Published in final edited form as:

Contemp Clin Trials. 2020 February ; 89: 105912. doi:10.1016/j.cct.2019.105912.

Program to Improve Mobility in Aging (PRIMA) study: Methods and Rationale of a Task-Oriented Motor Learning Exercise Program

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Abstract

Walking difficulty is a common and costly problem in older adults. A potentially important yet unaddressed strategy to enhance walking ability through exercise intervention is to add a timing and coordination component in gait training (i.e. task specific timing and coordination exercise intervention) to the usual strength, endurance, and flexibility training. We describe the methods and rationale of a randomized single-blind, physical therapist supervised, exercise intervention trial to compare the effects of a standard strength, endurance, and flexibility program to a standard plus timing and coordination program in community-dwelling older adults walking slower than the desired gait speed of 1.2 m/s. Exercise sessions are twice weekly for 12 weeks. Participants are assessed at baseline, 12 weeks (post intervention), 24 weeks and 36 weeks. The primary outcome is gait speed, secondary outcomes represent components of the interventions (strength, endurance, flexibility, timing and coordination), and tertiary outcomes are measure of activity and participation (Late Life Function and Disability Instrument and physical activity). The findings of this trial will (1) establish if a standard-plus task specific timing and coordination program is superior to a standard strength and endurance program in improving mobility, activity and participation and (2) determine if the improvements are sustained over time. The information derived from this project will provide valuable insight into the prevention and management of walking difficulty, which is so common in older Americans.

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Keywords

aging; exercise; physical therapy; disability; rehabilitation

INTRODUCTION

Walking difficulty is a common and costly problem in older adults. Almost half of all community-dwelling older adults report walking difficulty and of those without such difficulty, approximately 22% will develop new difficulty over one year.¹ Gait speed, a measure of mobility, is a strong predictor of walking difficulty, nursing home placement and death.^{2–5} Improvements in gait speed predict a substantial reduction in mortality⁶ and are related to fewer disabilities, hospitalizations and a reduction in healthcare costs.⁷

Walking is a complex task that places demands on multiple systems including the musculoskeletal, cardiopulmonary, and nervous systems.^{8,9} Current exercise interventions to improve mobility focus on underlying musculoskeletal, cardiopulmonary, and vascular mechanisms besides others, with little emphasis on neural control mechanisms such as motor sequencing and temporal dynamics.^{10,11} A motor skill based exercise approach uses task specific timing and coordination exercises to challenge the brain to adapt and learn the sequence of movements and timing with the postures and phases of gait to improve walking.^{12,13} Improvements in walking occur by restoring the pattern of brain and neuromuscular activation that optimizes the use of capacities to meet the demands of the task of walking. Given the widespread subclinical and clinical neurological abnormalities with aging,^{14–17} it is important to incorporate explicit motor control principles into exercise for older adults. Thus, a potentially important yet unaddressed strategy to promote walking ability through exercise intervention is to add a timing and coordination component in gait training (i.e. task-oriented timing and coordination exercise) to the usual strength, endurance, and flexibility exercise components. In previous pilot studies, task specific timing and coordination training had beneficial effects on mobility (gait speed) that were greater than a standard strength and endurance program immediately after completion.^{18–20} However, the impact of the intervention on activity and participation and the longer-term persistence of effects of the program after the intervention has ended are less known.²¹ Therefore, the objectives of the present study are to determine if a standard-plus program is more successful in improving walking ability (i.e. gait speed; primary outcome), and other process, activity and participation outcomes at 12 weeks after study entry compared to a standard exercise program; and to determine if whether the greater benefits will be observed in both slower and faster walkers and persist over time.

METHODS

Study Overview.

This is a randomized single-blind two arm intervention trial to compare the effects on mobility, activity and participation of a standard strength, endurance, and flexibility program to the standard plus timing and coordination program in community-dwelling older adults walking slower than the desired gait speed of 1.2 m/s.^{22,23} Physical therapist delivered

exercise sessions are twice weekly for 12 weeks. Participants are assessed at baseline, 12 weeks (post intervention), 24 weeks and 36 weeks. See Figure 1 for the study flow. The study is approved by the University of Pittsburgh Institutional Review Board and registered in clinicaltrials.gov (NCT02663778). All participants provided written informed consent prior to participation. The trial was initiated in April 2016 and data collection is ongoing.

