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Protocol

Study of Hyperkyphosis, Exercise and Function (SHEAF) Protocol of a Randomized Controlled Trial of Multimodal Spine Strengthening Exercise in Older Adults With Hyperkyphosis

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BACKGROUND: Hyperkyphosis negatively effects health status, physical mobility, and quality of life, but there is no standard protocol for treating hyperkyphosis. Treatment options include targeted exercise.

OBJECTIVES: This single-site randomized controlled trial (RCT) will determine the efficacy of a targeted multimodal spine strengthening exercise program, compared with no exercise intervention, among community-dwelling men and women aged ≥60 years.

DESIGN: The RCT is a parallel-group design, with 1:1 randomization to exercise or attentional control groups.

SETTING: One primary site (1 academic medical center partnered with 1 local community medical center).

PARTICIPANTS: One hundred men and women aged ≥60 years with thoracic kyphosis ≥40° will be randomized.

INTERVENTION: The targeted multi-modal spine strengthening exercise intervention includes exercise and postural training, delivered by a physical therapist in a group of 10 participants 3 times a week for 6 months. Controls receive monthly health education meetings in a group of 10 participants with monthly calls from study coordinator to monitor physical activity and any adverse events.

MEASUREMENTS: Primary outcome is change in Cobb angle of kyphosis measured from lateral spine radiographs at baseline and 6-months. Secondary outcomes include change in physical function (the modified Physical Performance Test, Timed Up and Go, Time Loaded Standing, 4-meter walk, Six-minute walk) and health-related quality of life (SRS-30 self-image domain, PROMIS Global Health Index and Physical Function Index). Additional secondary

outcomes include pain, physical activity level, spinal flexion and extension muscle strength, paraspinal extensor muscle density and adverse events.

LIMITATIONS: Blinding of the participants and instructors providing the intervention is not possible.

CONCLUSIONS: The efficacy of a high-quality, adequately powered exercise intervention in men and women with kyphosis ≥40° will be evaluated to determine whether targeted multi-modal spine strengthening exercise reduces hyperkyphosis in older adults, as well as improves important secondary outcomes of physical function and health-related quality of life.

Introduction

Age-related hyperkyphosis, an abnormal forward curvature in the thoracic spine, is a common progressive deformity of the spine that affects up to 50% of older adults.[1-3] Hyperkyphosis can lead to significant deterioration in health status, physical mobility and quality of life. Women with hyperkyphosis have slower walking speed, difficulty climbing stairs, impaired balance, and greater risk for falls, fractures and mortality.[2,4-8] Risk factors for hyperkyphosis include advanced age, low bone mass, degenerative disc disease, and prevalent vertebral fractures.[9-11] Furthermore, routine poor posture, decreased spinal extension mobility, and reduced back extensor muscle strength are other commonly cited potential causes of age-related hyperkyphosis,[12-14] and these impairments may be modifiable with exercise.

Despite the adverse effects on health, physical function and quality of life, hyperkyphosis has only recently started to be recognized by health care providers as a major health concern.[15] There is no standard of care for treating hyperkyphosis. Current treatment options include exercise and bracing. We conducted an uncontrolled pilot study of an exercise program targeting spinal muscle strength among older women with hyperkyphosis that resulted in a significant improvement in kyphosis, spinal muscle strength and physical performance.[16] A recent systematic review, including 7 randomized controlled trials (RCT) to determine the effects of exercise on kyphosis, found that exercise targeting back extensor muscle strength may result in a modest improvement in kyphosis.[17] However, a clear recommendation for a treatment intervention was not possible due to the small sample sizes, heterogeneity of the study subjects, and different and un-validated measurements of the outcome variable of kyphosis. There is a need to perform a high-quality RCT that is adequately powered and uses validated outcome

measurements of kyphosis, to determine whether targeted spine strengthening reduces hyperkyphosis in older adults. Furthermore, few of the prior studies included outcome measures of physical function and it is not known whether exercises designed to reduce kyphosis will also lead to improvement in physical function. Spinal orthoses reportedly reduce excessive kyphosis, improve spinal extensor muscle strength and physical performance although they have only been tested in women with underlying spinal osteoporosis.[18]

Based upon the results of our previous pilot study, we designed an adequately powered, high quality randomized trial to test the hypothesis that a targeted multimodal spine strengthening exercise program will lead to a clinically meaningful change in kyphosis in community-dwelling hyperkyphotic adults aged 60 years and older. The rationale underlying such an intervention is that hyperkyphosis increases with age, contributes to impaired physical function, and that hyperkyphosis will be improved by an exercise intervention targeting musculoskeletal impairments associated with hyperkyphosis.

