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Effect of Mind-body Exercise (Tai Chi) for Patients with Early Dementia: Protocol for a Randomized Controlled Study

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Effect of Mind-body Exercise (Tai Chi) for Patients with Early Dementia: Protocol for a Randomized Controlled Study

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ABSTRACT

Introduction

At present, there is no cure for most types of dementia. Many studies suggest that Tai Chi exercise is a safe and appropriate mind-body exercise for old people and efficiently slows down age-related cognitive decline. This trial is undertaken to create a set of Tai Chi exercise specially designed for people with cognitive impairments by a multidisciplinary team. We will also evaluate its effects on cognitive function, behavior/mood, fall risk and activities of daily living of patients with early dementia.

Methods and analysis

A set of Tai Chi program named “Cognition Protecting Tai Chi” (CPT) was developed by a research team comprised of geriatricians, neurologists, rehabilitation specialists, sports medicine experts, and Chinese medicine experts. Then a randomized controlled study will be conducted. Ninety patients with early dementia will be recruited and randomly divided into intervention group and control group. The intervention group will take this CPT three times a week for 20 minutes under guidance of the professional therapist. The control group will receive routine treatments. The study will last for 10 months. All participants will undergo a battery of neuropsychological and functional evaluations, including Mini-Mental State Examination, Montreal Cognitive Assessment, The World Health

Organization–University of California Los Angeles Auditory Verbal Learning test, Geriatric Depression Scale, Neuropsychological Inventory, Barthel Index, at baseline, 5 and 10 months. Fall incidence will also be recorded. Primary outcomes are changes of above psychometric assessments of the participants, and secondary outcome is fall incidence.

Ethics and dissemination This study was approved by the ethical review committee of the Beijing Geriatric Hospital (protocol number: 2015-021). Informed consents will be got from all participants or their guardians. Findings of this study will be published in peer-reviewed journals, academic conferences, and other healthcare settings where appropriate.

Trial registration number

ChiCTR-INR-16009872 (http://www.chictr.org.cn)

Strengths and limitations of this study

►This is the first study to create a Tai Chi program which is specifically designed for patients with cognitive impairments by a multidisciplinary professional team.

►We also design a randomized controlled trial to evaluate its effects. This will add evidence to nonpharmacological therapy for dementia.

►An open-label study design may result in bias though is difficult to make the Tai Chi intervention blind.

INTRODUCTION

Demented patients can show various clinical symptoms, with memory loss as the most common initial problem. Later on, complaints of inattention, miscalculation, unreasoning and disorientation become more and more evident[1]. Besides cognitive disorders, mental and behavioral disturbances, such as depression, anxiety and aggressiveness may happen. As disease going on, these syndromes progressively interfere with vital activities of daily living and resulting in independence. At present, there is no cure for most types of dementia. Current pharmacologic interventions that used to rescue cognitive function, such as acetylcholinesterase inhibitors and memantine, have limited efficacy and their adverse effects are not uncommon[2-5]. Meanwhile, typical and atypical antipsychotics for dementia have the same or even severe shortcomings.

According to neuroplasticity theory, the repetition of stimulate-reflect training helps demented patients with preservation and restoration of brain functions, even when their brains have been damaged to some extent[6]. Therefore, there is a considerable focus on investigation of non-pharmacological approach associated with enhancing cognition. Many studies suggest that mind-body exercise efficiently prevent and slow down age-related cognitive decline, and benefit the prognosis of dementia[7-10].

Tai Chi, one of Chinese traditional martial art, is an aerobic mind-body exercise with mild-to-moderate intensity and is safe for the elderly. It requires focus of concentration as well as shifting balance of the body in accordance with soft limb movements. Its gentle and smooth movements are coupled with steady breathing. In the theory of traditional Chinese medicine, qi and blood can both be mobilized and coordinated when practicing Tai Chi, this unique exercise. Excitability of the central nervous system is also improved while some parts of the brain areas being in working state and other parts being inhibited. Thus, most brain neurons can have enough relaxation, including those are getting atrophy. In this kind of alternate tension with relaxation, function of cerebral cortex is improved and progress of cognitive decline may get delayed. As strength and flexility of the body both increase, fewer falls happen, as well as other complications.

Tai Chi has been recommended as a preferred kind of exercise for fall prevention in the elderly by the American Geriatrics Society, because it improves not only muscular strength, co-ordination and balance, but also is an enjoyable activity with the potential for long-term insisting[11]. In a randomized trial carried out in non-demented Chinese elders, 40 weeks of Tai Chi exercise was proved to increase brain volume and improve cognition better than intervention of social interaction[12]. Evidences have also shown that Tai Chi is an appropriate exercise for

individuals with dementia in its early stage, which helps improving quality of life, brain function and even inducing reconstruction of neurons. It has the potential to serve as an alternative therapeutic approach for dementia persons[13-15]. Other studies reported that physical exercise like Tai Chi improved mood and alleviated psychiatric problems in early or middle stages of dementia and also significantly reduced caregiver distresses[16]. Sticky Hands Tai Chi, a special Tai Chi training technique practiced with a partner, promoted a comfortably intimate interaction between the two persons and improved exercise adherence and mood in demented older people[13].

China mainland is the origin of Tai Chi exercise and it has the biggest number of demented older people[17]. However, almost all the available evidence was conducted by foreign investigators. Moreover, though there have been various programs of Tai Chi exercise, none of them is designed for people with cognitive impairments. Our objective is to develop an appropriate Tai Chi program specifically for patients with mild dementia, which is called “Cognition Protecting Tai Chi” (CPT), and to evaluate its protective effects on cognitive function, behavior/mood, fall risk and activities of daily living. If results are positive, it will have potential to be recommended as a routine cost-effective exercise intervention for this population.

