1983;73(4):389-395.

5. Hart LG, Deyo RA, Cherkin DC. Physician office visits for low back pain. Frequency, clinical evaluation, and treatment patterns from a US national survey. *Spine.* 1995;20(1):11-19.

6. Docking RE, Fleming J, Brayne C, Zhao J, Macfarlane GJ, Jones GT. Epidemiology of back pain in older adults: prevalence and risk factors for back pain onset. *Rheumatology (Oxford).* Sep 2011;50(9):1645-1653.

7. Rundell SD, Sherman KJ, Heagerty PJ, Mock CN, Jarvik JG. The clinical course of pain and function in older adults with a new primary care visit for back pain. *J Am Geriatr Soc.* Mar 2015;63(3):524-530.

8. Jarvik JG, Gold LS, Tan K, et al. Long-term outcomes of a large, prospective observational cohort of older adults with back pain. *Spine J.* Sep 2018;18(9):1540-1551.

9. Reid MC, Williams CS, Gill TM. Back pain and decline in lower extremity physical function among community-dwelling older persons. *J Gerontol A Biol Sci Med Sci.* Jun 2005;60(6):793-797.

10. Hicks GE, Simonsick EM, Harris TB, et al. Trunk muscle composition as a predictor of reduced functional capacity in the health, aging and body composition study: the moderating role of back pain. *J Gerontol A Biol Sci Med Sci.* Nov 2005;60(11):1420-1424.

11. Leveille SG, Guralnik JM, Hochberg M, et al. Low back pain and disability in older women: independent association with difficulty but not inability to perform daily activities. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences.* 1999;54(10):M487-M493.

12. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med.* Mar 2 1995;332(9):556-561.

13. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol.* Mar 1994;49(2):M85-94.

14. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci.* Apr 2000;55(4):M221-231.

15. Studenski S, Perera S, Wallace D, et al. Physical performance measures in the clinical setting. *J Am Geriatr Soc.* Mar 2003;51(3):314-322.

16. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *Jama.* Jan 5 2011;305(1):50-58.

17. Hicks GE, Simonsick EM, Harris TB, et al. Cross-sectional associations between trunk muscle composition, back pain, and physical function in the health, aging and body composition study. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences.* 2005;60(7):882-887.

18. Bigos S, Bowyer O, Braen G, Brown K, Deyo R, Haldeman S. Acute low back problems in adults. Rockville, MD: Agency for Health Care Policy and Research. *Public Health Service, US Department of Health and Human Services.* 1994.

19. Brennan GP, Fritz JM, Hunter SJ, Thackeray A, Delitto A, Erhard RE. Identifying subgroups of patients with acute/subacute "nonspecific" low back pain: results of a randomized clinical trial. *Spine.* 2006;31(6):623-631.

20. Childs JD, Fritz JM, Flynn TW, et al. A clinical prediction rule to identify patients with low back pain most likely to benefit from spinal manipulation: a validation study. *Annals of internal medicine.* 2004;141(12):920-928.

21. Fritz JM, Delitto A, Erhard RE. Comparison of classification-based physical therapy with therapy based on clinical practice guidelines for patients with acute low back pain: a randomized clinical trial. *Spine.* 2003;28(13):1363-1371.

22. Long A, Donelson R, Fung T. Does it matter which exercise?: A randomized control trial of exercise for low back pain. *Spine.* 2004;29(23):2593-2602.

23. Paeck T, Ferreira ML, Sun C, Lin CW, Tiedemann A, Maher CG. Are older adults missing from low back pain clinical trials? A systematic review and meta-analysis. *Arthritis Care Res (Hoboken).* Aug 2014;66(8):1220-1226.

24. Bernard MA, Clayton JA, Lauer MS. Inclusion Across the Lifespan: NIH Policy for Clinical Research. *Jama.* Oct 16 2018;320(15):1535-1536.

25. Collins FS, Varmus H. A new initiative on precision medicine. *N Engl J Med.* Feb 26 2015;372(9):793-795.

26. Lowsky DJ, Olshansky SJ, Bhattacharya J, Goldman DP. Heterogeneity in healthy aging. *J Gerontol A Biol Sci Med Sci.* Jun 2014;69(6):640-649.

27. James RJE, Walsh DA, Ferguson E. Trajectories of pain predict disabilities affecting daily living in arthritis. *Br J Health Psychol.* Sep 2019;24(3):485-496.

28. Hicks GE, Pohlig RT, Coyle PC, et al. Classification of geriatric low back pain based on hip characteristics with a 12-month longitudinal exploration of clinical outcomes: Findings from Delaware Spine Studies. . *Physical Therapy.* In submission 2020.

