

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Li F, Harmer P, Fitzgerald K, et al. Tai chi and postural stability in patients with Parkinson's disease. *N Engl J Med* 2012;366:511-9.

(PDF updated February 9, 2012.)

Supplementary Appendix

This Supplementary Material section has been supplied by the authors to provide readers with additional information about the original research plan and results (including the Flow of Patients through the Trial, Tables 1 and 2).

The components in this Supplementary Material document are as follows:

1. Research Plan
2. Figure 1: Flow of Patients through the Trial.
3. An expanded version of Table 1.
4. Description of intervention sustainability with an expanded version of Table 2.

Online publication Supplementary Material for Li F, Harmer P, Fitzgerald K, et al. Tai Chi and postural stability in patients with Parkinson's Disease. *N Engl J Med* 2012; 366:511-519.

Research Plan

Note: The following research plan was prepared in 2007 and subsequently approved prior to the initiation of the trial by the Institutional Review Board of the Oregon Research Institute (dated August 2007).

Study Design Overview

Based on our preliminary work,^{1,2,3} we propose to conduct a 6-month randomized, controlled, single-blind clinical trial with three intervention arms: Tai Chi, strength training, and a low-impact exercise stretching control. The primary aim is to investigate whether a Parkinson's-specific Tai Chi program can improve primary outcome measures of balance and secondary outcome measures of physical function, lower-extremity muscle strength, and falls frequency in patients with mild-to-moderate Parkinson's disease (stages 1, 2, or 3 of the Hoehn and Yahr scale).⁴ Two secondary aims are to be examined: (a) whether gains in lower-extremity muscle strength following the Tai Chi intervention will mediate the relationship between the intervention and the endpoint of balance and (b) whether there will be sustainability of intervention effects at a 3-month follow-up. Randomized participants in each intervention arm will receive a twice weekly, 60-minute exercise program for 24 consecutive weeks. Primary and secondary outcome measures will be collected at baseline, 3 months, and at the 6-month trial termination, and again at 3 months postintervention. Based on theoretical considerations and previous research on Tai Chi, the overarching working hypothesis is that Tai Chi will show better performance results on primary outcome measures compared to both the strength training and low-impact exercise control groups.

The basic components of the study design flow are depicted in Figure 1. The study will use a staggered subject recruitment process, in which eligible participants will undergo initial screening, consent, and baseline assessments, and then be randomized based on a 1:1:1 ratio allocation schedule. Details regarding study population, subject recruitment, randomization, intervention components, and outcome assessments are described below.

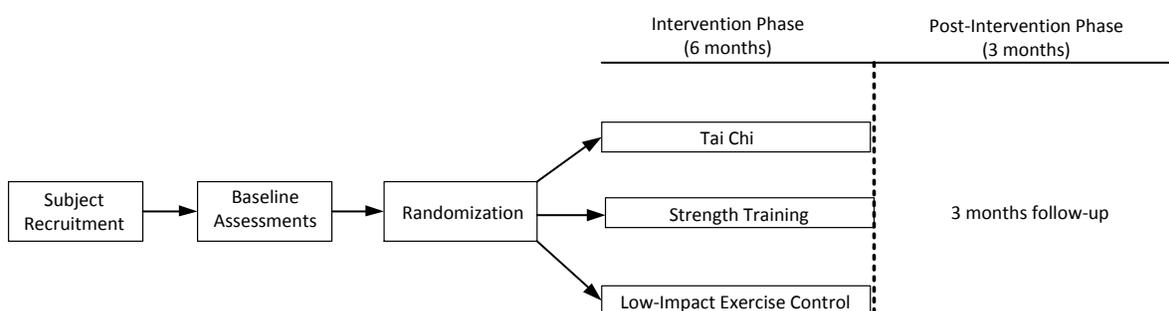


Figure 1. Study Design Flow

Study Population

The intervention will be directed toward individuals who have been diagnosed with idiopathic Parkinson's disease, with the following eligibility criteria.

Inclusion criteria will include (a) a clinical diagnosis of Parkinson's disease, with a disease severity rating of stage I to III on the Hoehn and Yahr scale;⁴ (b) age between 40 and 85 years old; (c) at least one score of 2 or more for at least one limb for the tremor, rigidity, postural stability, or bradykinesia items in the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS III);⁵ (d) stable medication usage; (e) ability to stand unaided or walk with or

without an assistive device; (f) medical clearance for participation; and (g) willingness to be assigned to any intervention condition. Exclusion criteria will include (a) current participation in any other behavioral or pharmacological study or instructor-led exercise program; (b) Mini-Mental State Examination⁶ score lower than 24; (c) debilitating conditions or vision impairment that would impede full participation in the study; and (d) being unavailable during the study period.

Recruitment Sources and Procedures

Potential study participants will be recruited through three major sources: (1) referrals from local medical clinics (i.e., physician/neurologist offices); (2) local Parkinson's disease support groups; and (3) advertisements in local newspapers. The study participants will be recruited from the Eugene-Springfield area in Lane County, Oregon. To reduce potential expectation bias, participants will be informed that the study will be comparing three different exercises and that they will be assigned to an exercise group at random.

To ascertain eligibility, a research assistant will make an initial telephone contact with those who are referred by their physicians/neurologists and local Parkinson's disease support groups, and those who respond to the study advertisements. This initial prescreen telephone contact is intended to determine basic eligibility set forth under the recruitment inclusion and exclusion criteria. Potentially eligible patients who meet initial inclusion criteria will be scheduled for a 2.5-hour in-office visit at our research laboratory.

Baseline Assessments

Those individuals who are eligible after screening will then be given informed consent materials followed by a baseline evaluation conducted by a study assessor. The baseline assessments will include blood pressure, weight and height, and collection of demographics, health status, and medication use. This will be followed by assessments of balance, physical function, muscle strength, and motor disability. At that time, the intervention activities involved with the study will be reiterated to the eligible individuals. Those who meet all study criteria, are clear about research procedures, have completed baseline assessments, and give final consent will then be randomized.