We are conducting a single-blinded randomized controlled trial of a multi-modal spine strengthening exercise intervention: 1) to determine if the exercise intervention improves kyphosis, measured as Cobb angle using lateral spine radiographs, 2) to determine if the exercise intervention improves secondary outcome measures of physical function and health related quality of life, measured using the modified Physical Performance Test, gait speed, Timed Up and Go, Timed Loaded Standing, and the PROMIS Global Health Index and Physical Function Index, and 3) to determine if the exercise intervention improves spinal muscle strength and/or spinal muscle density and if change in these factors is associated with change in physical

function.

Method

Study Setting

The study is conducted at the University of California San Francisco (UCSF), an academic medical center, with a second intervention location at the Kaiser Permanente Northern California (KPNC) San Francisco Medical Center.

Trial Design

This is a single-blinded randomized, controlled trial comparing a 3 times per week group exercise intervention with a monthly health education group class (Clinical trials, govidentifier NCT01751685 with a 1:1 allocation ratio. The study is enrolled in five waves of 20 participants, with 10 participants randomized to intervention and 10 participants to control in each wave (Figure 1). Participants are randomized in equal proportions to intervention or control using randomly permuted blocks of 2 and 4, stratified by age and sex. Treatment assignments are generated prior to the study, and placed in order in sealed, opaque envelopes with stratum-specific sequential ID numbers. Consenting participants fulfilling study eligibility criteria are assigned the next available ID number for the appropriate age and sex stratum by the study staff. The envelope is opened at the end of their baseline study visit. The date and time each envelope is opened is recorded in a log along with participant ID to ensure integrity of the randomization.

Participants

Individuals are eligible who are age 60 years and older, with kyphosis angle $\geq$ 40 degrees measured by the Debrunner kyphometer (Techmedica Inc, Camarillo, CA). After meeting preliminary study criteria, a study physician reviews the participant's medical history and a letter

is sent to their primary care provider for signed approval to participate in the planned exercise intervention. Exclusion criteria include inability to extend the thoracic spine at least 5 degrees, failure to comply with run-in procedures, non-English speaking, and a disorder or disease likely to prevent or interfere with safe participation in a group-based exercise class including painful vertebral fractures in the past 3 months, unexplained weight loss (>10 pounds in the past year), 3 or more falls in the past year, advanced disability or end-stage disease, major psychiatric illness, cognitive impairment (failed Mini-Cog),[19] alcohol or drug abuse (diagnosed by primary care provider), narcotic pain medications, diagnosed vestibular or progressive neurologic disorder, total hip or knee replacement or hip fracture within the previous 6 months, or oral glucocorticoid medications for 3 months or more the past year. Participants are excluded if unable to pass safety tests (gait speed <0.6 m/s, inability to stand with feet together for 30 seconds, inability to actively flex shoulders to 90 degrees, inability to move from standing to supine on a mat and return to standing independently or with the use of a nearby chair).

Intervention

The intervention is a multi-modal group-based kyphosis-specific exercise program that was developed and initially tested during our previous pilot study.[16] The exercise program targets multiple musculoskeletal impairments that are known to be associated with hyperkyphosis, including spinal extensor muscle weakness, decreased spinal mobility, and poor postural alignment (Table 1). The *spinal strengthening* component incorporates high-intensity strengthening exercise targeted to strengthen spinal extensor muscles and stabilize the trunk in neutral alignment. The *spinal mobility* component incorporates foam rollers and end-range exercises to increase spinal extension and rotation, and reduce mobility limitations in the anterior shoulders, chest and spine. Participants lie supine on foam rollers, and perform sidelying and

standing end-range thoracic extension and rotation to mobilize the spine during exercise. The *spinal alignment* component integrates spinal extensor strength and mobility into practice. The instructor trains participants to recognize neutral spinal alignment and maintain their best spinal alignment during the group exercise program and during activities of daily living. Participants are asked to practice good posture at least 3 times during the day, and to report compliance to the study coordinator on a weekly basis. Participants are instructed not to change their usual level of activity or exercise during study enrollment.

We standardized the protocol with a written pamphlet/script and a video. Each exercise session begins with 10 minutes of warmup activity, ended with 5 minutes of cool-down, and stretching the neck, chest and all extremities. A licensed physical therapist teaches the intervention. A research assistant is present during exercise class to assist the physical therapist.

Setting and supervison. A group-based intervention lead by a physical therapist is implemented to ensure that participants learn from a professional skilled at exercise instruction in an older population with multiple medical co-morbidities. The physical therapist is assisted by a trained research assistant to ensure a ratio of 5:1 participant/instructor. The instructors include auditory, visual and tactile feedback to participants to ensure safe performance of the exercises, and instructions to integrate good body mechanics and posture into the exercises and activities of daily living (ADLs). Exercises are progressed in frequency and intensity during the study, as long as participants are able to demonstrate good quality movement. If a participant has pain ≥6/10, he or she is instructed not to attend class, to contact their medical provider, and to use analgesic medications (Tylenol 1.5 grams up to 3.0 grams per day, or Voltaren gel applied over the painful area) and ice. If a participant has pain <6/10, exercises may be modified in order to ensure the ability to complete the exercises without increasing pain.