Participants.

We select older adults based on gait speed as it is an indicator of future morbidity and mortality.^{4,5} To be included in the study, walking speed has to be 0.6–1.2 m/s. The range restriction ensures older adults are at increased risk for negative outcomes but are walking sufficiently well to participate in the intervention.³ Desired gait speed is between 1.2–1.3 m/s;^{23,24} however, it is not uncommon for some older adults to walk faster than 1.3 m/s.⁴ We selected 1.2 m/s as the upper limit as it identifies older adults with walking speed less than desired and there is room for meaningful improvement.²⁵ We exclude persons who are unable to participate in testing, have medical conditions that make testing or participation in an exercise program unsafe, or who have plans to permanently leave the area during the study period. See Table 1 for a comprehensive list of inclusion/exclusion criteria.

Recruitment and Retention.

Participants are recruited through the Pittsburgh Pepper Center Registry of over 2200 older adults who have *consented to be directly contacted* by participating researchers about mobility research studies. Registry participants are diverse in gender, age and ethnicity and have a wide range of self-reported mobility. To maximize participation and retention, participants are reimbursed for travel expenses related to the study.

Screening.

Initial phone contact uses a structured questionnaire to identify inclusion and exclusion criteria by self-report. Individuals who meet criteria are scheduled for an in person examination to identify additional potential exclusions. Prior to the in person examination, safety of participation is reviewed and approved by the candidate's physician. The in person exam includes a review of systems, current medications, vital signs, neurological exam, lower extremity range of motion and strength testing, visual screening, and cognitive status²⁶. Eligibility is determined based on a 4 meter gait speed measured using a stopwatch. Two trials are completed and the mean gait speed is calculated to determine eligibility.

Data Collection.

Data collection for baseline, 12, 24, and 36 weeks is identical. The primary, secondary and tertiary outcomes (Table 2) described below are collected by assessors masked to group assignment.

Mobility Primary Outcome:

Gait Speed.

The primary outcome is gait speed because of its strong psychometric properties, significant association with morbidity and mortality, and the continuous nature of the variable with desirable distributional properties. Gait speed is a reliable,^{27,28} valid, sensitive²⁵ and specific²⁹ measure that correlates with functional ability and balance confidence. Gait speed is not only strongly associated with future disability, falls, hospitalization, nursing home admission and mortality,^{2–5} but also a responsive measure sensitive to change over time.^{6,25,30} Thus, an improvement in gait speed is likely a good indicator of the effectiveness of an exercise program. In addition, gait speed was chosen by a panel of experts as the standardized assessment to measure locomotion for the Motor Function Domain of the National Institutes of Health (NIH) Toolbox.³¹

Usual pace gait speed is assessed with an instrumented walkway (Protokinetics LLC, Havertown, PA). After explanation and demonstration, the participant completes two practice walks the length of the walkway to become accustomed to walking on the walkway. Each walk is considered one pass. The subject then completes six passes on the walkway at their usual, self-selected walking speed. Gait speed is averaged over the six passes. The test-retest reliability of gait speed measured using an instrumented walkway by intraclass correlation coefficient (ICC) is 0.98.²⁷

Process Secondary Outcomes:

In order to assess the integrity of the intervention, we selected measures that represent the main components of the intervention (i.e. strength, endurance, flexibility, and timing and coordination) as our secondary outcomes.

Strength and Power.

The Keiser A420 (Keiser Corporation, Fresno, CA) electronic pneumatic leg press machine is used to measure lower extremity strength and power. Leg strength is measured by determining the 1 repetition maximum (1RM) for each leg individually. The maximum value observed on the graphical display of either side is recorded as the peak leg strength. For power, we follow the protocol previously described by Callahan et al, 2007.³² First, the 1RM for each leg is determined. Then power testing at 40% of 1RM and 70% of 1RM is conducted for each leg. Rest breaks of a minimum of 90 seconds are given between each test. Leg press power is measured as the peak power graphically recorded when the individual performs a single leg press repetition pushing out as quickly as possible at 40% and 70% of 1RM. Five repetitions are recorded for each leg at each resistance. The highest recorded power of all repetitions (either side, either resistance) is operationally defined as leg press power. Leg press power at 40% and 70% of 1RM is recorded.