Randomization and Blinding

Eligible participants will be randomized to one of the interventions with an allocation of 1:1:1, through a permuted block randomization. Concealment of allocation will be implemented. The randomization schedule, generated by the project data analyst, will be kept by a project staff who will deliver it, in a sealed envelope, to a research assistant who will then assign qualified individuals to intervention groups. Randomization will occur after informed consent is obtained and baseline assessments have been completed.

All study assessors who will collect study outcome measures will be blinded to study hypotheses and group allocation. Blinding will be strictly maintained by emphasizing to assessors the importance of minimizing assessment bias and regular checking of the blinding status. Efforts will be also made to maintain separation between the study assessors and research assistants who deal with administrative activities and class safety monitoring, and between study assessors and class instructors who deliver the intervention. Participants will be instructed not to reveal their group status to the study assessors at any time. The investigators and the data analyst will be blinded to group designation and review coded data with names of participants replaced by numbers.

Interventions

The protocol will ensure that each exercise group has a consistent intervention schedule on key training parameters involving duration (60 minutes per session), frequency (2 times per week), and training structure (i.e., a 5- to 10-minute warm-up, core activities, and a 5-minute cool-down). Participants in all three conditions will be instructed not to engage in any additional home practice.

Tai Chi. The protocol consists of six Tai Chi forms,² integrated into an 8-form routine (a well-established program from our prior work^{1,7}) in the late stages of the study. The names of six forms are as follows:

- *Form One:* Wave Hands like Clouds (Stepping sideways: left and right);
- *Form Two:* Part the Wild Horse's Mane (Stepping diagonally forward: left and right);
- *Form Three:* Hold a Ball (Stepping diagonally forward: left and right);
- *Form Four:* Repulse Monkey (Stepping diagonally backward: left and right);
- *Form Five:* Fair Lady Works at Shuttles (Stepping diagonally forward: left and right);
- *Form Six:* Grasp the Peacock's Tail (Stepping diagonally forward: left and right).

After 3-4 months of training, the protocol will proceed to the integration of the 8-form routine with the names listed below:

- *Form One:* Hold a Ball (Stepping sideways: left and right);
- *Form Two:* Part the Wild Horse's Mane (Stepping diagonally forward: left and right);
- *Form Three:* Single Whip (Stepping sideways: left and right);
- *Form Four:* Wave Hands like Clouds (Stepping sideways: left and right);
- *Form Five:* Repulse Monkey (Stepping diagonally backward: left and right);
- *Form Six:* Brush Knees (Stepping diagonally forward: left and right).
- *Form Seven:* Fair Lady Works at Shuttles (Stepping diagonally forward, left and right)
- *Form Eight:* Grasp the Peacock's Tail (Stepping diagonally forward, left and right)

Because the goal of the protocol is to assist patients in retraining balance and postural stability, the protocol is specifically designed to challenge balance control and train gait patterns. Exercising forms and movements will be integrated therapeutically by performing symmetrical and coordinated movements such as trunk rotation and weight shifting from foot to foot, controlled and coordinated displacement of the body's center of mass over the base of support, ankle sway toward and around the perimeter of the base of support, dynamic eye and head movements, and anterior-posterior and medial-lateral stepping with rhythmical weight shifting. The early stage of the program (i.e., the first 10 weeks) will emphasize primarily learning and practicing single forms with multiple repetitions, whereas the later stage will focus on performing individual forms to strengthen postural balance and increase locomotion. Natural breathing will also be emphasized as part of the exercise and integrated into the Tai Chi movement routine. Instruction will cover learning new forms and reviewing and practicing forms learned in previous sessions.

Resistance. This training protocol is developed from recommendations on muscle strengthening and falls prevention for older adults^{8,9,10,11} and patients with Parkinson's disease.¹² It consists of lower-extremity exercises that focus on strengthening the extensor muscles that are important for posture, balance, and gait. Specific training will involve the hip (flexion, extension, abduction, adduction), knee (flexion, extension), and ankle (dorsi and plantar flexion). No added resistance will be used in the first 9 weeks of training. Added resistance (weighted vests, ankle weights) will be introduced at week 10. Weighted vest resistance will be initially set

at 1% of body weight and gradually increased (approximately 1%-2%, depending on each participant's tolerance, every 5th week) until 5% of body weight is achieved. Ankle weights will start at 1 lb per limb and be gradually increased to 3 lbs. The routine will involve 8-10 exercises including forward/side stepping, squats, forward/side lunges, chair raises, and toe raises, performed primarily in a standing position. All training exercises will be performed in 1-3 sets with 10-15 repetitions in each. Rate of progression will be modified for participants with physical limitations (e.g., joint pain).

Stretching. The rationale for using this modality is to provide participants with a low-intensity exercise program that would contain identical social interaction, enjoyment, and physical activity (i.e., by traveling to and from the training centers) and changes in lifestyle secondary to study participation that will be inherent components in the two exercise interventions without providing comparable lower-extremity weight-bearing strength or balance training benefits. The validity of this program has been demonstrated in previous studies which showed no significant effects on physical performance measures.^{1,3} The program will consist of breathing, stretching, and relaxation, with the majority of activities performed in a seated position. Each session will begin with a set of warm-up exercises such as arm, neck, and leg circles; trunk rotation; and light walking. The core part of the training session will consist of exercises that encompass a variety of seated-and-standing combined stretches involving upper body (neck, upper back, shoulder, chest, and arm), lower extremities (quadriceps, hamstring/calf, and hip), and gentle and slow trunk rotations. Also included will be deep abdominal breathing exercises that emphasize inhaling and exhaling to maximum capacity, as well as progressive relaxation of major muscle groups.