Frequency and duration. Participants assigned to the intervention attend a group exercise program for 1 hour three times per week for 6 months, followed by 6 months of usual physical activity. Those assigned to the control attend a group education program for 1 hour once a month for 6 months. After the 6-month post-intervention testing visit, control participants meet with the study physical therapist and receive 1-1 instruction in the kyphosis-specific exercise program, receive an exercise DVD of the study exercise program, handouts with pictures of the exercises and concepts of postural alignment, and exercise equipment (a roller and theraband). The intervention participants receive the same DVD, handouts and exercise equipment after their 6-month testing visit.

Intensity. The strengthening regimen incorporates high-intensity strengthening exercise at a Borg Scale intensity of 4-5, based upon 70-80% of perceived exertion,[20,21] a stimulus recommended to produce significant strength gains, and often results in improved endurance, in upper and lower extremity muscles in older adults.[22] For all strengthening exercises (quadruped arm and leg lift, prone trunk lift, sidelying thoracic rotation/extension and sidelying leg lifts) we implement a gradual, ramped protocol for the first 6-weeks, beginning without resistance, while participants learn the exercises, and gradually progressing the intensity of the exercise with theraband or resistance with weights to light (30-40%), moderate (50-60%), then high (70-80%) intensity resistance based upon perceived exertion until a Borg Scale intensity of 4-5 is reached.[23,24] When exercising at a Borg Scale intensity of 4-5, within the first 2 repetitions, one typically rates the level of difficulty as *"somewhat hard"* to "hard". If the participant rates the difficulty less than "somewhat hard", the resistance will be increased, or if the participant rates difficulty as more than "hard", resistance will be reduced. The goal is to perform 2 sets of good quality movements in the range of 70-80% of maximum until momentary muscle fatigue at 8

repetitions.[23,24] Weights are increased from one pound, in one-pound increments, and theraband resistance is increased, progressing from yellow to red to green to blue theraband (corresponding to 2 to 10 pounds of force for each percentage of theraband strain).[25] Resistance is increased throughout the trial to maintain a "somewhat hard" to "hard" level of exertion.

Comparator. The control group was designed to approximate the social interaction and attention received during the exercise intervention. Control participants receive monthly health education classes in a group class format to provide social interaction. Sample topics include bone health, managing urinary incontinence, fall prevention, and stress management. Additionally, the study coordinator calls participants on a monthly basis to record 7-days of pedometer reading, and collect safety log information for monitoring adverse events.

Blinding. Participants and class instructors in this study cannot be blinded. However, the primary outcome measurement of change in Cobb angle of kyphosis from lateral spine radiographs will be made by an investigator blinded to group allocation. Furthermore, all measurements of physical function are collected by an investigator blinded to group allocation.

Data Collection and Management

Operating procedures, informed consent, scripts for telephone screening and teaching the exercise intervention, data forms, and checklists for visits are in the Study of Hyperkyphosis, Exercise and Function (SHEAF) Study Manual. The study schedule, the hypotheses and analyses are shown in Tables 2 and 3, respectively. A research assistant/coordinator initially screens participants for the study on the telephone or via an online screening tool followed by a telephone screen. Study staff obtains informed consent and performs an in-person clinic screen to ensure that participants meet all study criteria, and collect baseline demographic and health information. Once approval to participate is obtained from the primary care provider, participants

attend a run-in meeting, where they receive a reference manual with study contact information, time and location for testing and class visits, and a pedometer with instructions to wear for 7-days prior to their baseline testing.

A UCSF Clinical Research Center (CRC) exercise physiologist performs the physical performance tests. Data is entered via Research Electronic Data Capture (Redcap) forms into a secure database. Every hour, pre-programmed error-checking programs scan incoming forms for completeness, data ranges, and logic sequences, and study personnel are notified to correct any errors. The data are stored and accessible to the data analyst for transforming the data to SAS for viewing, reporting, and analyses.

Primary Outcome

The primary outcome is change in kyphosis from baseline to 6-months, measured using the gold standard Cobb angle of kyphosis derived from standing lateral spine radiographs and a standardized protocol for thoracic kyphosis (T4-T12).[26] We will perform exploratory analyses using the centroid method for measuring Cobb angle from lateral spine radiograph and the Debrunner kyphometer external measurement of kyphosis.[27]

Secondary outcomes. Secondary outcomes are 3-, 6-, and 12-month changes of physical function and health-related quality of life.