Endurance.

The Six Minute Walk Test (6MWT) of distance walked (meters) in six minutes, including time for rest as needed, is used to assess endurance.³³ The 6MWT has established

psychometric properties, including test-retest reliability (Pearson $r=.95$) in older adults,^{29,34} and construct validity for graded exercise test and functional classification.³⁵ We chose the 6MWT because it is responsive to change,^{25,36} widely used, and included in the NIH Patient-Reported Outcomes Measurement Information System project of establish measures for clinical assessment.³⁷ Greater distance covered during the six minutes is better.

Flexibility.

The Chair Sit-and-Reach Test, a measure of hamstring flexibility, is the measure of flexibility.³⁸ Subjects sit on the edge of a chair with their preferred leg extended and the other leg bent with the foot flat on the floor. Subjects bend forward at the hips, keeping the spine as straight as possible. The distance reached in relation to the foot is recorded in cm. The test was selected because it does not require the older adult to sit on the floor, which may be difficult for some. The test has established psychometric properties of test-retest reliability (ICC=0.92–0.96) and criterion validity with comparison to the sit-and-reach test ($r=0.74$).³⁸ Values can be positive or negative with positive numbers indicating greater flexibility.

Timing and Coordination of walking.

Smoothness of walking is an integrated measure of motor control of walking,^{39,40} and is assessed during usual over ground walking. Linear acceleration of the body is measured along three axes (vertical, anterior-posterior and medial-lateral) using a tri-axial accelerometer attached to the skin over the third lumbar spine (L3) segment. Trunk accelerations are sampled at 200 Hz and are used to calculate the harmonic ratio following the methodology of Menz.³⁹ The harmonic ratio (HR) is derived in the vertical, medial-lateral and anterior-posterior directions. Higher HRs are better.

Gait variability, defined as fluctuations in gait characteristics from one step to the next,⁴¹ is an important indicator of impaired mobility in older adults^{42,43} and is a second indicator of timing and coordination. Gait variability is quantified for temporal and spatial gait characteristics including stance time, step length, and step width. Variability is calculated as the between-step standard deviation of the set of steps recorded over six passes on an instrumented walkway (described above under gait speed). Approximately 32 steps or more are collected from six passes on the walkway which is more than adequate to achieve a stable measure of gait variability. Our prior work has shown that 20 steps are sufficient to achieve a reliability of 0.75 and 30 are sufficient for 0.80.^{44,45} In general, lower variability is better although there are exceptions.^{42,43,46}

The Figure of 8 Walk (F8W) was designed to measure motor skill (speed, amplitude and accuracy of movement) in walking and is a task specific measure of timing and coordination.^{47,48} The test involves walking a figure of eight pattern about two markers placed 5 feet apart. Performance is scored based on the time to complete the figure 8 walk and the number of steps to complete the walk. The F8W has demonstrated interrater reliability and test-retest reliability (interrater ICCs of .90 and .92 and test-retest ICCs of .84 and .82, for time and number of steps, respectively). Construct validity has been previously demonstrated by

associations with physical function in daily life, activity restriction, and performance of activities of daily living.⁴⁷ A faster time and fewer steps are better.

Activity Tertiary Outcomes:

Using the World Health Organization's International Classification of Functioning, Disability and Health (ICF)⁴⁹ model, we include measures of activity (execution of a physical task) as tertiary outcomes. Activity levels are assessed with the Late Life Function and Disability Instrument functioning component (LFDI-F).⁵⁰ The LFDI-F is a self-report measure for assessing physical function in older adults with acute or chronic problems, and designed to be more sensitive to change than similar measures. It has 32 items in three domains, basic lower extremity, advance lower extremity and upper extremity. We selected the LFDI-F because 1) it includes a wide variety of life tasks in various social areas thus extending beyond the traditional focus of just activities of daily living, 2) the scale was designed with sufficient breadth of items and increments of rating in order to minimize ceiling and floor effects and maximize the scale's ability to detect change over time, and 3) it is a continuous outcome which gives us greater statistical power than a dichotomous outcome to detect change over time. The LFDI-F has established known groups validity and the test-retest reliability is extremely high (ICC=0.91–0.98).⁵⁰ Scores range from 0–100; higher scores represent a greater level of function.