METHODS

Settings: This study is conducted at Center for Cognitive Disorders of Beijing Geriatrics Hospital (BGH). This hospital is a tertiary hospital with 900 inpatient beds located in Haidian District of Beijing City. The Center for Cognitive Disorders of BGH is a department serving for the elderly with cognitive impairments, which is also the Guidance Center for Cognitive Rehabilitation of the Haidian District.

Study design

There are two steps in this study design (Figure 1).

Firstly, a Tai Chi exercise program was specifically designed for cognitively impaired patients by a research team comprised of geriatricians, neurologists, rehabilitation specialists, sports medicine experts, and Chinese medicine experts. We deleted those unsafe and complex actions in traditional 8 style Tai Chi programs and added actions which were thought more beneficial to cognitive functions based on theories of traditional Chinese medicine science. This set of Tai Chi exercise was named “Cognition Protecting Tai Chi” (CPT). It has mainly 8 styles of actions, and each action can be divided into three motions. Then, CPT was performed in 5 patients with mild dementia who were invited to do the pre-experiment for 4 weeks. We modified those Tai Chi actions further where necessary according to their compliance and feedback till the final version was done.

There are mainly 8 styles of actions in the final version of CPT except routine Starting Posture and Closing Form, which includes Raising Both Hands, Forearm Rollings on Both Sides, Brush Knee and Twist Step on Both sides, Grasp the Bird's Tail-Left Side and then Right Side, Cloud Hands, Single Whip, Work at Shuttles on Both Side, and Raising Left and then Right Hands (Figure 2).

Secondly, we will conduct a randomized controlled trial in participants who have mild dementia.

Recruitments of participants

Participants will be recruited from long-term care facilities near Beijing Geriatric Hospital, including Wenquan senior apartment, Lengquan senior apartment, and Hexihui senior apartment. Residents who meet the inclusion criteria will be recruited and written consent forms will be signed by all participants or their guardians.

Inclusion criteria

Patients aged no less than 60 years and in early stage of dementia (diagnosis based on The Diagnostic and Statistical Manual of Mental Disorders, 4th edition) with a Clinical Dementia Rating score of less than 2 are enrolled in this study.

Exclusion criteria

Patients who have severe visual and auditory impairments, serious physical disease in important organs (such as heart, lung, kidney, liver

and so on), movement disorders, and are unable to accept assessments or interventions which are required in this study for any reasons.

Randomization

Participants enrolled will be randomly divided into intervention group or control group at a ratio of 1:1. A computer-generated list will be used to do the randomization by a study assist who has no idea of the subsequent allotment.

Intervention

The intervention group will perform Tai Chi exercise three times a week for 20 minutes under the guidance of the professional therapists. The control group will receive routine treatments. The study will last for 10 months.

Assessment

The Chinese version of Mini Mental State Examination (MMSE)[18] is a 30-point questionnaire that is used to measure cognitive impairment. It examines functions of attention and calculation, recall, language, ability to follow simple commands and orientation.

The Montreal Cognitive Assessment (MoCA) Beijing version (www.mocatest.org) is another 30-point test for assessing cognitive function. It includes items of short-term memory recall, visuospatial abilities, multiple aspects of executive functions, attention, concentration and working memory, language and orientation to time

and place. More difficult and multiple tasks make it more sensitive to mild cognitive changes than MMSE.

The World Health Organization–University of California Los Angeles Auditory Verbal Learning test (WHO-UCLA-AVL)[19] is a tool to assess immediate recall and delayed recall with 15 words independent in meaning. Immediate recall is performed by asking subject to remember and recall those 15 words just after each auditory learning, and this learning-recall process is repeated for three times. An average performance is recorded. Delayed recall is performed by asking subject to recall those 15 words in 30-45 minutes after the immediate recall being done.

The Geriatric Depression Scale (GDS)[20] is a 30-item self-report assessment used to identify depression in the elderly, of which questions are answered "yes" or "no." It is simple enough to be used when testing older individuals with mild or moderate cognitive impairment.

The Neuropsychiatric Inventory (NPI)[21] assesses common psychiatric and behavioral symptoms in dementia. Its items include hallucinations, delusions, agitation/aggression, dysphoria/depression, anxiety, irritability, disinhibition, euphoria, apathy, aberrant motor behavior, sleep and night-time behavior disturbance, appetite and eating disorders. The NPI is administered by the clinician to the caregiver who has detailed knowledge of the patient's performance. Besides, the caregiver is also

asked to rate their own distress associated with daily care of the patient. The Barthel Idex (BI)[22] is an ordinal scale used to measure performance in activities of daily living (ADL). The ten variables describing ADL and mobility addressed in the Barthel scale are presence or absence of fecal incontinence, presence or absence of urinary incontinence, help needed with grooming, help needed with toilet use, help needed with feeding, help needed with transfers (e.g. from chair to bed), help needed with walking, help needed with dressing, help needed with climbing stairs and help needed with bathing.

All participants will undergo above assessments at 0 (baseline), 5 and 10 months. Fall incidence will also be recorded.

Outcomes

The primary outcome is score of such psychometric tools and the secondary outcome is fall incidence.

Sample size

The sample size was calculated based on the results of pre-experiment of this study. Using a type I error of 0.05 and a power of 80%, a sample size of 40 per groups is enough for both primary outcomes and secondary outcome. Considering a 10% dropout rate may happen, a total number of 90 participants will be recruited.