Physical function. The *modified Physical Performance Test (modified PPT)* is a composite measure of several aspects of physical function in aging adults.[28] The modified PPT includes 7-item timed standardized tasks: 50-foot floor walk, putting on and removing a lab coat, picking up a penny from the floor, standing up five times from a 16-inch chair without the use of arms, lifting a 7-pound book to a shelf, climbing one flight of stairs, and standing with feet together, and two additional untimed tasks: climbing up and down four flights of stairs and performing a

360º turn. A *4-meter walk* test is administered to measure gait speed (m/s).[29] *The Timed Up and Go* test measures the time (s) to rise from a 48 cm height armchair, walk 3 m, turn and return to a fully seated position in the chair.[30] *Timed Loading Standing* is a test of combined trunk and arm endurance that measures the time (s) a person can stand while holding a two-pound dumbbell in each hand with the arms at 90 degrees of shoulder flexion and the elbows extended.[31] The *Six-minute Walk* test is a measure of aerobic capacity, and records the distance in feet covered walking for 6 minutes.[32]

Health related quality of life (HRQoL): We administer the modified Scoliosis Research Society SRS-30 instrument, self-image domain,[33] to measure self-image, and PROMIS global health and physical function indices to measure overall health and physical function quality of life.[34]

Other measures. Questionnaires are used to collect demographic data and medical history (eg. current medications and medical co-morbidities in the past 5 years) at the screening and baseline study visit. We measure height and weight using standard methods, and bone density of the hip and spine using the GE Lunar Prodigy Dual X-ray Absorptiometry at the baseline visit. We are using a standardized protocol for spine muscle flexor and extensor strength[16] with the Biodex 3 (Biodex Medical Systems Inc.) computerized dynamometer and the spine attachment to measure peak torque to body weight muscle strength. (RSI Systems, Boulder, CO). We are obtaining axial images from abdominal quantitative computed tomography lateral scout scans at the L4-L5 disc space (GE9800 Advantage; General Electric, Milwaukee, WI) and calculating spinal extensor muscle density (HU) using specialized proprietary software. Vertebral fractures will be calculated from T4 to L4 baseline standing lateral spine radiographs. Physical activity level is measured at baseline, 3-month, 6-month and 12-month study visits using the Physical Activity

Scale for the Elderly (PASE) questionnaire,[35] and an Omron step counter for 7 days. Pain and pain interference data is collected at each visit.

Harms. Participants are asked to report adverse events to the study staff. Safety logs are administered by the study coordinator on a weekly basis in the intervention group and monthly in the control group. Participants complete an event log documenting change in pain, falls and other injuries. Events are categorized as occurring during a study visit, occurring outside of study visit, pre-existing, or new event. Serious adverse events (death, life-threatening adverse experiences, related inpatient hospitalization) will be reported to the UCSF Committee on Human Subjects Research within 5 days.

Recruitment. Participants are recruited from community talks at local senior centers, communication with primary care physicians at Kaiser Permanente Northern California (KPNC) San Francisco Medical Center, flyers posted in the UCSF Departments of Physical Therapy, Department of Medicine – Division of General Internal Medicine, and Orthopedics and Spine Clinic, as well as the San Francisco Veterans Affairs Medical Center and KPNC San Francisco Medical Center; and letters sent to people 60 years and older in a UCSF registry of patients who have previously agreed to be contacted about research and a KPNC San Francisco diagnosis-unspecified database established for the study.

Strategies to enhance retention. All participants are remunerated $100 upon completion of the study. All participants also receive a copy of the study exercises on DVD, an exercise manual with study concepts and photographs of the exercises, a foam roller and theraband. Participants in the intervention group receive up to 72 1-hour group exercise classes, and participants in the control group receive 4 1-hour health education meetings and an individual 1-hour session with the study physical therapist after their 6-month testing visit. Both groups receive copies of their

DXA and x-ray reports upon completion of the study. Throughout the study, parking is reimbursed for study visits or taxi vouchers are provided for the testing visits.

Sample size estimation. We calculated the minimal effects detectable with 80% power in 2-sided tests with a type-I error rate of 5%, in a sample size of 100 subjects, allowing for within-subject correlation of the baseline and 6-month outcomes, and loss to follow-up of 20% of participants. Results shown in Table 4 strongly suggest that the study is powered to detect clinically meaningful effects.

The minimum detectable effects for kyphosis and Physical Performance Test (PPT) in Table 4 are consistent with our uncontrolled pilot study results, even if regression to the mean and spontaneous improvement accounted for ½ of the mean improvement of 6 degrees in kyphosis and 2 points in PPT. Standard methods for ANCOVA, positing reductions in residual variance by a factor of $1-r^2$ due to adjustment for the baseline value of the outcome, were used to obtain these estimates with r representing the within-subject correlation. Using data from the pilot study, we estimated r as 0.8 for kyphosis and PPT, and 0.85 for gait speed; we also used pilot data to obtain residual standard deviations (5, 2.6, and 0.18 respectively).