Participation Tertiary Outcomes:

Guided by the ICF⁴⁹ model, we include LFDI Disability (LFDI-D) components as measures of participation (involvement in life situations).⁵¹ LFDI-D is a self-report measure for assessing disability in older adults with acute or chronic problems, and designed to be more sensitive to change than similar measures. LFDI-D has 16 items representing frequency of performance and limitation in performance of life tasks domains. We use disability frequency and disability limitation domains in our study. Within the disability limitations domain, we also employ social role, personal role, instrumental role and management role domains because they may provide insight into the impact of the disability on frequency of performance and perceived limitations.⁵¹ LFDI-D scales have established known groups validity and the test-retest reliability is moderate to high (ICC=0.68–0.82).⁵¹ Scores range from 0–100; higher scores represent less disability.

The Actigraph Accelerometer (Actigraph, Pensacola, FL) is used to assess the participants' usual daily physical activity. The ActiGraph is often used in physical activity research and has recently been shown to be more reliable than other devices.⁵² The Actigraph has been validated in a variety of laboratory and field settings.^{53–55} Accelerometers are electronic sensors that measure the quantity and intensity of ambulatory movement.⁵⁶ The Actigraph Accelerometer is worn on the waist during waking hours for 7 consecutive days, and the participants are instructed to remove the monitor only for sleeping, during imaging studies, and or during swimming and bathing activities. For pre-intervention physical activity assessment, the participants are given the accelerometer during the baseline assessment. They are asked to return the accelerometer during their first intervention visit. For post-intervention testing, the subject receives the accelerometer during the last intervention visit

and are asked to return it during the post-intervention assessment. For the 24- and 36-week follow-up assessments, the participant is given the accelerometer during their visit and are asked to return it by mail in a postage paid envelope. The continuous data that are available through actigraphy provide many possible measures for analysis. We focus on 1) total activity counts, 2) percentage of time spent in sedentary activity and 3) number of bouts of moderate intensity activity as our outcomes. Wear time will be also be recorded and all activity outcomes will be adjusted for wear time.

Interventions.

Sessions are twice weekly for 12 weeks supervised by a physical therapist (PT). The PTs are trained by the intervention developers in all aspects of the interventions and they are responsible for delivering the interventions to both arms of the study. All sessions last about 50–65 minutes and include a warm-up, 40–55 minutes of the exercise intervention, and a cool down period. Both intervention groups also receive a physical activity behavioral change program (Group Lifestyle Balance™) described below.

Modified Group Lifestyle Balance™ (modified GLB).

The Group Lifestyle Balance (GLB) program is a behavioral lifestyle intervention which is modeled closely on the original and highly successful Diabetes Prevention Program.⁵⁷ The Diabetes Prevention Program is a NIH funded study that demonstrated small changes in lifestyle such as healthy eating and increased physical activity could lower the risk of developing type 2 diabetes in those at high risk for the disease. GLB was designed to help individuals reach a balance between two parts of their lifestyle--eating and physical activity.⁵⁸ We focus only on the physical activity component of the GLB program (i.e. modified GLB). The physical activity goal of the GLB program is for participants to achieve and maintain a weekly physical activity level of at least 150 minutes of moderate intensity activity similar to a brisk walk. Participants in both interventions participate in 16 modified GLB sessions. The first 12 sessions are weekly, individual sessions. The final 4 sessions are delivered in person or over the phone over a 12-week period as follows: every other week for 4 weeks (2 sessions) and once every 4 weeks for 8 weeks (2 sessions). Sessions cover topics such as *Jump Start Your Activity Plan*, *Problem Solving*, *Ways to Stay Motivated* and *Stress and Time Management*.

Standard Intervention.