29. Hicks GE, Sions JM, Velasco TO. Hip Symptoms, Physical Performance, and Health Status in Older Adults With Chronic Low Back Pain: A Preliminary Investigation. *Arch Phys Med Rehabil.* Jul 2018;99(7):1273-1278.

30. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med.* Feb 5 2013;158(3):200-207.

31. Hoeymans N, Feskens EJ, van den Bos GA, Kromhout D. Measuring functional status: cross-sectional and longitudinal associations between performance and self-report (Zutphen Elderly Study 1990-1993). *J Clin Epidemiol.* Oct 1996;49(10):1103-1110.

32. Reuben DB, Seeman TE, Keeler E, et al. Refining the categorization of physical functional status: the added value of combining self-reported and performance-based measures. *J Gerontol A Biol Sci Med Sci.* Oct 2004;59(10):1056-1061.

33. Stretton CM, Latham NK, Carter KN, Lee AC, Anderson CS. Determinants of physical health in frail older people: the importance of self-efficacy. *Clin Rehabil.* Apr 2006;20(4):357-366.

34. Latham NK, Mehta V, Nguyen AM, et al. Performance-based or self-report measures of physical function: which should be used in clinical trials of hip fracture patients? *Arch Phys Med Rehabil.* Nov 2008;89(11):2146-2155.

35. Beurskens AJ, De Vet H, Köke AJ, van der Heijden GJ, Knipschild PG. Measuring the functional status of patients with low back pain. Assessment of the quality of four disease-specific questionnaires. *Spine.* 1995;20(9):1017-1028.

36. Peters DM, Fritz SL, Krotish DE. Assessing the reliability and validity of a shorter walk test compared with the 10-Meter Walk Test for measurements of gait speed in healthy, older adults. *Journal of geriatric physical therapy.* 2013;36(1):24-30.

37. Takacs J, Garland SJ, Carpenter MG, Hunt MA. Validity and reliability of the community balance and mobility scale in individuals with knee osteoarthritis. *Physical therapy.* 2014;94(6):866-874.

38. van Dorn A. COVID-19 and readjusting clinical trials. *The Lancet.* 2020;396(10250):523-524.

39. McDermott MM, Newman AB. Preserving clinical trial integrity during the coronavirus pandemic. *Jama.* 2020;323(21):2135-2136.

40. Delitto A, George SZ, Van Dillen L, et al. Low back pain. *J Orthop Sports Phys Ther.* Apr 2012;42(4):A1-57.

41. Hoeksma HL, Dekker J, Ronday HK, et al. Comparison of manual therapy and exercise therapy in osteoarthritis of the hip: a randomized clinical trial. *Arthritis Rheum.* Oct 15 2004;51(5):722-729.

42. MacDonald CW, Whitman JM, Cleland JA, Smith M, Hoeksma HL. Clinical outcomes following manual physical therapy and exercise for hip osteoarthritis: A case series. *J Orthop Sports Phys Ther.* Aug 2006;36(8):588-599.

43. Khayambashi K, Mohammadkhani Z, Ghaznavi K, Lyle MA, Powers CM. The effects of isolated hip abductor and external rotator muscle strengthening on pain, health status, and hip strength in females with patellofemoral pain: a randomized controlled trial. *journal of orthopaedic & sports physical therapy.* 2012;42(1):22-29.

44. Hicks GE, Sions JM, Velasco TO, Manal TJ. Trunk Muscle Training Augmented With Neuromuscular Electrical Stimulation Appears to Improve Function in Older Adults With Chronic Low Back Pain: A Randomized Preliminary Trial. *Clin J Pain.* Oct 2016;32(10):898-906.

45. Services USDoHaH. Common Terminology Criteria for Adverse Events (CTCAE), version 6.0. 5 ed; 2017.

46. Kreidler SM, Muller KE, Grunwald GK, et al. GLIMMPSE: online power computation for linear models with and without a baseline covariate. *Journal of statistical software.* 2013;54(10).

47. Rubin DB. Inference and missing data. *Biometrika.* 1976;63(3):581-592.

48. Twisk J, de Boer M, de Vente W, Heymans M. Multiple imputation of missing values was not necessary before performing a longitudinal mixed-model analysis. *Journal of Clinical Epidemiology.* 2013/09/01/ 2013;66(9):1022-1028.

49. Hedeker D, Gibbons RD. Application of random-effects pattern-mixture models for missing data in longitudinal studies. *Psychological Methods.* 1997;2(1):64-78.

50. Deyo RA, Dworkin SF, Amtmann D, et al. Report of the NIH Task Force on research standards for chronic low back pain. *J Pain.* Jun 2014;15(6):569-585.

51. Creavin ST, Wisniewski S, Noel-Storr AH, et al. Mini-Mental State Examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations. *Cochrane Database Syst Rev.* Jan 13 2016(1):Cd011145.

52. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* Sep 2001;16(9):606-613.