Intervention Instructors

All Tai Chi instructors will be trained and certified, through a 2-day instructional workshop, by the Principal Investigator. Instructors who deliver resistance training and stretching classes will be recruited through local communities and required to have at least 10 years of community teaching experience with middle aged and older adults and be certified by a recognized organization (e.g., American College of Sports Medicine). Additional requirements for instructing classes will include (a) being first-aid/CPR certified and (b) being able to follow instructional guidelines specified by the research project.

Because of the behavioral trial, blinding instructors will not be possible. However, the instructors will not be provided with any information related to the objectives of the study, nor will they participate in any outcome assessments.

Class Size

A class size of 8-12 is planned in order to provide adequate instructional attention to each participant and to allow the class instructor to carry out the required training routines.

Class Location

All intervention classes will be held at either our exercise laboratory at the Oregon Research Institute or a local community facility.

Intervention Adherence

Each study participant will be expected to commit for 9 months (6 months of intervention and 3 months of post-intervention follow-up). Participants will be encouraged to attend all intervention sessions (48 total), and an adherence rate of over 75% is expected. Class attendance will be closely monitored by a research assistant biweekly in the first month and monthly thereafter. Participants will be considered drop-outs if they withdraw during the intervention, fail to return for evaluations, or miss more than four consecutive weeks of their assigned intervention. All participants who stop attending the intervention sessions will be immediately contacted and encouraged to return for all evaluations. All drop-outs will receive an exit interview to determine the reason for leaving the study.

Drop-outs

Unavoidable drop-outs, such as death, onset of severe illness, and other medical complications, are anticipated. Based on our prior studies involving Tai Chi, we estimate a 15% dropout rate for the overall study. The proposed sample size will take into account this anticipated dropout rate.

System for Program Fidelity

A standardized intervention protocol and a process evaluation checklist, developed via prior trials,^{1,3} will be implemented. These measures focus primarily on intervention fidelity and involve issues such as (a) instructor qualification and training, (b) teaching distribution of the individual forms or movements, (d) exercise intensity and consistency in training dosage across different sites, and (e) weekly class attendance checking and monitoring. The evaluation will be conducted monthly by authorized staff personnel.

Outcome Measure

All primary and secondary measures will be ascertained at baseline, 3 months (midpoint), 6 months (intervention termination), and 3 months following the completion of the intervention.

Primary Outcome

Limits of stability. This will include two indicators: (1) maximum excursion and (2) directional control, assessed by computerized dynamic posturography (Balance Master[®] System). Maximum excursion, a measure of the cone of stability, assesses the limits of self-initiated (voluntary) movements as patients shift/lean their center of gravity toward the theoretical limit (100%) in each of eight target directions without falling. The average value, expressed in a percent of limits of stability, of the eight target positions will be used, with higher percent scores indicating the maximum excursion achieved in reaching by the patients during the task. Directional control provides a measure of movement accuracy by comparing the amount of movement in the intended direction (toward the target) to the amount of extraneous movement, presented as a percentage (%), with higher values indicating a straight path toward the intended target.

Secondary Outcome:

Muscle Strength: Muscle strength of bilateral knee extensors/flexors and ankle plantar/dorsiflexors will be measured on an isokinetic dynamometer (Biodex System 3, Biodex

Corporation, Shirley, New York). Each test of strength will be performed on the participants' right limb followed by the left limb at angular velocities of 60°s^{-1} and 120°s^{-1} .

*Functional Reach:*¹³ This measure assesses the maximal distance a participant can reach forward beyond arm's length while maintaining a fixed base of support in a standing position. The average of two trials will be used, with higher scores indicating better balance.

*Timed Up&Go:*¹⁴ This measure assesses the time taken to rise from a chair, walk 10 feet, return, and sit down. Lower scores indicate better mobility.

*Unified Parkinson's Disease Rating Scale (III – Motor Examination):*⁵ This is a well-established clinical measure that assesses motor symptoms of Parkinson's disease. The scale has 14 items, each scored on a 5-point Likert scale ranging from 0 to 4, with 0 representing "no impairment" and 4 representing "marked impairment." Scores range from 0 to 56, with lower values indicating less motor disability.

Falls: Frequency of falls will be monitored via daily self-report "fall calendars."³ A fall is defined as unintentionally coming to rest on the floor or the ground or falling and hitting objects such as stairs or pieces of furniture. The measure will be collected monthly throughout the intervention or until a participant withdraws from the study.

Other Baseline, Process, and Outcome Measures

Participant characteristics. Demographic and health characteristics of participants will be collected at baseline to describe the sample, compare conditions, and investigate characteristics associated with outcomes. These measures will include age, gender, marital status, education, race/ethnicity, health status, existing medical condition, use of medication, resting blood pressure, body weight (kg), and body height (cm). Blood pressure will be measured with the use of an automated device (Omron HealthCare). Body weight and height will be assessed through the use of digital scales (Health o Meter[®]).

Habitual physical activity: The Physical Activity Scale for the Elderly (PASE)¹⁵ will be used to assess levels of habitual physical activity during the course of intervention. The PASE measures physical activity in the areas of leisure, household, and occupational activity during the previous 7 days. Higher scores indicate higher levels of habitual physical activity.

Medication use: Dose and frequency of medication during the trial will be closely monitored via the Medication Change Questionnaire (MCQ).¹⁶ The MCQ records patients' ingested prescription anti-Parkinson's disease medication over a period of 7 days. As a measure of monitoring change in medication use, the MCQ will be collected on a monthly basis. Trained coders will then assign a code to classify each medication into a particular category. The total number of medications per participant will be calculated.