The Standard Intervention includes a brief warm-up period (5 minutes), lower extremity strengthening exercise (10–15 minutes), endurance exercise (30–40 minutes), and a brief cool down period (5 minutes) for a total of 50–65 minutes of intervention. The warm-up and cool down periods contain gentle stretching exercises for the lower extremity and trunk. The strengthening exercise is conducted on stacked weight training equipment (leg extension/curl combo, leg press machine, and multi-hip combo) and can include the following exercises: knee extension, knee flexion, leg press, hip abduction and hip extension. When participants could complete 2 sets of 15 repetitions with light effort (i.e. Rating of Perceived Exertion [RPE]⁵⁹ < 10), resistance is increased for progression of the exercises; the aim to exercise in a perceived effort range of RPE, 11–13, 'somewhat hard'. Participants complete exercises for hip abduction and hip extension plus an additional one to two exercises for the

lower extremity muscle groups, which are selected by the physical therapist based on the individual participant's needs. The endurance exercise consists of treadmill walking at a somewhat difficult submaximal workload with a RPE of 10–13. When participants can tolerate a 10–13 RPE level for 15 minutes, the workload is increased. The goal is to achieve 40 minutes of continuous treadmill walking exercise at the somewhat difficult level of exertion.

Standard Plus Task Specific Timing and Coordination Intervention (Standard-Plus).

Participants receiving the Standard-Plus Intervention will complete task specific timing and coordination exercise in addition to Standard Intervention described above. In order to keep the total intervention time and the time spent in walking/standing activities equal between the two intervention arms, the participants in the Standard Plus intervention complete a 5 minute warm-up, 10–15 minutes of lower extremity strengthening exercises, 15–20 minutes of endurance exercises, 15–20 minutes of timing and coordination exercise, and a 5 minute cool-down for a total of 50–65 minutes of intervention.

The timing and coordination exercise is based on principles of motor learning that enhance “skill” or smooth and automatic movement control.^{60–65} This program uses goal-oriented, progressively more difficult stepping and walking patterns to promote the timing and coordination of stepping, integrated with the phases of the gait cycle. Conceptually, the exercise is intended to achieve its effects by shifting the center of pressure posterior-lateral then forward, encouraging hip extension prior to stepping, loading the trailing limb, coordinating activation of the abductors of the soon to be swing leg with adductors of the stance limb, and shifting the center of pressure in medial stance to unload the stepping limb. Progression is based on first separately increasing the speed, amplitude or accuracy of performance prior to undertaking a more complex task.^{12,13,18,20} For example, the progression of stepping patterns is, 1) self-paced step forward and across, 2) increase stepping speed, 3) alternate side of stepping, and 4) alternate forward with backward stepping. Walking patterns incorporate patterns of muscle coordination and interlimb timing similar to the stepping exercises into walking. Walking patterns progress by separately altering speed, amplitude (e.g. narrowing oval width), or accuracy of performance (e.g. without straying from the desired path), and then to complex walking patterns involving walking past others and with upper extremity object manipulation tasks added, such as carrying, bouncing or tossing a ball.⁶⁵

Key Differences between Interventions.

The standard impairment-based intervention aims to increase physiologic capacity in body systems that contribute to walking but does not include task specific exercise necessary to make use of the physiological capacity in body systems (i.e. musculoskeletal and cardiopulmonary systems) for the walking. Whereas, the task specific timing and coordination intervention aims to improve the motor skill of walking by re-aligning biomechanical and neuromotor programs, and improving feedback for adjusting movements.^{13,18} In a sense, an impairment-based intervention can be thought of as “installing a bigger engine” whereas the task specific timing and coordination intervention is comparable to a “tune-up” of an engine for optimal performance.¹²

Treatment Fidelity.

A developer (JVS) of the task oriented timing and coordination program monitors treatment fidelity. The individual reviews the intervention data sheets biweekly, observes interventions being delivered quarterly and conducts annual meetings with the physical therapist (PT) interventionists, with the goal of ensuring adherence to the specific protocols. Treatment fidelity data provides information on the adherence of the physical therapists to the interventions, and the adherence of the participants to the prescribed activities. Monitoring treatment fidelity also provides an opportunity to detect and address potential study problems early, optimizing potential for benefit and ensuring accurate interpretation of findings.