Analyses

Reporting will be in accordance with SPIRIT guidelines. The primary analyses will be by treatment assignment, without regard to adherence to the intervention. Changes in Cobb angle of kyphosis at 6 months will be the primary endpoint. Given fiscal and feasibility limitations on this single-site study, tests of treatment effects on 6 additional physical function and 3 HRQoL measures (Aim 2), as well as muscle strength and density (Aim 3), and all comparisons at 1 year, will be regarded as secondary and analyzed without penalty for multiple comparisons, but with results clearly presented as hypothesis-generating. We will use t-tests, Wilcoxon, chi-square, and

exact tests as appropriate to compare the treatment and control groups in terms of baseline age, gender, co-morbidities, vertebral fractures, degenerative disc disease, and level of kyphosis. If between-group imbalances are found, sensitivity analyses will be conducted adjusting for the imbalanced covariates. However, the primary analysis will be unadjusted, to avoid inflation of type-I error and erosion of confidence in the results due to model selection. ANCOVA will be used to assess effects of the intervention on changes from baseline to 6 months in the primary and secondary endpoints. The models will include fixed effects for treatment, the baseline value of the outcome, and wave of recruitment. Normality and equality of variance of the residuals will be checked and achieved using transformation if necessary. We will also check for non-linearity in the effect of baseline value of the outcome, as well as its interaction with treatment assignment. In secondary analysis, the same approach will be used for changes from baseline to 1 year. In exploratory sub-group analyses, we will assess differences in the treatment effect by baseline kyphosis, split at the 75^{th} percentile, number of co-morbidities ($\geq$2 vs 0-1), and presence of vertebral fracture. Finally, we will use the methods of Bland and Altman to assess the agreement of radiographic and Debrunner kyphosis measurements, then assess treatment effects using the Debrunner measurements. After we assess intervention effects on muscle strength and density, we will then use structural equation modeling to assess the pathways through which the intervention affects physical function. We hypothesize that the intervention will have direct effects on function, as well as indirect effects on function via kyphosis, muscle strength, and density; we also hypothesize an indirect effect of the intervention on kyphosis via strength and density. These analyses will control for potential confounders of the changes in kyphosis and strength including age, baseline kyphosis severity, degenerative disc disease, physical function, and vertebral fractures.

Trial monitoring. The principal investigator has primary responsibility for the overall conduct of the study, the study manual and chairing study meetings with the co-investigators. The principal investigator and lead investigators meet after each wave of the study to review the progress of the study and address any human subject issues that occur. These discussions may involve adverse event prevention measures, subject accrual issues, research staff training on protection of human subjects, and occurrence of adverse events. Lead investigators will contribute expertise in design and analysis, and contribute to overall study progress.

Data Safety Monitoring Board. The Data Safety Monitoring Plan provides for an external, objective Data and Safety Monitoring Board (DSMB) comprised of 3 arm's length members who review safety of study participants after each wave of the study. Blinded safety data is communicated to all DSMB members. The DSMB reviews annual reports prepared by the PI, statistician, and data management staff on the progress of the project including data on enrollment, comparison of target to actual enrollment, overall status of the study participants, adherence to the study interventions, and information on race/ethnicity, gender, adverse events, and serious adverse events. The DSMB determines whether the study should continue, be terminated, or modified based on observed beneficial or adverse effects.

Ethics and Confidentiality

The study has received approval from the University of California at San Francisco and Kaiser Permanente Northern California Institutional Review Boards (IRB), as well as the Research Committee of the San Francisco Veterans Affairs Medical Center. Any study modifications are approved by the IRB before implementation, consent forms are revised, and the protocol

revisions are reported on the clinicaltrials.gov site. Participants for the current trial are assigned an ID to be used on all forms and in the database management system. De-identified data is stored in a secure database and is backed up daily. Hard copies of records with personal identifiers are kept separately from the data. Data is entered into the data management system by a research assistant/coordinator. Only the research assistant/coordinator and the database service provider are able to view participants' data and identifiers in the database. Trial investigators have no relevant financial or competing interests.

Discussion and Dissemination

We propose to evaluate the efficacy of a single-site randomized trial of a targeted multi-modal spine strengthening exercise program in community-dwelling adults 60 years and older with hyperkyphosis. A recent systematic review of the effects of exercise on hyperkyphosis supports the need for an adequately designed randomized controlled trial examining the effect of exercise on hyperkyphosis.[17] Furthermore, efforts to prevent or treat osteoporosis related spinal kyphosis have identified the need for more comprehensive assessment of health outcomes in older adults with excessive kyphosis, including comprehensive assessment of symptoms, impact, and treatment benefit for kyphosis.[15]

The population is aging although physical function status is not keeping pace.[36] Individuals are living longer with greater impairments in physical mobility. There is sparse quality evidence of the effects of targeted spine strengthening exercise on kyphosis. Few trials have assessed the effects of a multi-modal spine strengthening exercise program on physical function, specifically mobility function, which is known to be impaired in individuals with hyperkyphosis. We are conducting a high-quality randomized controlled trial that is adequately powered and utilizes

validated outcome measurements of kyphosis, to investigate the effects of a multi-modal spine strengthening exercise program on both our primary outcome of kyphosis as well as secondary outcomes of physical function. If the exercise intervention results in a change in kyphosis and/or physical function, we will examine the pathways of change in order to determine whether changes in kyphosis, spinal muscle strength and/or density are responsible for the change in physical function. Furthermore, if we find that hyperkyphosis and physical function can be improved by a multi-modal spine strengthening exercise program, this evidence could enable providers to recommend early intervention for hyperkyphosis to prevent or delay hyperkyphosis associated physical disability.