Quality control and quality assurance

Diagnosis of each participant will be made by at least three dementia

specialists. All data will be monitored and reviewed by the PI or co-investigators. Training will be provided to all researchers. Consistency coefficients in scoring assessment scales between researchers should be no less than 0.85. Data entry of all the case report forms will be verified by a second person of the study team.

Statistical method

All analyses will be performed using SPSS version 16.0. Comparisons of score variations of psychometric assessments over time between two groups will be conducted using repeated measurement of variance analysis. Difference of fall incidences between groups will be analyzed using Chi-squire test.

CONCLUSION

In this protocol, we describe a "Cognition Protecting Tai Chi" (CPT) exercise developed by our research team including geriatricians, neurologists, rehabilitation specialists, sports medicine experts, and Chinese medicine experts. Moreover, a randomized controlled trial will be conducted to evaluate the effect of this CPT on patients with dementia in early stage.

Contributors

Jihui Lyu conceived the idea and supervised this study and is the guarantor. Jihui Lyu, Xiangjiang Rong, Xueli Chen, Fangling Li, Wenjie Li

and Lian Wei were involved in the design. Wenjie Li, Yanna Huang and Xiangjiang Rong prepared draft manuscript and Jihui Lyu revised the manuscript. Wenjie Li, Mo Li and Xiangjiang Rong carried out the statistical calculation. All authors approved submission of this manuscript.

Funding

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Competing interests

None declared.

Ethical approval: This study was approved by the ethical review committee of the Beijing Geriatric Hospital (Beijing, China).

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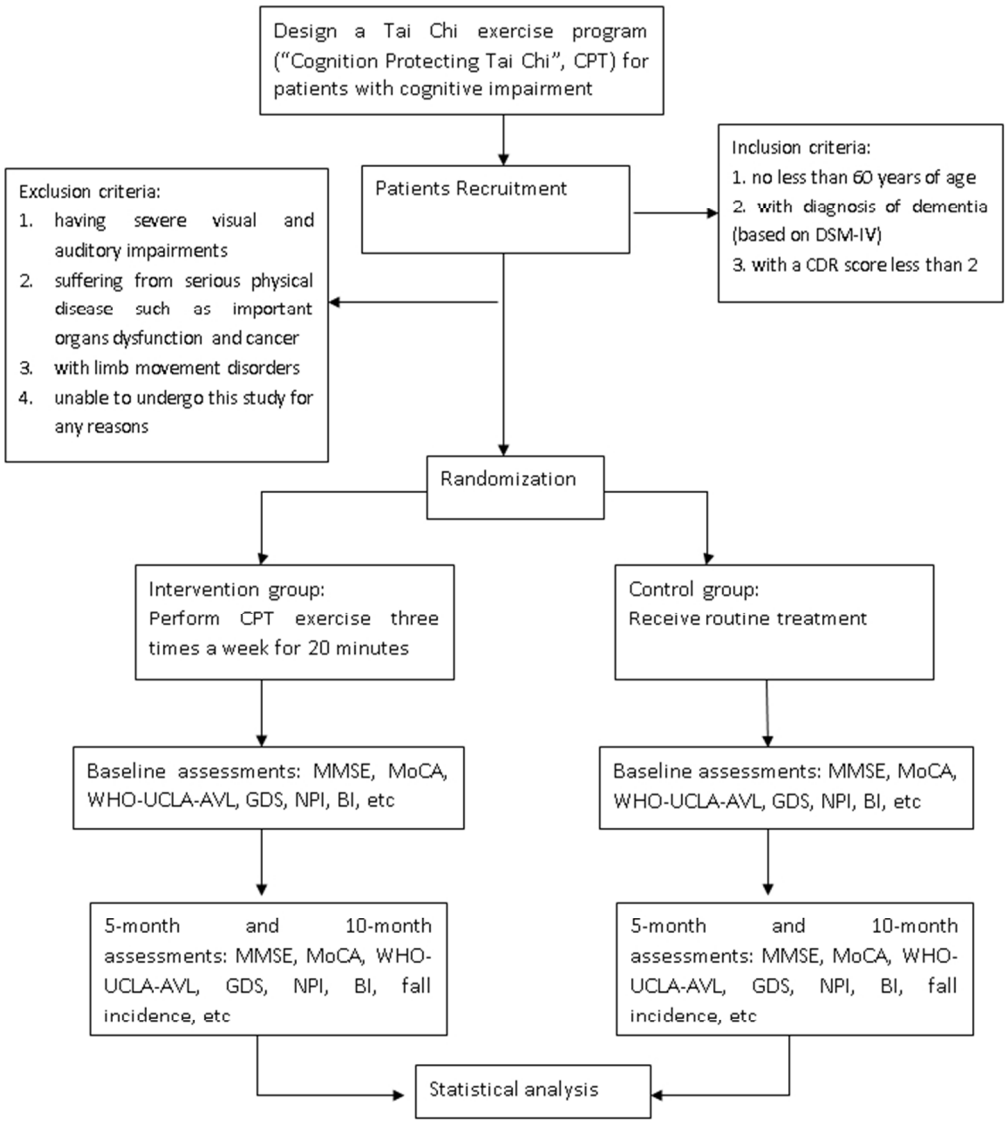