Randomization.

We randomize participants to standard and standard-plus interventions in a 1:1 ratio, stratified by whether a slower (<1.0 m/s) or faster (≥ 1.0 m/s) walker at baseline. Within each baseline gait speed stratum, we use a blocked randomization scheme with block sizes randomly chosen from small even numbers to force continued approximate balance between the numbers of subjects in each arm during recruitment. Exact block sizes will be revealed after unmasking the data. The randomization scheme was built into the study data management system. At the time of randomization, the system first determines the stratum of the participant being randomized, and then assigns the group dictated by the next unused randomization sequence number for the stratum. The system does not allow access to the group assignment to blinded study team members (outcomes assessors).

Sample Size Justification and Statistical Power.

Total sample size of 248 was estimated based on preliminary data from our pilot studies; our ability to detect statistical significance in two-tailed tests conducted at the $\alpha=0.05$ level; standard sample size and power computation methods available in the literature and commercial software (PASS® 2012; Number Cruncher Statistical Systems, Inc., Kaysville, Utah); and conservative expected dropout rates of 10, 15 and 20% during the 12-, 24- and 36-week follow-up. Thus, we conservatively anticipate 111, 105 and 99 participants in each intervention arm to complete the 12-, 24- and 36-week assessments. Our primary outcome on which the sample size justification is based is gait speed. The preliminary data estimate the standard deviation in baseline to follow-up change in gait speed is 0.15 m/s.^{19,20} Moreover, a meaningful change in gait speed is approximately 0.10 m/s.²⁵ With the proposed number of 124 randomized to each intervention, we will have $>99\%$ power to detect statistical significance of a between-intervention difference of such magnitude in 12-week change (primary outcome and endpoint). Anticipating that half of the participants will belong to the slower baseline gait speed stratum, we will be able to detect a between-intervention difference in 12-week change within each stratum (slower/faster baseline gait speed) with 93% power. For 24- and 36-week gait speed change, we will have 92% and 90% statistical power, respectively, within each stratum. If the anticipated split between slower and faster walker strata turns out to be no worse than 55%–45%, we will still have at least 90% power for both strata; and if it is no worse than 67%–33%, at least 80%.

Regarding other outcomes, our preliminary data showed standard deviations in baseline measures of 0.9 s for Figure 8 Walk time, 8.8 points for LFDI function, 12.1 points for LFDI disability limitation and 53.1 m for 6-minute walk test.¹⁹ Baseline to follow-up change standard deviations, respectively, were 1.08 s, 5.5 points, 11.8 points and 42.8 m.¹⁹ With the proposed sample size, we will be able to detect differences as small as 0.43 s, 2.2 points, 4.7 points and 17.2 m, respectively, in 36-week changes with 80% power. They correspond to small-moderate Cohen's effect sizes of 0.25–0.48.⁶⁹ Statistical power for more proximal endpoints is even greater due to greater numbers of participants in study at earlier time points.

Data Analysis.

Overview.—All statistical analyses will be performed based on the intention-to-treat philosophy. First, the baseline pre-intervention values of participant characteristics and measurements will be compared between the two arms with and without consideration of gait speed stratum using analysis of variance, Kruskal-Wallis, chi-square and/or Fisher's exact tests, as appropriate, depending on type and distribution of variables. Any significant differences will be noted and accounted for by controlling for them as additional covariates in supplements to the main analyses. We will not alter the main analyses to preserve its a priori and predictable nature. Next, main analyses to address the specific aims and hypotheses will be performed. If an analysis of residuals reveals violations of standard assumptions of linear models, we will use a Box-Cox transformation⁷⁰ to the response variable before fitting the models. Multiple imputation will be used to account for any missing data in the main analysis.^{71,72} Finally, many exploratory follow-up analyses will be performed as outlined below.