Quality of life. The SF-12¹⁷ will be used to assess physical and mental dimensions of quality of life. The scale contains 12 self-report items, reflecting what participants are able to do functionally, how they feel, and how they evaluate their health status. Two component scores, referred to as the physical and mental health summary scores, will be calculated according to published scoring algorithms. Each subscale will be transformed into a scale from 0-100, where higher scores indicate better physical and mental health.

Fear of falling. Fear of falling will be measured by the Survey of Activities and Fear of Falling in the Elderly (SAFFE).¹⁸ The SAFFE contains 11 activities representing ADLs and IADLs (e.g., taking a tub bath or shower), mobility (e.g., walking for exercise), and social activities (e.g., visiting friends or relatives). For each activity, several questions are asked: (a) "Do you currently do it?"; (b) "If you do the activity, how worried are you that you might fall?";

(c) “If you do not do the activity, do you not do it because you are worried that you might fall?”; (d) “If you do not do the activity because of worry, are there also other reasons that you do not do it?”; and (e) “If you are not worried, what are the reasons that you do not do it?” The SAFEE contains two indicators: (a) fear of falling and (b) levels of activity.

Sensory Organization Test. Balance Master® (NeuroCom) will be used to conduct the Sensory Organization Test that measures an individual’s ability to (a) individually use visual, vestibular, and somatosensory inputs to control upright stance and (b) suppress each of the systems when they provide inaccurate information about the body’s orientation in certain sensory conditions. To measure these abilities, the participant will be required to stand on a moveable dual-force plate facing into a three-sided enclosure that can also be moved using a “sway-referencing” technique that involves programming the forceplate or visual surround to follow the movement of the subject’s center of gravity sway in a forward and backward direction. Three trials will be performed by each participant under six sensory conditions. The composite equilibrium score, the weighted average of the scores of all sensory conditions, will be calculated to characterize the overall level of performance.

Intervention class attendance. Class attendance will be recorded for each participant at each class session and evaluated biweekly by research staff. A measure of compliance with the intervention protocol will be calculated at the end of the intervention using the class attendance information.

Study Assessors

All study assessors will be oriented and trained to follow the general assessment guidelines and protocols established by the research project. Training will be conducted by the Principal Investigator. Following the established assessment protocol,¹⁹ the assessors will also be trained by a board-certified neurologist to use the Unified Parkinson’s Disease Rating Scale. Inter-rater reliability among assessors will be established via an intraclass correlation method.

Testing Procedures

The assessment protocol will be standardized to ensure measurement consistency between assessors and across different sites and to minimize effects of motor fluctuations. Efforts will be made to schedule all assessments at the same time of day and to perform them in the same order to control for variations in performance because of the medication cycle. Participants will be instructed to follow their normal schedule of medications and physical activity, including not to start any new exercise or drug treatment program throughout the course of the study. All assessments will be conducted during typical “on” cycle medications phases.

Monitoring of Adverse Events

In this trial, major serious adverse events will be defined as death, hospitalization required, or participant left with permanent adverse outcome. Minor-to-moderate adverse events will be those where participants indicate limitations not requiring treatment, experience a fall with no fracture or not requiring medical attention, muscle soreness or pain that persists for more than 48 hours, dizziness or faintness, or hypertension or hypotension during an exercise session. Adverse events, major or minor, during a class session or outside classes (home, lab testing) will be documented in a project adverse log and, in the event of observing a major adverse event, reported immediately to the Oregon Research Institute Institutional Review Board and the funding agency (the National Institutes of Health).

In-class exercise safety will be closely monitored during the entire length of the trial by research staff and class instructors. Staff will make periodic visits to classes to check safety status and address concerns related to the exercise programs. Intervention instructors will be asked to monitor participants for symptoms of any discomfort or signs of falling. Modifications in the training protocol will be made, upon approval of the research staff, on an individual basis as necessary.

Statistical Plan

Preliminary analysis. Before addressing the main questions of the study, we will examine whether attrition influenced the representativeness of the remaining study sample, whether the intervention conditions were different on demographic variables that are not controlled for in the random assignment procedure, and whether any of the baseline characteristics (e.g., age, gender, stage of disease) need to be accounted for in the primary analyses. In addition, we will carefully evaluate whether outcomes of interest will be affected by change in medication use and habitual physical activity. Group comparisons on baseline demographic descriptors and primary and secondary outcome measures will be performed using analysis of variance for continuous variables and the chi-square (or Fisher's Exact) test for categorical variables.

Main analysis. To evaluate the effects of Tai Chi on the a priori specified outcomes, a repeated-measures, mixed-effects model will be used, which will include all assigned participants consistent with the principle of intention-to-treat. The dependent variables will be measures of primary and secondary outcomes collected at baseline, 3 months, and 6 months, operationalized as continuous variables. Falls will be the only count variable—i.e., number of falls that occurred during the intervention period (from baseline to 6 months)—and therefore will be analyzed using negative binomial regression analysis, with allowance for overdispersion attributable to variation between participants. Intervention type will be entered into the negative binomial regression model as two dummy vectors, with the reference group being the stretching control group. Independent variables will be restricted to basic design features: fixed effects for treatment group and time. In the presence of significant baseline differences in the outcome variables, they will be used as covariates in the analyses. The same analytical procedures will be employed to examine the sustainability of the intervention effects. SPSS software, version 17, will be used to model the continuous variables, and Stata, version 11, will be used to model the count variable with negative binomial regression analysis.

Power and sample size. The power calculation is based on (a) a desired power of at least 80%; (b) an alpha level of 0.05 (type I error rate); and the assumptions that (c) observations in primary study outcome variables are independently and identifiably distributed; (d) there is equal variance in the three groups (i.e., a common variance); (e) there is equal sample size in all groups; and (f) there is a constant correlation (0.5) among repeated measurements. Sample size is set at 45 participants per group to detect a group difference of 6 points in maximum excursion and 10 points in directional control from baseline to 6 months (assuming 15% attrition, 2-tailed α level of 0.05, at least 80% power). These predicted points equate to a medium effect size of 0.30 or greater (as the difference between two means divided by the pooled standard deviation for the data).