Figure 1. The study flow

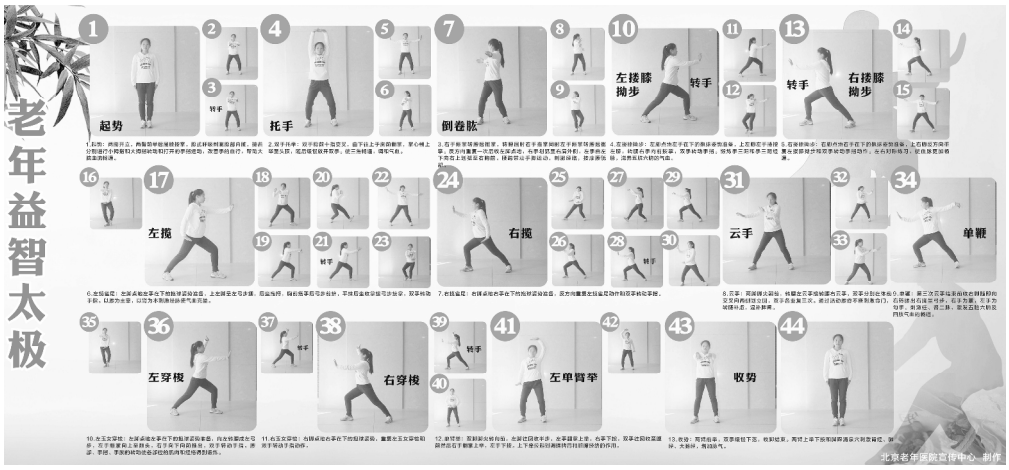

Figure 2. Main actions of Cognitive Protection Tai Chi (CPT)

3256x1493mm (72 x 72 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4
	2b	Specific objectives or hypotheses	5-6
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	7
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Not applicable
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	11
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Not applicable
Sample size	7a	How sample size was determined	11
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Not applicable
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	9
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	9
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	9

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	9
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Not applicable
	11b	If relevant, description of the similarity of interventions	Not applicable
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	12
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	12
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Not applicable for a protocol
	13b	For each group, losses and exclusions after randomisation, together with reasons	Not applicable
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Not applicable
	14b	Why the trial ended or was stopped	Not applicable
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Not applicable
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Not applicable
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Not applicable
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Not applicable
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Not applicable
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Not applicable
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Not

			applicable
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Not applicable
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Not applicable
Other information			
Registration	23	Registration number and name of trial registry	3
Protocol	24	Where the full trial protocol can be accessed, if available	This is a protocol
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	13

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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The Efficacy of Practicing Tai Chi for Older People with Mild Dementia: Protocol for a Pilot Randomized Controlled Study

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Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Neurology, Rehabilitation medicine
Keywords:	Tai Chi, cognitive function, Dementia < NEUROLOGY

The Efficacy of Practicing Tai Chi for Older People with Mild Dementia: Protocol for a Pilot Randomized Controlled Study

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Key words: dementia, Tai Chi, cognitive function

Word count: 2932

ABSTRACT

Introduction

Many studies suggest that Tai Chi exercise is a safe and appropriate mind-body exercise for older people and effectively slows down age-related cognitive decline. A set of bespoke Tai Chi exercise named "Cognition Protecting Tai Chi" (CPT) has been created for older people with cognitive impairments by the research team of geriatricians, neurologists, rehabilitation specialists, experts of sports medicine, and experienced practitioners of traditional Chinese medicine. This trial is designed to evaluate its effects on cognitive function, behavior/moods, risk of falls and activities of daily living of the participants with mild dementia.

Methods and analysis

A randomized controlled study will be conducted. Eighty participants with mild dementia will be recruited and randomly allocated to an intervention group and a control group. The intervention group will practice the CPT three times a week for 20 minutes each time under the guidance of professional therapists. The control group will continue receiving their routine treatments. The duration of this study will be 10 months. All participants will be assessed with a battery of neuropsychological and functional evaluations, which include Mini-Mental State Examination, Montreal Cognitive Assessment, the

World Health Organization–University of California Los Angeles Auditory Verbal Learning test (WHO-UCLA-AVLT), Trail Making Test (TMT), Geriatric Depression Scale, Neuropsychological Inventory and Barthel Index, at the baseline, five and ten months during the study period. Fall incident will also be recorded. The primary outcome will be the WHO-UCLA-AVLT delayed recall score. The secondary outcome will be the TMT score.

Ethics and dissemination

This study has been approved by the ethical review committee of the Beijing Geriatric Hospital (protocol number: 2015-021). Informed consent will be obtained from all participants or their guardians. The authors intend to submit the findings of the study to peer-reviewed journals or academic conferences to be published.

Trial registration number

ChiCTR-INR-16009872 (http://www.chictr.org.cn)

Strengths and limitations of this study

► The bespoke CPT is specially designed for older people with mild dementia by the research team of multidisciplinary professionals. The team consist of geriatricians, neurologists, rehabilitation specialists, experts of sports medicine, and experienced practitioners of traditional Chinese medicine.

► The randomized controlled trial design minimizes the risk of selection bias.

►As the sample size is calculated based on the primary outcome, this pilot study may fail to demonstrate statistical differences of secondary outcomes.

► An open-label study design is often viewed as leaning towards bias, however it is not feasible to achieve a blinded intervention for this study. Therefore special measures for randomization and data collection process will be incorporated into the study to reduce bias.