53. Löwe B, Unützer J, Callahan CM, Perkins AJ, Kroenke K. Monitoring depression treatment outcomes with the patient health questionnaire-9. *Med Care.* Dec 2004;42(12):1194-1201.

54. Davenport TE, Cleland JA, Yamada KA, Kulig K. Measurement Properties of the Low Back Activity Confidence Scale (LoBACS). *Evaluation & the health professions.* 2016;39(2):204-214.

55. Sullivan MJ, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. *Psychological assessment.* 1995;7(4):524.

56. George SZ, Valencia C, Beneciuk JM. A psychometric investigation of fear-avoidance model measures in patients with chronic low back pain. *journal of orthopaedic & sports physical therapy.* 2010;40(4):197-205.

57. Corbett DB, Simon CB, Manini TM, George SZ, Riley JL, 3rd, Fillingim RB. Movement-evoked pain: transforming the way we understand and measure pain. *Pain.* Apr 2019;160(4):757-761.

58. Fischer AA. Pressure algometry over normal muscles. Standard values, validity and reproducibility of pressure threshold. *Pain.* Jul 1987;30(1):115-126.

59. Jones DH, Kilgour RD, Comtois AS. Test-retest reliability of pressure pain threshold measurements of the upper limb and torso in young healthy women. *J Pain.* Aug 2007;8(8):650-656.

60. Chesterton LS, Sim J, Wright CC, Foster NE. Interrater reliability of algometry in measuring pressure pain thresholds in healthy humans, using multiple raters. *Clin J Pain.* Nov-Dec 2007;23(9):760-766.

61. Pua YH, Wrigley TV, Cowan SM, Bennell KL. Intrarater test-retest reliability of hip range of motion and hip muscle strength measurements in persons with hip osteoarthritis. *Arch Phys Med Rehabil.* Jun 2008;89(6):1146-1154.

62. Thorborg K, Petersen J, Magnusson SP, Hölmich P. Clinical assessment of hip strength using a hand-held dynamometer is reliable. *Scand J Med Sci Sports.* Jun 2010;20(3):493-501.

63. Harada ND, Chiu V, Stewart AL. Mobility-related function in older adults: assessment with a 6-minute walk test. *Arch Phys Med Rehabil.* Jul 1999;80(7):837-841.

64. Unver B, Kahraman T, Kalkan S, Yuksel E, Karatosun V, Gunal I. Test-retest reliability of the 50-foot timed walk and 30-second chair stand test in patients with total hip arthroplasty. *Acta Orthop Belg.* Sep 2015;81(3):435-441.

65. Nilsdotter AK, Lohmander LS, Klässbo M, Roos EM. Hip disability and osteoarthritis outcome score (HOOS)–validity and responsiveness in total hip replacement. *BMC musculoskeletal disorders.* 2003;4(1):1-8.
66. Cella D, Riley W, Stone A, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. *Journal of clinical epidemiology.* 2010;63(11):1179-1194.
67. Amtmann D, Cook KF, Jensen MP, et al. Development of a PROMIS item bank to measure pain interference. *Pain.* 2010;150(1):173-182.
68. Hahn EA, DeVellis RF, Bode RK, et al. Measuring social health in the patient-reported outcomes measurement information system (PROMIS): item bank development and testing. *Quality of Life Research.* 2010;19(7):1035-1044.

Table 1: Inclusion/Exclusion Criteria

Inclusion Criteria	• Low back pain > 3months for at least ½ of the days in the last 6 months[50] • Moderate low back pain intensity (>3 on a scale of 0-10) • Normalized isometric hip internal rotation strength <0.26[a] • Hip Disability and Osteoarthritis Outcome Score >5 on pain-related items P4-P8[a]
Exclusion Criteria	• Previous hip fracture with repair • Hip fracture within the last 15 years without repair • Total hip replacement • Known spinal pathology other than spinal stenosis and/or osteoarthritis • Severely impaired mobility (ie, requires the use of a wheelchair)

	• Folstein Mini-Mental State Examination Score <24[51] • Severe visual or hearing impairment • Red flags such as fever, significant unintentional weight loss > 10 pounds, pain that awakens or keeps one awake at night, trauma that preceded the onset of pain, or signs and symptoms of cauda equina • Significant pain in the legs greater than the back • Acute illness (eg, COVID-19) • Inability to participate in the study for the full six months (eg, moving residences) • Receipt of manual or exercise therapy for low back or hip within the last 3 months
[a]Criteria defined from decision tree analysis	