Reference Cited

1. Li F, Fisher KJ, Harmer P, Irbe D, Tearse RG, Weimer C. Tai Chi and self-rated quality of sleep and daytime sleepiness in older adults: A randomized controlled trial. *J Am Geriatr Soc* 2004;52:892-900.
2. Li F, Harmer P, Fisher KJ, et al. Tai Chi-based exercise for older adults with Parkinson's Disease: A pilot program evaluation. *J Aging Phys Activ* 2007;15:139-151.
3. Li F, Harmer P, Fisher KJ et al. Tai Chi and fall reductions in older adults: A randomized controlled trial. *J Gerontol: Med Sci* 2005;60(A(2)):187-194.
4. Hoehn M, Yahr M. Parkinsonism, onset, progression and mortality. *Neurology* 1967;17:427-42.
5. Fahn S, Elton RI, Members of the UPDRS Development Committee. Unified Parkinson's Disease Rating Scale. In: Fahn S, Marsden, CD, Calne DB, Goldstein M, editors. *Recent Developments in Parkinson's Disease*, vol. 2. Florham Park, NJ: Macmillan Health Care Information, 1987;153-163.
6. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State": A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189-198.
7. Li F, Harmer P, Glasgow R, et al. Translation of an effective Tai Chi intervention into a community-based falls prevention program. *Am J Pub Health* 2008; 98(7):1195-1198.
8. Greendale G, Salem GJ, Young JT, Damesyn M, Marion M, Wang M-Y, Reuben DB. A randomized trial of weighted vest use in ambulatory older adults: Strength, performance, and quality of life outcomes. *J Am Geriatr Soc* 2000;48:305-311.
9. Nelson ME et al. Physical activity and public health in older adults: Recommendation from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc* 2007;39:1435-1445.
10. Rubenstein LZ, Josephson KR, Trueblood PR, et al. Effects of a group exercise program on strength, mobility, and falls among fall-prone elderly men. *J Geronto: Med Sci* 2000;55A:M317-M321.
11. Shaw JM, Snow CM. Weighted vest exercise improves indices of fall risk in older women. *J Geronto: Med Sci* 1998;53:M53-M58.
12. Hirsch MA, Toole T, Maitland CG, Rider RA. The effects of balance training and high-intensity resistance training on persons with idiopathic Parkinson's Disease. *Arch Phys Med Rehabil* 2003;84:1109-1117.
13. Duncan PW, Weiner DK, Chandler J, et al. Functional reach: A new clinical measure of balance? *J Gerontol A Biol Sci Med Sci* 1990;45:192-197.
14. Podsiadlo D, Richardson S. The timed "Up & Go": A test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991;39:142-148.
15. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): Development and evaluation. *J Clin Epidemiol* 1993;46(2):153-62.
16. Paterson C, Symons L, Britten N, Bargh J. Developing the Medication Change Questionnaire. *J Clin Pharm Ther* 2004;29:339-349.
17. Ware JE, Kosinski M, Keller SD. *SF-12: How to score the SF-12 physical and mental health summary scales* (2nd ed.). Boston, MA: The Health Institute, New England Medical Center. 1995.
18. Lachman ME, Howland J, Tennstedt S, Jette A, Assmann S, Peterson, EW. Fear of falling and activity restriction: The Survey of Activities and Fear of Falling in the elderly (SAFFE). *J Gerontology: Psy Sci* 1998;53: P43-P50.

19. Goetz CG, Stebbins GT, Chmura TA, Fahn S, Klawans HL, Marsden CD. Teaching tape for the motor section of the Unified Parkinson's Disease Rating Scale. *Mov Disord* 1995;10:263-266.
20. Deane K, Jones DE, Ellis-Hill C, Clarke CE, Playford ED, Ben-Shlomo Y. Physiotherapy for Parkinson's' disease: A comparison of techniques. *Cochrane Database of Syst Rev* 2001, Issue 1. Art. No.: CD002815.