Main Analysis.—We will fit a series of linear mixed models using the SAS® MIXED procedure with change from baseline in each of the continuous outcome measures as the dependent variable; intervention arm (standard/standard plus), follow-up time point (12-/24-/36-week) and their interaction as fixed effects; baseline value of outcome as an additional fixed effect covariate; and a participant random effect. We will appropriately construct means contrasts to compare the intervention gains at 12, 24 and 36 weeks. The tests of significance at $\alpha=0.05$ for the 12-week gait speed means contrast will be considered the formal test of the primary hypothesis. Next, we will repeat the above mixed model analysis entirely, but with stratification by baseline gait speed ($<1.0/1.0+$ m/s) for secondary within-subgroup comparisons. Statistical significance of 24- and 36-week means contrasts and other outcomes will be considered as tests of the secondary hypotheses involving process, activity and participation outcomes as well as persisting effects.

Exploratory Analyses.—To examine subgroup-specific intervention effects, we will repeat the main analyses after stratification by various other baseline participant characteristics (besides baseline gait speed) to identify, if any, subgroups which are most/least likely to benefit from interventions. A priori, we anticipate that stratification by baseline walking confidence and cognitive function may show differential gains. We are aware that any definitive subgroup analyses should be supported by strong evidence in the form of a significant interaction effect.⁷³ Tests of interaction generally have low statistical

power, and it is not a main goal in the present trial to recruit a large number of participants required for definitive subgroup analyses beyond the already included pre-planned subgroups based on baseline walking speed. Thus, we plan to interpret our subgroup analyses with caution and an exploratory rather than a confirmatory philosophy, whose results are to be confirmed in a larger subsequent trial.

DISCUSSION

Standard impairment-based strength and endurance exercise interventions to improve walking, which ignore the timing and coordination of the movement control of walking, have a real but modest impact on walking ability in older adults.^{74–79} Aging and disease alter timing and coordination as reflected by slowed neuromotor performance, increased gait variability and reduced smoothness of movement.^{80–83} A task oriented timing and coordination exercise intervention that includes practice in the coordination and timing aspects of gait across varied walking conditions (eg straight and curved paths) has the potential to improve the smooth motor skill and efficiency of walking ability greater than a standard exercise program.^{19,20}

Why would we expect both slower and faster walkers to reap greater benefits from Standard-Plus?

It is important to note the goal of considering subgroups based on baseline walking speed is different from that of a traditional subgroup analysis. Typically, the goal is to examine whether the between-intervention difference is greater in one subgroup compared to another which is accomplished through a test of subgroup $\times$ intervention interaction. If the interaction test is significant, one estimates subgroup-specific between-intervention differences. In contrast, our goal was to demonstrate that both subgroups benefit to a greater degree with the Standard-Plus intervention. The rationale being that older adults with both mild (i.e. gait speed between 1.0 and 1.2 m/s) and moderate (i.e. gait speed between 0.60 and 1.0 m/s) walking difficulty are likely to have subclinical or clinically overt neurological impairments which contribute to their walking difficulty and which could benefit from the timing and coordination intervention.^{19,20}

Why would the standard-plus intervention impact activity and participation?

Walking underlies many activities of daily living and walking difficulty is associated with reduced activity and participation.^{50,84} The timing and coordination component of the standard-plus intervention, is a task-oriented approach which emphasizes the sequence of movements and timing with the postures and phases of gait to improve walking. The ultimate goal of the timing and coordination training is to make the older adult a skilled, “expert” walker. For motor tasks, expert movers, or those with greater motor skill for a specific activity, tire less easily than novices because of the greater efficiency of skilled motor performance.^{60,85,86,87} Older adults who are “expert walkers” (i.e. skilled walkers) have efficient gait, tire less easily and as a result will likely walk more, participate in more activities and report less disability.²¹

Why would the benefits of the standard-plus intervention be sustained after the intervention has ended?