INTRODUCTION

There are various clinical symptoms of people with dementia, which usually start with cognitive impairments, such as memory loss, and then complaints of inattention, miscalculation, lack of logical reasoning and disorientation[1]. Besides cognitive impairments, people with dementia may also experience some changes psychologically and physically. There might be changes in personality, mood swings, ability to communicate and behaviors. It is often observed that patients with dementia feel anxious, depressed and may become verbally and physically aggressive. As the disease progresses, these symptoms gradually affect their ability in maintaining their activities of daily living, which leads to loss of independence. Current pharmacologic interventions used to maintain cognitive function, such as acetylcholinesterase inhibitors and memantine, have limited efficacy, and there are usually side effects[2-5]. Meanwhile, typical and atypical antipsychotics for dementia have the same or even severe side effects.

According to neuroplasticity theory, the repetition of stimulate-reflect training can help patients with dementia in preservation and restoration of brain functions, even when the brain has pathological damage to some extent[6]. There has been a considerable focus on the non-pharmacological approach to enhancing cognition. Many studies suggest that mind-body exercise can efficiently prevent the onset of

dementia by delaying age-related cognitive decline, and benefit the prognosis of dementia[7-10].

As one of traditional Chinese martial arts, Tai Chi is an aerobic mind-body exercise with mild-to-moderate physical movements that are safe for older people[11]. Tai Chi requires mind concentration and shifting the balance of body in accordance with gentle and smooth movements and steady breathing. In the theory of traditional Chinese medicine, Qi (Qi is one of the fixed technical terms in traditional Chinese medicine, referring to behavioral patterns seen to occur through the spatial extension of a physical medium, which is both activity and active substance) and blood are the two most fundamental materials to maintain human life activities. Qi and blood can both be mobilized coordinately when practicing Tai Chi, which helps maintain the balance of Yin and Yang (the two opposite properties of all natural things in traditional Chinese medicine) and improves harmony of human body[12]. As the nature of Tai Chi exercise strengthens the muscles of lower limbs of the body, it helps improve stability and minimize the risk of falls[11]. Tai Chi is a recommended exercise for fall prevention in older people by the American Geriatrics Society, because it not only improves muscular strength, co-ordination and balance, but also is an enjoyable activity with a potential as a long-term exercise regime[13]. A randomized trial in older Chinese people without dementia carried out by Mortimer, et al in

2012 suggest that Tai Chi increases brain volume and improves cognitive function more effectively than the intervention of social interaction[14]. Evidence has also shown that Tai Chi is an appropriate exercise for individuals with dementia in early stages, which helps improve quality of life, brain function inducing reconstruction of neurons, and Tai Chi could become an emerging alternative therapy for people with dementia[15-17]. Other studies reported that physical exercise like Tai Chi improved mood and alleviated psychiatric problems in early or middle stages of dementia and also significantly reduced caregiver distresses[18]. For example, Sticky Hands Tai Chi, a special Tai Chi training technique practiced with a partner, promoted a comforting intimate interaction between the two persons and improved exercise adherence and mood in older people with dementia[15].

China has the largest number of older people with dementia[19] and Tai Chi is originated from China. Tai Chi experts in China have developed various programs of Tai Chi, but none is especially designed for older people with cognitive impairments. Therefore, a set of Tai Chi program named “Cognition Protecting Tai Chi” (CPT) has been designed by the research team of multidisciplinary professionals in the first stage of this study. The second stage of this study is to test the effectiveness of the CPT program in improving cognitive function, and to evaluate its effects and impacts on psychological behavior, mood swings, risk of falls and

ability in maintaining activities of daily living for people with mild dementia with comparison to usual care. If results are positive, it would demonstrate the potential to become a routine cost-effective exercise for older people with mild dementia.

METHODS

Settings: This study is designed at Center for Cognitive Disorders of Beijing Geriatric Hospital (BGH). The Case Report Forms will be kept and research data will be analyzed by BGH. This hospital is a tertiary hospital which is the highest rank in China's hospital system in terms of capacity of beds and research capability. BGH has 900 inpatient beds and is located in Haidian District of Beijing. The Center for Cognitive Disorders of BGH is a department serving older people with cognitive impairments. It is also the Guidance Center for Cognitive Rehabilitation of Haidian District. The recruitment, assessment, intervention, and follow-ups of participants will be conducted at three long-term care facilities near BGH at where the participants reside.

Patient and Public Involvement

Information leaflets of the study will be available at the three long-term care facilities. The leaflets explain in full detail the aims and objectives of the study, selection criteria and the processes that the study will be adhering to. The research team will provide an individual face to face

consultation to all applicants or their guardian to answer any questions they may have. The applicants can then discuss this with their family if they wish and make a decision to opt in or opt out the study prior to signing the consent form. The findings of this study will be made available to the participants and their guardians.

Study design

There are two stages in this study design (Figure 1).

The first stage is the development of the CPT program by the research team. The CPT program was specifically designed for cognitively impaired patients by a research team of geriatricians, neurologists, rehabilitation specialists, experts of sports medicine, and experienced practitioners of traditional Chinese medicine in 2016. The team has modified the traditional Chinese Tai Chi to suit people with mild dementia. Any unsafe and complex actions in the traditional eight style Tai Chi program was removed, and some movements which were thought to be more beneficial for cognitive functions were added based on theories of traditional Chinese medical science. For example, the researchers removed the posture of standing on one foot and added some movements of rotating wrists and fingers in consideration of the suitability and safety aspects of the program for people with dementia. The CPT program contains eight styles of Tai Chi movements and each movement can be divided into three different maneuvers. Between

January 2017 and May 2017, the CPT has been piloted with five patients with mild dementia who were invited to learn and practice the CPT program for four weeks. The CPT has been further modified where necessary based on the comments and the feedback provided by the participants before the completion of final version of the CPT.