Our study has some limitations including that we are recruiting a healthy community-based group of adults 60 year and older and are excluding individuals with co-morbidities that could interfere with safe participation in a group exercise class. Therefore the results of this study will not be generalizable to frail adults 60 years and older with hyperkyphosis. Another limitation is that blinding the participants and the instructors providing the intervention is not possible. While this is not uncommon in exercise trials, we have ensured that the investigators measuring kyphosis and performing the physical function testing are blinded to group allocation.

To ensure that the results of our study will inform physical therapists in practice and have an impact on patient care, results will be presented at scientific conferences and published in academic journals. We will also disseminate the results of this clinic trial to professional groups including the American Physical therapy Association, American Society of Bone and Mineral Research and the National Osteoporosis Foundation. These professional organizations may incorporate findings from this research into evidence-based exercise prescriptions and clinical practice guidelines for older adults with hyperkyphosis.

Our goal is to conduct a clinical trial that will provide clinicians with evidence of the efficacy of a targeted multi-modal spine strengthening exercise program on hyperkyphosis and physical function. Exercise trials have often used lower extremity strengthening exercise to improve physical function in older adults. In contrast, we are focusing on decreasing spinal hyperkyphosis. If our exercise intervention is successful, our approach to improving hyperkyphosis could represent a fundamental paradigm shift in exercise intervention strategies to improve physical function for older adults. Results from our trial may provide new insights into the effects of exercise on physical function and quality-of life that are important outcomes for patients and if successful, could assist providers' in individualized clinical decision making.

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Dr Katzman conceived of the study. Dr Katzman, Dr Vittinghoff, Dr Kado, and Dr Lane initiated the study design, and Dr Lane, Dr Schafer, Ms Wong, and Dr Gladin helped with implementation. Dr Katzman is the grant holder. Dr Vittinghoff provided statistical expertise in clinical trial design and conducted the primary statistical analysis. All authors contributed to refinement of the study protocol and approved the final manuscript. The authors appreciate Dr Roger Long's oversight reviewing participant medical histories and safety logs.

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Figure 1. Flowchart of the randomized control trial