Figure 1: Flow of Patients through the Trial

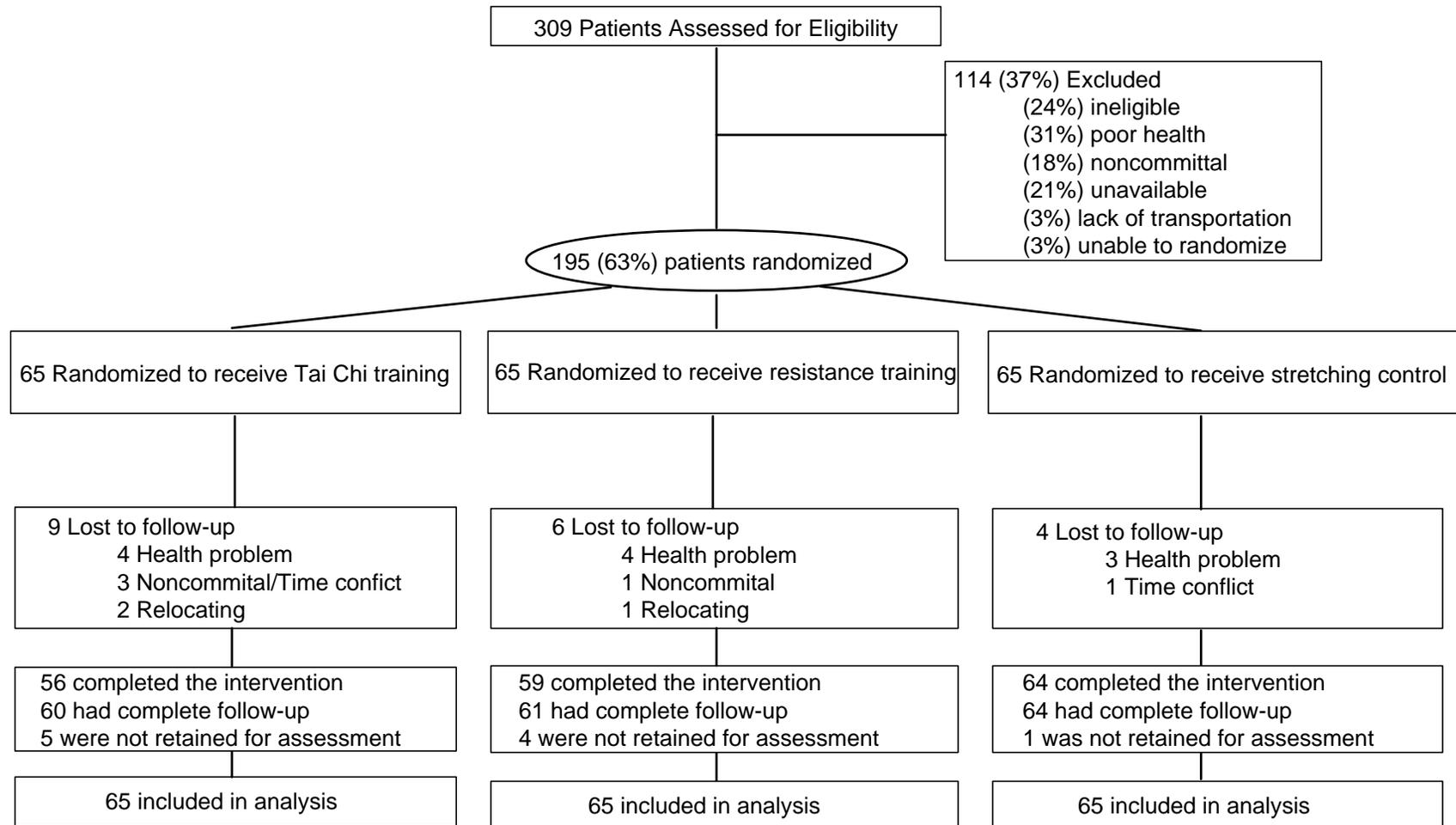


Table 1. Demographic and Clinical Characteristics of the Study Population at Baseline* (an expanded version)

Characteristics	Tai Chi (n = 65)	Resistance (n = 65)	Stretching (n = 65)
Female, No. [†] (%)	20 (31)	27 (42)	26 (40)
Age, mean (SD), y	68 (±9)	69 (±8)	69 (±9)
Education, No. [†] (%)			
High school	16 (25)	16 (25)	15 (23)
> High school	49 (75)	49 (75)	50 (77)
Married, No. [†] (%)	52 (80)	47 (72)	49 (75)
Body mass index, [‡] kg/m ² (SD)	28 (±5)	27 (±5)	27 (±5)
Hoehn and Yahr stage, No. [†] (%)			
Stage 1 – 1.5	9 (13.9)	14 (21.5)	8 (12.3)
Stage 2 – 2.5	34 (52.3)	27 (41.6)	28 (43.1)
Stage 3 or greater	22 (33.8)	24 (36.9)	29 (44.6)
Age at initial diagnosis, mean (SD), y	61 (±12)	65 (±9)	65 (±11)
Disease duration, mean (SD), y	8 (±9)	8 (±9)	6 (±5)
Parkinson's medications taken, No. [†]			
Levodopa/Carbidopa	43	50	50
Pramipexole or Ropinirole	20	21	12
Other PD medication	10	16	20
Blood pressure, mean (SD)			
Systolic, mm Hg	130 (±18)	131 (±18)	134 (±20)
Diastolic, mm Hg	78 (±11)	78 (±11)	78 (±11)
Self-report health status, No. [†] (%)			
Poor/fair	35 (53.8)	31 (47.7)	28 (43.1)
Good	23 (35.4)	28 (43.1)	29 (44.6)
Very good/excellent	7 (10.8)	6 (9.2)	8 (12.3)
Self-report habitual physical activity, [§] mean (SD)	123 (±67)	107 (±54)	116 (±62)
Self-report chronic medical conditions, [¶] No. [†] (%)			
0	12 (18.5)	9 (13.8)	12 (18.5)
1	24 (36.9)	17 (26.2)	16 (24.6)
≥2	29 (44.6)	39 (60)	37 (56.9)

*The chi-square test was used for categorical variables and 1-way analysis of variance for continuous variables. There were no statistically significant between-group differences in any baseline characteristics (P values not shown).

[†]Values indicate number of patients.

[‡]Body mass index is calculated as weight in kilograms divided by height in meters squared (kg/m²).

[§]This is measured by the Physical Activity Scale for the Elderly,³⁵ with higher scores indicating higher levels of habitual physical activity.

[¶]These include arthritis, heart disease, high blood pressure, lung disease, diabetes, osteoporosis, depression, chronic back pain, and cancer; range 0-9.

MAINTENANCE OF INTERVENTION GAINS

One hundred twenty-two participants (62%) continued exercises upon completion of the 6-month intervention. Of these participants, 47 continued participating in a Tai Chi class and the remaining 75 participated in either low-impact or strength training exercise classes.

Improvements observed in the Tai Chi group during intervention were maintained on all primary and secondary outcome measures during a 3-month postintervention follow-up. The changes from baseline to 3-month postintervention follow-up showed that the Tai Chi group continued to perform significantly better than either the stretching or resistance groups in maximum excursion (13.83%, 95% CI, 8.38 to 19.29; 5.92%, 95% CI, 0.38 to 11.45, respectively) and directional control (9.94%, 95% CI, 3.28 to 16.63; 8.71%, 95% CI, 1.28 to 16.14, respectively) (see Table 2 online supplement). Outcome scores indicated no significant change for the Tai Chi group from the 6-month termination to the 3-month postintervention follow-up. At the 3-month follow-up, the Tai Chi group experienced fewer falls compared to the stretching group (IRR = 0.31, 95% CI, 0.14 to 0.67, P = 0.003) and the resistance group (IRR = 0.40, 95% CI, 0.18 to 0.88, P = 0.02).