In addition to routine Starting Posture and Closing Form, there are eight styles of Tai Chi movements in the CPT, including Raising Both Hands, Forearm Rolling on Both Sides, Brush Knee and Twist Step on Both sides, Grasp the Bird's Tail-Left Side and then Right Side, Cloud Hands, Single Whip, Work at Shuttles on Both Sides, and Raising Left and then Right Hand (Figure 2).

The second stage is a randomized controlled trial which will be conducted to test the effectiveness of the CPT program.

Recruitment of participants

Participants will be recruited from long-term care facilities near BGH. These facilities are Wenquan nursing home, Lengquan nursing home, and Hexihui nursing home. There are altogether more than one thousand older residents living in these nursing homes, thus sufficient samples can be provided. Residents who meet the inclusion criteria will be recruited. Written consent forms will be signed by all participants or their guardians.

Inclusion criteria

Residents aged 60 years or older with mild dementia (diagnosis is based on The Diagnostic and Statistical Manual of Mental Disorders, 4th edition), who have a Clinical Dementia Rating score less than 2 will be enrolled into this study.

Exclusion criteria

Residents who have severe visual or auditory impairment, serious medical conditions in major organs (such as heart, lung, kidney, liver and so on), illnesses affecting mobility, or are unable to accept assessments or interventions which are required in this study for any reasons.

Randomization and allocation sequence

Participants will be enrolled by dementia specialists. The randomization will be carried out by an independent research assistant who will not be involved in the enrollment, assessment, or intervention of the participants. Random number sequences will be generated using SAS software. Sealed envelopes with the serial number outside and group number inside will be produced and kept in a locked drawer which will be inaccessible to all the researchers. The envelopes will be opened sequentially by the independent research assistant after baseline assessments and participants will be assigned to two groups (i.e. one intervention group and one control group) at a ratio of 1:1 according to the group number printed inside the envelopes. Outcome evaluators and data analysts will be blinded to the group assignment.

Intervention

This study is designed as a 10 month-randomized controlled trial. In addition to their routine treatment and usual care for ADL, the intervention group will perform the CPT exercise three times a week for 20 minutes each time under the guidance of the professional therapists at where the participants reside. The intervention will be practiced in groups with one therapist to five to eight participants. The control group will only receive routine treatments and usual care for ADL. The intervention to the participant should be discontinued if any complication that could affect the outcomes of the CPT occurs. The participants will be encouraged to complete follow-ups. The participants and their representatives have access to the research team anytime if they need to discuss any issues or concerns during the study period. The participants will be explained that they can discontinue with the intervention at any time during the period of the study. Demographic information of participants who withdraw from the study after randomization and the reasons for their withdrawal will be collected.

Assessment

The trial will utilize the most commonly used tools (see below) that have been carefully selected to assess the efficacy of CPT. The Chinese version of Mini Mental State Examination (MMSE)[20] is a 30-point questionnaire which is used to measure cognitive impairments. It examines functions

of attention, calculation, recall, language, ability to follow simple commands and orientation.

The Montreal Cognitive Assessment (MoCA) Beijing version (www.mocatest.org) is also a 30-point test for assessing cognitive function. MoCA includes cognitive domains for short-term memory recall, visuospatial abilities, multiple aspects of executive functions, attention, concentration and working memory, language and orientation to time and place. Because there are more difficult and multiple tasks in MoCA, MoCA is more sensitive to detect mild cognitive changes than MMSE does[21].

The World Health Organization–University of California Los Angeles Auditory Verbal Learning test (WHO-UCLA-AVL)[22] is a tool to assess immediate recall and delayed recall with 15 words independent in meaning. Immediate recall is performed by asking the participants to remember and recall those 15 words just after each auditory learning, and this learning-recall process is repeated for three times to generate an average performance score. An average performance is recorded. Delayed recall is performed by asking the participants to recall those 15 words 30-45 minutes after the immediate recall has been completed.

The study utilizes the method of the Trail Making Test (TMT) which is a neuropsychological test of visual attention and task switching. It can provide information on visual search speed, scanning, speed of

processing, mental flexibility, as well as executive functioning. A Chinese version of Shape TMT was used in this study. This Shape TMT shows numbers from 1 to 25 twice, once in a circle and once in a square. The participants are asked to connect them in sequential order alternately between circles and squares (circle 1, square 1, circle 2, square 2, etc.) [23]. This Shape TMT has been proved to be a sensitive test of visual search and sequencing[24].

The Geriatric Depression Scale (GDS)[25] is a 30-item self-report assessment used to identify depression in the elderly, of which questions are answered in a "yes" or "no" format. It is appropriate to test older individuals with mild or moderate cognitive impairment using GDS.

The Neuropsychiatric Inventory (NPI)[26] assesses common psychiatric and behavioral symptoms in dementia. Its items include hallucinations, delusions, agitation/aggression, dysphoria/depression, anxiety, irritability, disinhibition, euphoria, apathy, aberrant motor behavior, sleep and night-time behavior disturbance, appetite and eating disorders. Information can be obtained from caregivers who have in-depth knowledge of the patients' performance. The caregivers will also be asked to rate their own distress level associated with daily care and support provided by them to the patients.

The Barthel Idex (BI)[27] is an ordinal scale used to measure performance in ADL. The ten variables describing ADL and mobility

addressed in the Barthel scale are: presence or absence of fecal incontinence, urinary incontinence, grooming, toileting, feeding, transferring (e.g. from chair to bed), walking, dressing, climbing stairs and bathing. The scoring is based on information provided by the participant's informant, who can be his/her family members or caregivers.