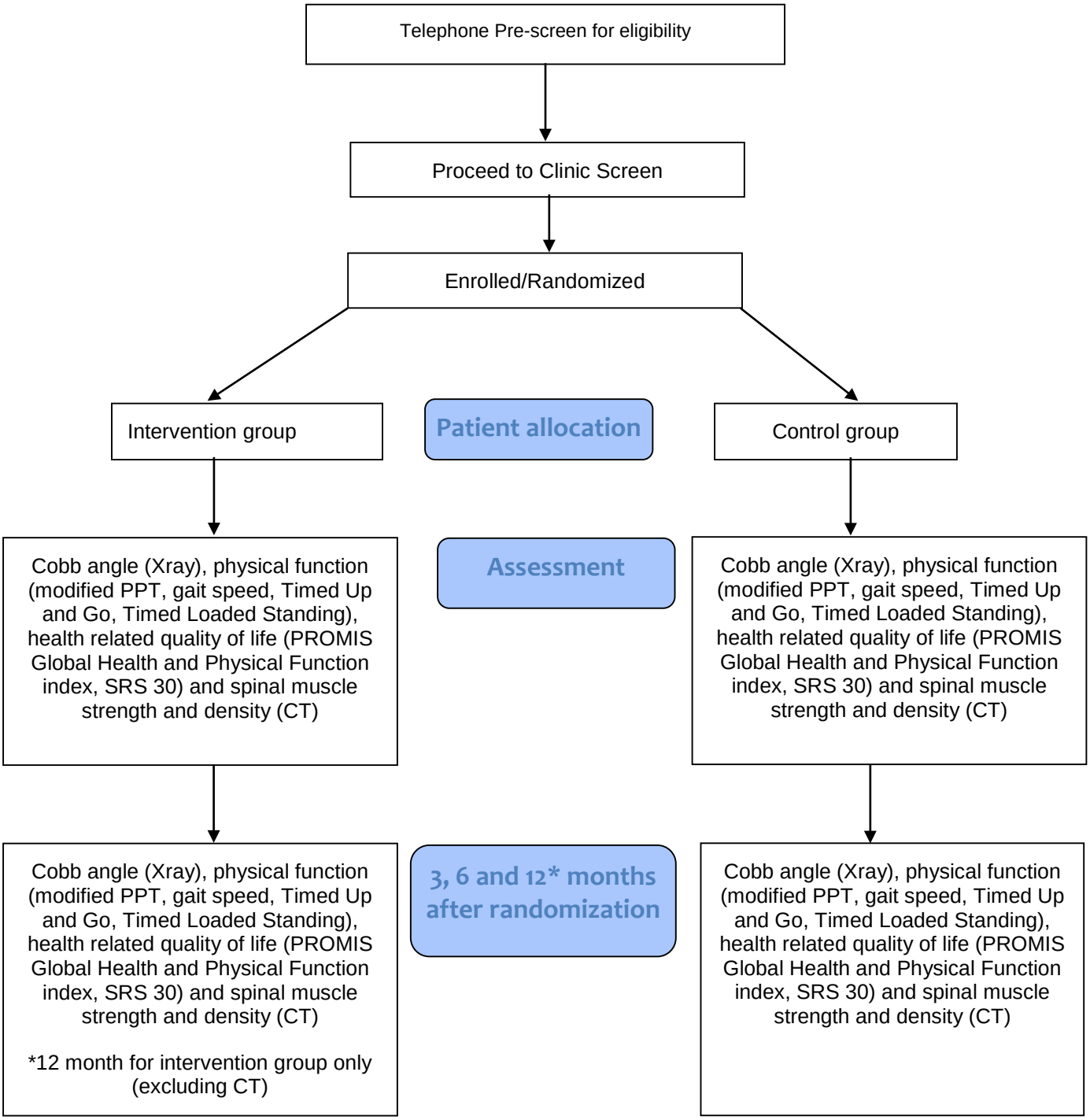

Table 1. Multi-modal spine strengthening exercise intervention framework

Exercise	Target	Repetitions	Equipment
Spinal strengthening: Strengthening trunk muscles (20 mins) **Progress weights and theraband to "somewhat hard to hard" 70-80% max**			
Supine transversus abdominus on roller	Stability of trunk with mobility of extremities; strengthen transverses abdominus	10 reps x1	Roller
Quadruped arm and leg lift	Stability of trunk with mobility of extremities; strengthen lower trapezius, spinal extension, multifidus, and transverses abdominus stabilization	8 reps x 2	Cuff weights
Prone trunk lift to neutral	Thoracic, lumbar and hip extension strengthening	8 reps x 2	Bolster, cuff weights
Side-lying thoracic rotation/extension	Thoracic extension and rotation with scapulothoracic retraction/depression strengthening, and mobility in extension and rotation	8 reps x 2	Theraband
Sidelying hip abduction/external rotation	Strengthen gluteus medius for stability in stance	8 reps x 2	Cuff weights
Spinal alignment: Warm-up, integrate postural stability into mobility training (20 mins)			
Marching on roller	Increase heart rate and warm-up "core" muscles"	10 reps x1	Roller
Unilateral overhead reaching on roller	Increase heart rate and increase shoulder flexibility	10 reps x1	Roller
Bilateral pull down supine on roller	Increase heart rate and improve shoulder and chest flexibility	10 reps x1	Theraband, roller
Shoulder flexion/thoracic extension at wall	Stability of trunk with mobility in shoulders and thoracic spine; strengthen lower	10 reps x1	Body weight

	trapezius/serratus anterior muscles		
Wall push-ups	Stability of trunk with mobility in arms; scapular stabilization	10 reps x1	Body weight
Single leg stance	Stability of trunk during unilateral stance	10 reps x1	Body weight
Spinal mobility: ROM exercises using a stretch strap as needed (15 min)			
Chest/spine stretching supine/roller	Lengthen pectoralis major; expand ribcage and anterior chest wall	During warm-up	Roller
Gluteal stretching	Lengthen posterior hip capsule and gluteal muscles	Passive 30s hold x1	-
Supine straight-leg raise	Lengthen hamstrings and gastroc-soleus	Passive 30s hold x1	Stretch strap
Prone hip/quadriceps stretch	Lengthen iliopsoas and quadriceps	Passive 30s hold x1	Stretch strap
Quadruped thoracic extension stretch	Increase thoracic spine extension and lengthen anterior chest wall musculature	Passive 30s hold x2	-
Neck/chest stretch standing	Cool-down; lengthen trapezius and anterior chest wall musculature	Passive 30s hold x3 positions	-
Diaphragmatic breathing: coordinated throughout; breathing into the concavity; exhaling with pelvic floor and deep abdominal muscle contraction			
Postural correction: Practice at least 3 times a day during activities of daily living			