Intervention strategies challenge the brain to improve walking performance in different ways. An impairment-based intervention, such as the standard strength and endurance program, challenges the brain to use increased capacity in body systems to compensate for gait difficulties. Walking performance likely improves secondary to increased ability to produce muscle forces, to move joints through a greater range of motion, and to deliver more oxygenated blood to the active tissues. The use of greater capacity of body systems for walking makes the outcome of the impairment-based intervention approach potentially inefficient and difficult to sustain. A motor skill based approach challenges the brain to adapt and learn the sequence of movements and timing with the postures and phases of gait to improve walking. Improvements in walking occur by restoring the pattern of brain and neuromuscular activation that optimizes the use of capacities to meet the demands of the task of walking. The task-oriented focus of the motor skill based approach has the potential to lead to not only an efficient and automatic motor sequence pattern for walking, but also reward-based adaptive changes in the brain, which may be sustainable.¹³ Recently, in a randomized controlled trial comparing strength exercises to task-oriented exercises in older women, improvements in functional task performance were sustained for six months after the end of training only in the task-oriented group.⁸⁸

CONCLUSION

Exercise recommendations for older adults rarely focus on motor learning or other forms of exercise that promote neurological function. Standard strength, endurance and flexibility exercises has had only modest effects on mobility likely because it does not address all of the underlying systems involved in walking. To our knowledge, ours is the first large, adequately powered clinical trial to focus on a novel but scientifically justified intervention to improve the timing and coordination of gait, and to assess its capacity to improve mobility, and promote activity and participation in older adults. The findings will (1) establish if a standard-plus task specific timing and coordination exercise intervention program is superior to a standard strength and endurance program in improving mobility, activity and participation and (2) determine if the improvements are sustained over time. The information derived from this project will provide valuable insight into the prevention and management of walking difficulty, which is so common in older Americans. If the findings are encouraging, we will pursue avenues of dissemination such as an implementation project incorporating the standard-plus task specific timing and coordination walking exercise intervention into physical therapy clinical practice.

ACKNOWLEDGEMENTS

This work was supported by the National Institutes of Health (R01 AG045252A, K24 AG057728, P30 AG024827, K23 AG049945).

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Figure 1.
Study flow diagram

Table 1.

Inclusion and exclusion criteria

Inclusion Criteria (all criteria must be met)		Exclusion Criteria (one or more)	
1	65 years of age and older	1	Inability to participate in testing or exercise intervention:
2	Ambulatory without an assistive device or the assistance of another person	a.	persistent lower extremity pain that is present on most days of the week and crepitus, tenderness or enlargement of joints of the lower extremity (arthritis) ⁸⁹
3	Usual 4-meter gait speed > 0.60 m/s and < 1.2 m/s	b.	back pain that is present on most days of the weeks and interferes with walking and activities of daily living or back pain that increases with walking (lumbar stenosis)
4	Physician clearance to participate in a moderate intensity exercise program	c.	calf pain or cramping which worsens with walking and is relieved by rest (peripheral arterial disease)
		d.	refuse to walk on a treadmill
		e.	plans to move out of the area in the next year
		1	Safety concerns:
		a.	dyspnea at rest or during activities of daily living or use supplemental oxygen (congestive heart failure, chronic obstructive pulmonary disease)
		b.	any acute illness or medical condition that is not stable according to the approving physician
		c.	resting systolic blood pressure ≥ 200 mm Hg or diastolic blood pressure ≥ 100 mm Hg or resting heart rate > 100 or < 40 beats per minute ⁹⁰
		d.	diagnosis of any dementia or cognitive impairment defined as Modified Mini-Mental State examination score < 79
		e.	hospitalized in the past 6 months for acute illness or surgery, other than minor surgical procedures
		f.	severe visual impairment as indicated by difficulty navigating the clinic
		g.	history of stroke
		h.	fixed or fused lower extremity joints such as hip, knee or ankle
		i.	lower extremity strength <3/5 on manual muscle testing
		j.	lower extremity amputation
		k.	progressive movement disorder such as multiple sclerosis or Parkinson's disease

Table 2.

Primary, secondary and tertiary outcome measures.

Outcome Category	Construct	Measure
Primary	Mobility	Gait speed
Secondary	Strength	Leg press strength (1 repetition max) and power (at 40% and 70% of 1 repetition max).
	Endurance	Six-minute walk test
	Flexibility	Chair Sit-and-Reach Test
	Timing and Coordination	Smoothness of walking, Gait variability, Figure 8 Walk
Tertiary	Activity	Late Life Function and Disability Instrument – Function
	Participation	Late Life Function and Disability Instrument – Disability Daily physical activity