All participants will undergo all above assessments at 0 (baseline), five and ten months within the current study period. Fall incident will also be recorded. Fall will be defined as the experience of a sudden, involuntary, unintentional change of position, down on the ground or on a lower plane. When assessing a definite fall, the team will try to get an eyewitness account or records of security cameras (all the areas of the nursing homes where participants live will be monitored by 24-hour security cameras).

Outcomes

The psychometric tools used in this study will be analyzed to assess the efficacy of the CPT. The primary outcome is the WHO-UCLA-AVLT delayed recall score. The secondary outcome is the score of the TMT. The fall incident will be analyzed to assess the safety of this Tai Chi program. Complaints of medical symptoms related to the intervention will be documented and treated when necessary, including fatigue, pain, dizziness, and so on.

Sample size

The sample size was calculated by Power Analysis and Sample Size Calculation Statistical Software V13.0 based on the results of pre-experiment of this study. Using a type I error of 0.05 and a power of 80%, a mean difference of 2 points is expected between two groups after 10 months. The results show a sample size of 34 per groups is adequate for testing the primary outcome (WHO-UCLA-AVLT delayed recall score). Considering a 15% dropout rate, a total number of 80 participants will be recruited.

Quality control and quality assurance

At least three dementia specialists will work together to examine the participants and provide diagnosis for each participant. All data will be monitored and reviewed by the PI or research coordinators. Training will be provided to all researchers. Consistency coefficients in scoring assessment scales between researchers should be no less than 0.85. Data entry will be verified by a second researcher in the team. To protect participants' confidentiality, only supervisors, researchers of this study and the ethics committee will be authorized to have access to the personal information and medical records of the participants.

Statistical method

All analyses will be carried out using SPSS version 16.0. The variations of scores of psychometric assessments over time between two groups will

be examined using repeated measurement of variance analysis. The association between intervention and incidence of falls will be analyzed using Chi-Square test.

CONCLUSION

This protocol outlined the objectives of the study and explained the CPT exercise developed by the research team including geriatricians, neurologists, rehabilitation specialists, experts of sports medicine, and experienced practitioners of in traditional Chinese medicine. The study is designed as a randomized controlled trial in order to evaluate the effects of this especially designed CPT on the participants with mild dementia.

Contributors

Jihui Lyu conceived the idea and supervised this study and is the guarantor. Jihui Lyu, Xiangjiang Rong, Xueli Chen, Fangling Li, Wenjie Li and Lian Wei were involved in the design. Wenjie Li, Nayan Huang and Xiangjiang Rong prepared draft manuscript. Jihui Lyu, Mei Champ, and Qian Xiong revised the manuscript. Wenjie Li, Mo Li and Xiangjiang Rong carried out the statistical calculation. All authors approved submission of this manuscript.

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Competing interests

None declared.

Ethical approval: This study was approved by the ethical review committee of the Beijing Geriatric Hospital (Beijing, China).

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Figure legends:

Figure 1 Trail Flow Chart.

Figure 2 Main movements of the "Cognition Protecting Tai Chi" (CPT).