All effects remained significant after adjusting for baseline and time-varying covariates.

Table 2. Study Primary and Secondary Outcomes at Baseline, 3 Months (midpoint), 6-Months Intervention Termination, 3-Months Postintervention Follow-up, and Group Differences (an expanded version)

	Tai Chi (n = 65)	Resistance (n = 65)	Stretching (n = 65)	P Value [†]	Between-Group Difference in Mean Change from Baseline to 3-months follow-up (95% CI) [‡]
Maximum excursion (%)[‡]					
Baseline	64.05±16.60	64.02±18.53	64.35±17.22		Tai Chi vs. Stretching
3 months	66.09±14.30	65.20±16.02	65.66±21.12		13.83 (8.38 to 19.29) ^{****}
6 months	73.62±13.44	68.03±18.48	61.94±16.39		Tai Chi vs. Resistance
3-months follow-up	72.06±14.49	66.11±20.41	58.52±18.46		5.92 (0.38 to 11.45) [*]
3-months follow-up – Baseline [¶]	8.01±12.62 ^{***}	2.09±18.69 ^{ns}	-5.83±18.30 ^{**}	<0.001	
3-months follow-up – 6 months [‡]	-1.55±10.03 ^{ns}	-1.92±16.58 ^{ns}	-3.42±14.81 ^{ns}		
Directional control (%)[§]					
Baseline	65.75±20.16	65.12±21.60	65.93±17.23		Tai Chi vs. Stretching
3 months	68.15±17.74	63.25±24.85	61.51±25.31		9.95 (3.28 to 16.63) ^{**}
6 months	73.77±11.49	62.69±22.82	62.56±21.62		Tai Chi vs. Resistance
3-months follow-up	71.88±18.99	62.54±23.67	62.10±24.66		8.71 (1.28 to 16.14) [*]
3-months follow-up – Baseline [¶]	6.12±19.86 ^{**}	-2.58±22.84 ^{ns}	-3.83±18.56 ^{ns}	0.01	
3-months follow-up – 6 months [‡]	-1.89±13.89 ^{ns}	-0.15±20.64 ^{ns}	-0.46±16.95 ^{ns}		
Stride length (cm)[#]					
Baseline	115.61±19.73	114.47±21.05	115.69±18.60		Tai Chi vs. Stretching
3 months	115.98±20.25	116.59±19.53	113.74±18.86		10.63 (5.98 to 15.27) ^{****}
6 months	125.86±20.30	118.79±20.65	113.61±18.54		Tai Chi vs. Resistance
3-months follow-up	123.37±20.49	113.81±20.80	112.82±17.92		8.41 (3.61 to 13.20) ^{***}
3-months follow-up – Baseline [¶]	7.76±14.01 ^{****}	-0.65±13.61 ^{ns}	-2.86±12.73 ^{ns}	<0.001	
3-months follow-up – 6 months [‡]	-2.49±14.88 ^{ns}	-4.97±11.21 ^{**}	-0.79±10.43 ^{ns}		
Gait velocity (cm/sec)[§]					
Baseline	110.11±21.03	109.15±25.42	110.87±21.68		Tai Chi vs. Stretching
3 months	111.05±23.54	111.30±21.55	108.89±23.20		18.69 (13.09 to 24.30) ^{****}
6 months	120.55±21.47	119.10±24.02	106.37±20.24		Tai Chi vs. Resistance
3 months follow-up	118.02±22.43	110.60±22.12	101.09±19.80		6.46 (0.17 to 12.75) [*]
3 months follow-up – Baseline [¶]	7.91±17.22 ^{****}	1.45±18.98 ^{ns}	-10.78±15.01 ^{****}	<0.001	
3 months follow-up – 6 months [‡]	-2.52±13.80 ^{ns}	-8.49±15.91 ^{****}	-6.28±11.71 ^{****}		
Peak Knee Extension Torque (Nm)^{††}					
Baseline	61.81±31.45	59.21±37.02	61.62±37.37		Tai Chi vs. Stretching
3 months	75.48±40.49	64.61±38.54	62.89±35.67		16.89 (6.3. to 27.48) ^{**}