Table 2. Schedule of enrollment, intervention and assessments

Activity	Staff Member	Time Point in Study Schedule						
		Screening/Consent	**Run-In**	**Baseline Testing**	**Study Classes/ Lectures**	**3-month Testing**	**6-month Testing**	**12-month Testing***
Recruitment and screening								
Telephone pre-screening	Recruiter	X						
Clinic screening, kyphosis measurement	Research Assistant	X						
Clinic screening, gait speed and safety exams	Research Assistant	X						
Clinic screening, demographic, medical history and Mini-Cog questionnaires	Research Assistant	X						
Informed consent	Research Assistant	X						
Assessments								
Pedometer allocation/ readings	Research Assistant		X	X		X	X	X
Height and Weight measurement	Research Exercise Physiologist			X		X	X	X
Modified Physical Performance Test	Research Exercise Physiologist			X		X	X	X
Time Loaded Standing	Research Exercise Physiologist			X		X	X	X
Timed Get Up and Go	Research Exercise Physiologist			X		X	X	X
6-minute walk	Research Exercise Physiologist			X		X	X	X
4meter walk	Research Exercise Physiologist			X		X	X	X
Biodex (isokinetic extension and flexion)	Research Exercise Physiologist			X		X	X	X
Debrunner kyphosis and lordosis	Research Exercise Physiologist			X		X	X	X
Lateral spine radiograph	Radiologist			X			X	X

Computed Tomography at L4	Radiologist			X			X	X
DXA-hip and lumbar spine	Research Exercise Physiologist			X				
Randomization	Research Assistant			X				
PASE questionnaire	Participant			X		X	X	X
Scoliosis Research Society SRS-30, self image domain	Participant			X		X	X	X
PROMIS global health and physical function	Participant			X		X	X	X
Adverse event protocol	Research Coordinator	As needed throughout study						
Intervention/Comparator Intervention								
Intervention Group								
Intervention Classes	Physical Therapist and Research Assistant				1 hr class 3x/wk for 6 mos			
Safety Logs	Research Coordinator				Weekly for 6 mos			
Control Group								
Lectures	Physical Therapist/MD/RN				1hr/mo for 4 mos			
Safety Logs	Research Coordinator				Monthly for 4 mos			

*Intervention Group Only

Table 3. Variables, hypotheses, outcomes, methods of analysis

Variable/Outcome	Hypothesis	Outcome Measure	Method of analysis
Primary			
Kyphosis	Improvement in intervention relative to control group	Radiographic Cobb angle	ANCOVA
Secondary			
Composite physical function	Improvement in intervention relative to control group	Modified Physical Performance Test score (7 items)	ANCOVA
Gait speed	Improvement in intervention relative to control group	4-meter walk	ANCOVA
Mobility	Improvement in intervention relative to control group	Timed Up and Go	ANCOVA
Spine endurance	Improvement in intervention relative to control group	Timed Loaded Standing	ANCOVA
Aerobic capacity/endurance	Improvement in intervention relative to control group	Six Minute Walk Test	ANCOVA
Spinal muscle strength	Improvement in intervention relative to control group	Biodex computerized dynamometer	ANCOVA
Spinal muscle density	Improvement in intervention relative to control group	Spinal extensor muscle attenuation from CT scans (HU)	ANCOVA
Spine specific health-related quality of life	Improvement in intervention relative to control group	SRS 30 self-esteem domain	ANCOVA
General health related quality of life	Improvement in intervention relative to control group	PROMIS Global Health Index and Physical Function Index	ANCOVA
Kyphosis	Improvement in intervention relative to control group	Kyphosis derived from Debrunner kyphometer	ANCOVA
Other outcomes			
Enrollment	We will recruit 100 participants	Number recruited	Descriptive statistics
Retention	We will retain at least 75% of the sample	Number who completed the study testing visit 2	Descriptive statistics

Adherence	The mean proportion of exercise sessions completed will be 60%	Mean proportion of completed exercise visits	Estimates based upon mean (95% CI)
Adverse events	No difference between groups	Self-report of adverse events	Chi-square test
Subgroup or sensitivity analyses			
Level of baseline kyphosis (split at 75th percentile)	No difference in outcomes	≥ 75th vs <75th percentile of kyphosis	Interaction term of the variable x treatment group
Number of co-morbidities	No difference in outcomes	≥2 vs 0-1 co-morbidities	Interaction term of the variable x treatment group
Presence or absence of vertebral fracture on baseline lateral spine radiographs	No difference in outcomes	≥1 or 0 vertebral fractures	Interaction term of the variable x treatment group
Physical activity level at baseline	No difference in outcomes	Step count at testing visit 1	Interaction term of the variable x treatment group
Change in physical activity at 6-months	No difference in outcomes	Change in step count from testing visit 1 to testing 2	Interaction term of the variable x treatment group

Table 4. Minimum detectable effects with sample size = 100

Outcome measures	Absolute / percent of mean change
Kyphosis (degrees)	1.88 / 3.3%
Modified Physical Performance Test (points)	0.98 / 3.3%
Gait speed (meters/second)	0.059 / 4.4%

Study of Hyperkyphosis, Exercise and Function (SHEAF) Protocol of a Randomized Controlled Trial of Multimodal Spine Strengthening Exercise in Older Adults With Hyperkyphosis

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