Table 2: Outcome Measures

Test	Domain	Description	Scoring
Quebec Back Pain Disability Scale (QBPD)[35a]	Low back pain-related disability	Questionnaire: 20 items related to daily activities, which are grouped into 6 categories	Higher scores = greater disability
10 Meter Walk Test (10MWT)[36, 37a]	Gait speed	Participants walk along a linear pathway at their 'usual pace' and 'as quickly as possible.'	Higher gait speeds = better outcomes
Patient Health Questionnaire-9 item (PHQ-9)[52, 53]	Depressive symptoms	Questionnaire: 9 items related to depressive symptoms	Scores of ≥ 10/27 are indicative of major depression
Low Back Activity Confidence	Self-efficacy	Questionnaire: 15 items scored according to participant's level of	Higher scores = greater self-efficacy

Scale (LOBACS)[54]		confidence in performing activities	
Pain Catastrophizing Scale (PCS)[55, 56]	Pain perception	Questionnaire: 13 items scored as three subscales to evaluate the constructs of rumination, magnification, and helplessness.	Higher scores = increased catastrophizing
Movement-evoked Pain[57]	Pain provocation with activity	Participants reported pain intensity before, during, and after 6MWT and 30 Second Chair Stand Tests	Smaller increases in pain = lower pain provocation with activity
Quantitative Sensory Testing[58-60]	Pain pressure threshold	Algometer used to measure pressure pain sensitivity at four sites bilaterally: upper trapezius, posterior superior iliac supine, greater trochanter, and tibialis anterior	Higher values = higher pain pressure threshold
Hip Strength[61, 62]	Strength	Hip strength (abduction, extension, internal and external rotation, flexion) taken with a hand-held dynamometer, normalized to body weight.	Higher forces = greater strength
6 Minute Walk Test (6MWT)[63]	Functional Mobility	Participants walk around a pre-determined course, trying to cover as much ground as possible in 6 minutes	Longer distances = better outcome
30 Second Chair Stand Test[64]	Functional mobility	Participants perform as many sit-to-stands as possible in 30 seconds while their arms are folded across their chest	More sit-to-stands = better functional mobility
Hip Disability and Osteoarthritis Outcome Score (HOOS)[65]	Hip-related disability	Questionnaire: 40 items across five domains (pain, symptoms, activities of daily living, sport and recreation function, hip-related quality of life)	Higher scores = better hip outcomes
Patient-Reported Outcomes Measurement Information System (PROMIS-29)[66-68]	Health-related quality of life	Questionnaire: 29 items across eight domains (physical function, anxiety, depression, fatigue, sleep disturbance, ability to participate in social roles and activities, pain interference, and pain intensity)	Higher scores = greater presence of each outcome
[a]Primary outcome measure			

Table 3. Summary of intervention components

	Component	Description
Hip-Focused		
On-site (45 min)	Hip manual therapy	Four hip mobilization techniques (bilateral) • Long-axis distraction (Grade III sustained) plus manipulation • Anterior-posterior oscillatory mobilizations (Grade III/IV) • Lateral femoral glide (Grade III sustained) with hip internal rotation oscillatory mobilizations (Grade III/IV) • Posterior-anterior oscillatory mobilizations (Grade III/IV) Manual stretches (bilateral) • Hamstrings • Hip flexors
	Functional hip exercises	Two phases • Visits 1-8: partial wall squats, hip abduction with elastic band, forward step-ups • Visits 9-16: wall squats, side-stepping with band, lateral step-ups
Home Exercise Program Education (15 min)	Hip strengthening exercises with elastic band	Hip abduction Hip extension Hip internal rotation Hip external rotation
	Trunk muscle training exercises	Bracing Anterior trunk (e.g., curl-ups) Posterior trunk (e.g., alternating arm lifts in quadruped) Lateral trunk (e.g., side bridges)
Spine-Focused		
On-site (45 min)	Lumbar manual therapy	Central posterior-anterior oscillatory mobilizations (Grade I-II) to L1-L5 levels Effleurage to thoracolumbar area
	Trunk muscle training exercises	Bracing Anterior trunk (e.g., curl-ups) Posterior trunk (e.g., alternating arm lifts in quadruped)
		Stationary cycle without resistance for submaximal intensity

	Stationary cycling	
Home Exercise Program Education (15 min)	Lumbar flexibility exercises	Generalized stretches to enhance lumbar mobility
	Trunk muscle training exercises	Same as above, but lateral trunk exercises omitted

Table 4. Internal Review Processes

Process	**Type**	**Reviewer**	**Description**
Automated	Chart	Web-based Application	Significant deviations from standardized protocols (e.g., omission of treatment components) are automatically flagged in real-time by the electronic data capture system.
Manual	Chart	Study Staff Member	≥25% of charted treatment sessions are reviewed for fidelity to treatment prescription and progression in months 1-6; ≥10% of treatment sessions every year thereafter.
On-site	Live	Study Staff Member	≥5 audits per interventionist in the first year are observed for fidelity to treatment prescription and progression; ≥2 evaluations per year per interventionist thereafter.