6 months	75.73±38.69	73.76±40.03	62.05±30.77		Tai Chi vs. Resistance
3-months follow-up	74.77±37.24	73.47±37.41	57.69±24.52		-1.29 (-11.90 to 9.31) ^{ns}
3-months follow-up – Baseline [†]	12.96±32.63 ^{****}	14.25±28.33 ^{****}	-3.93±28.24 ^{ns}	<0.001	
3-months follow-up – 6 months [†]	-0.96±22.14 ^{ns}	-0.29±18.48 ^{ns}	-4.36±15.63 [*]		
Peak Knee Flexion Torque (Nm) ^{††}					
Baseline	32.55±19.09	29.11±17.00	32.55±19.09		Tai Chi vs. Stretching
3 months	35.03±23.02	30.78±16.02	30.12±18.40		9.04 (3.31 to 14.78) ^{**}
6 months	37.69±19.30	37.99±18.21	29.95±17.88		Tai Chi vs. Resistance
3-months follow-up	36.64±18.57	36.19±17.57	27.59±15.05		-3.00 (-9.14 to 3.14) ^{ns}
3-months follow-up – Baseline [†]	4.09±16.77 [*]	7.09±18.57 ^{**}	-4.96±16.28 [*]	<0.001	
3-months follow-up – 6 months [†]	-1.05±15.91 ^{ns}	-1.79±11.51 ^{ns}	-2.36±10.35 ^{ns}		
Functional Reach (cm) ^{††}					
Baseline	24.43±6.91	24.41±6.51	24.96±7.31		Tai Chi vs. Stretching
3 months	25.74±7.25	24.71±6.78	24.41±8.10		5.66 (3.59 to 7.73) ^{****}
6 months	29.41±5.45	26.59±6.51	25.01±7.27		Tai Chi vs. Resistance
3-months follow-up	28.61±5.23	26.09±5.58	23.48±7.32		2.50 (0.41 to 4.60) [*]
3-months follow-up – Baseline [†]	4.18±6.01 ^{****}	1.68±6.06 [*]	-1.48±5.94 [*]	<0.001	
3-months follow-up – 6 months [†]	-0.79±3.82 ^{ns}	-0.50±4.33 ^{ns}	-1.53±5.07 [*]		
Timed Up&Go (sec) ^{††}					
Baseline	8.60±2.90	8.95±2.72	8.69±3.18		Tai Chi vs. Stretching
3 months	8.25±2.85	8.47±2.65	8.64±3.24		-1.19 (-1.79 to -0.61) ^{****}
6 months	7.55±2.69	7.95±2.60	8.67±3.45		Tai Chi vs. Resistance
3-months follow-up	7.75±2.69	8.10±2.57	9.04±3.61		-0.004 (-0.51 to 0.50) ^{ns}
3-months follow-up – Baseline ^{§§}	-0.85±1.66 ^{****}	-0.84±1.24 ^{****}	0.35±1.76 ^{ns}	<0.001	
3-months follow-up – 6 months ^{##}	0.19±0.89 ^{ns}	0.15±1.05 ^{ns}	0.37±1.01 ^{**}		
UPDRS ^{§§}					
Baseline	15.28±5.59	15.32±6.04	15.06±6.17		Tai Chi vs. Stretching
3 months	12.35±6.33	12.71±6.39	13.35±7.15		-4.80 (-6.69 to -2.91) ^{****}
6 months	8.86±4.12	10.25±4.83	13.66±7.54		Tai Chi vs. Resistance
3-months follow-up	9.71±4.92	11.17±5.53	14.29±5.53		-1.42 (-3.54 to 0.71) ^{ns}
3-months follow-up – Baseline ^{§§}	-5.57±5.49 ^{****}	-4.15±6.67 ^{****}	-0.77±5.42 ^{ns}	<0.001	
3-months follow-up – 6 months ^{##}	0.85±4.29 ^{ns}	0.92±4.57 ^{ns}	0.63±4.26 ^{ns}		

*P < 0.05, **P = 0.01, ***P = 0.001, ****P < 0.001, ^{ns} = not statistically significant.

†Generated from mixed repeated-measures analysis of variance (Group by Time) with baseline, 3 month (midpoint), 6-month intervention termination, and 3-month postintervention follow-up outcome scores; results are with intention-to-treat, with the last observation carried forward

for missing data for 10 patients lost to follow-up (during the 6-month intervention) (n=5 in Tai Chi, n=4 in Resistance, n=1 in Stretching. Refer to Fig. 1) and 19 additional patients lost during the 3-month postintervention follow-up (n=7 in Tai Chi, n=6 in Resistance, n=6 in Stretching).

‡Point estimates and estimates falling within the 95% confidence interval were generated from independent t-test for group differences in mean change scores from baseline to 3-months postintervention follow-up.

‡A measure of limits of stability that assesses the furthest distance displaced by participant's center of gravity while performing the leaning/reaching tasks. Values range from 0% to 100%, with higher percentages indicating better balance.

‡Difference scores generated by subtracting baseline scores from the 3-month postintervention follow-up scores, with positive values indicating improvements.

‡Difference scores generated by subtracting 6-month intervention termination scores from the 3-month postintervention follow-up scores, with negative values indicating the amount of loss during the postintervention follow-up.

§A measure of limits of stability in which the amount of movement in the intended direction (toward the target) is compared to the amount of extraneous movement (away from the target), defined by the ratio of (amount of intended movement – amount of extraneous movement)/(amount of intended movement), expressed in percentage accuracy. The composite score of the eight directions was used for analyses. The scores range from 0% to 100%, with higher percentages indicating better movement control.

#Measures the distance between the heel points of two consecutive footprints of the same foot with the unit of measure being centimeters. Higher scores indicate greater stride length.

§Measured by dividing the distance traveled by the ambulation time, with the unit of measure in centimeters per second. Higher scores indicate greater gait (walking) velocity.

‡‡Peak knee extension torque, measured in the unit of newton meter, generated by averaging scores for the right- and left-sided measures of strength performed at 60°/second of concentric knee isokinetic extensions.

‡‡Peak knee flexion torque, measured in the unit of newton meter, generated by averaging scores for the right- and left-sided measures of strength performed at 60°/second of concentric knee isokinetic flexions.

‡Measures the maximal distance a participant can reach forward beyond arm's length while maintaining a fixed base of support in a standing position. Higher scores indicate better balance.

‡Measures the time taken to rise from a chair, walk 10 feet (3 meters), return, and sit down. Higher scores indicate better mobility.

‡‡Difference scores generated by subtracting baseline scores from the 3-month postintervention follow-up, with negative values indicating improvements.

‡‡Difference scores generated by subtracting 6-month intervention termination scores from 3-month postintervention follow-up scores, with positive values indicating the amount of loss during the postintervention follow-up.

‡‡Unified Parkinson's Disease Rating Scale (III – Motor Examination, 14 items), scored on a 5-point Likert scale from 0 to 4, with 0 representing “no impairment” and 4 representing “marked impairment.” Scores ranged from 0 to 56, with lower values indicating less motor disability. A change score of 5 points or greater from baseline is considered clinically meaningful.²⁰