A1-3: Raising Both Hands

B1-3: Forearm Rolling on Both Sides

C1-3: Brush Knee and Twist Step on Both sides

D1-3: Grasp the Bird's Tail-Left Side and then Right Side, Cloud Hands

E1-3: Cloud Hands

F1-3: Single Whip

G1-3: Work at Shuttles on Both Sides

H1-3: Raising Left and then Right Hand

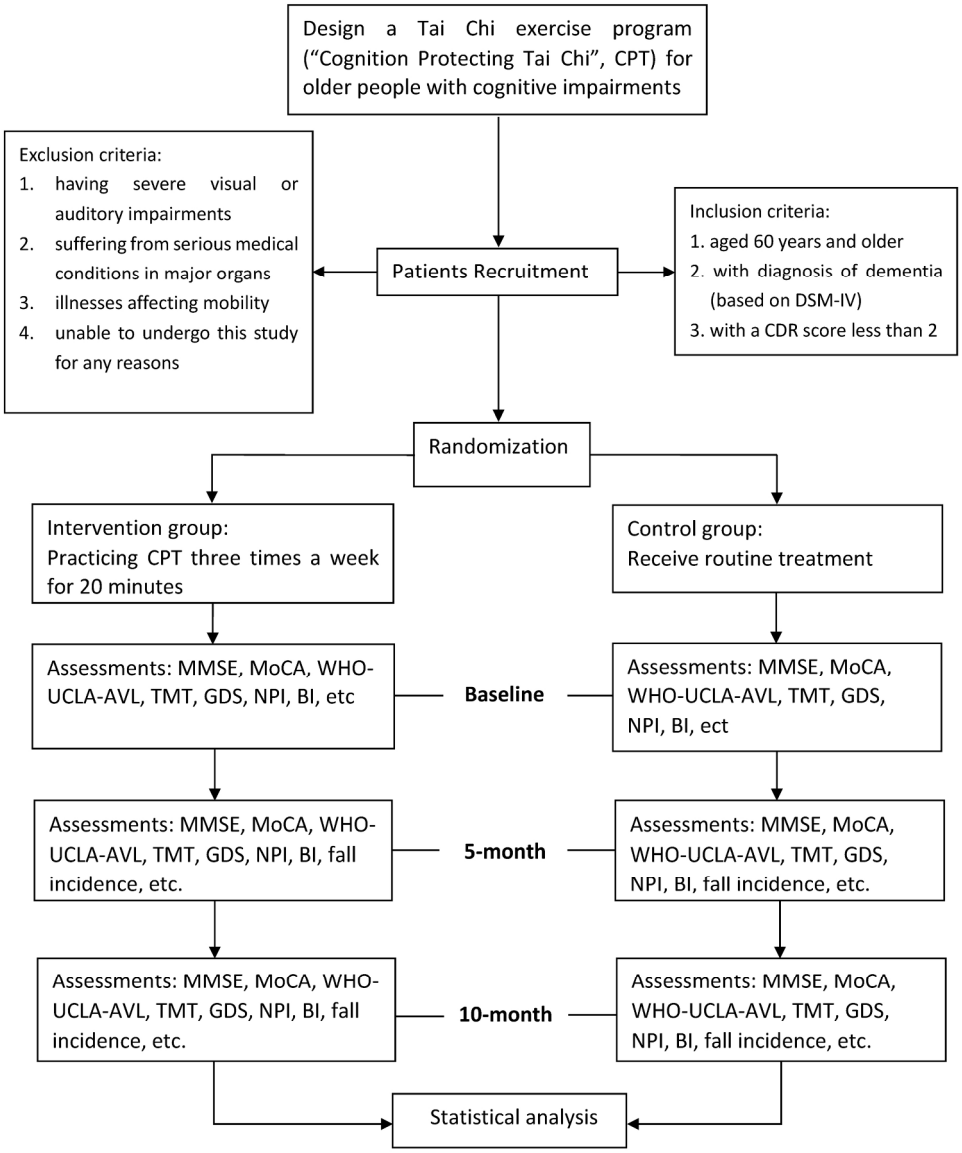

Figure 1 Trail Flow Chart.

221x266mm (300 x 300 DPI)

Figure 2 Main movements of the "Cognition Protecting Tai Chi" (CPT).
A1-3: Raising Both Hands
B1-3: Forearm Rolling on Both Sides
C1-3: Brush Knee and Twist Step on Both sides
D1-3: Grasp the Bird's Tail-Left Side and then Right Side, Cloud Hands
E1-3: Cloud Hands
F1-3: Single Whip
G1-3: Work at Shuttles on Both Sides
H1-3: Raising Left and then Right Hand

292x223mm (300 x 300 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	18
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	6-8
	6b	Explanation for choice of comparators	9
Objectives	7	Specific objectives or hypotheses	8, 9
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	10, 11
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	9
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	11, 12
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	13
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	13
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	13
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	13
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	16
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1. Trail flow chart

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	11
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	12
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	12
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	12
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	12
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-16
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	17
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17, 18
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	NA
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	16
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	4, 19
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	NA

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	4
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	NA
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	4
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

BMJ Open

The Efficacy of Practicing Tai Chi for Older People with Mild Dementia: Protocol for a Randomized Controlled Study

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Complete List of Authors:	Lyu, Jihui; Beijing Geriatric Hospital, Center for Cognitive Disorders; Capital Medical University, Alzheimer's disease Center, Beijing Institute for Brain Disorders Li, Wenjie; Beijing Geriatric Hospital, Center for Cognitive Disorders Rong, Xiangjiang; Capital University of Physical Education and Sport, School of Kinesiology and Health Wei, Lian ; Capital University of Physical Education and Sport, Graduate School Huang, Nayan; Beijing Geriatric Hospital, Center for Cognitive Disorders; Capital Medical University, Alzheimer's disease Center, Beijing Institute for Brain Disorders Champ, Mei; University of the West of England, Department of Nursing and Midwifery Xiong, Qian; Lancaster University, Centre for Ageing Research, Division of Health Research, Faculty of Health and Medicine Chen, Xueli; Beijing Geriatric Hospital, Department of Rehabilitation Li, Mo; Beijing Geriatric Hospital, Center for Cognitive Disorders Li, Fangling; Beijing Geriatric Hospital, Department of Traditional Chinese Medicine
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Neurology, Rehabilitation medicine
Keywords:	Tai Chi, cognitive function, Dementia < NEUROLOGY

The Efficacy of Practicing Tai Chi for Older People with Mild Dementia: Protocol for a Randomized Controlled Study

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Key words: dementia, Tai Chi, cognitive function

Word count: 3033

ABSTRACT

Introduction

Many studies suggest that Tai Chi exercise is a safe and appropriate mind-body exercise for older people and effectively slows down age-related cognitive decline. A set of bespoke Tai Chi exercise named "Cognition Protecting Tai Chi" (CPT) has been created for older people with cognitive impairments by the research team of geriatricians, neurologists, rehabilitation specialists, experts of sports medicine, and experienced practitioners of traditional Chinese medicine. This trial is designed to evaluate its effects on cognitive function, behavior/moods, risk of falls and activities of daily living of the participants with mild dementia.

Methods and analysis

A randomized controlled study will be conducted. Eighty participants with mild dementia will be recruited and randomly allocated to an intervention group and a control group. The intervention group will practice the CPT three times a week for 20 minutes each time under the guidance of professional therapists. The control group will continue receiving their routine treatments. The duration of this study will be 10 months. All participants will be assessed with a battery of neuropsychological and functional evaluations, which include Mini-Mental State Examination, Montreal Cognitive Assessment, the

World Health Organization–University of California Los Angeles Auditory Verbal Learning test (WHO-UCLA-AVLT), Trail Making Test (TMT), Geriatric Depression Scale, Neuropsychological Inventory and Barthel Index, at the baseline, five and ten months during the study period. Fall incident will also be recorded. The primary outcome will be the WHO-UCLA-AVLT delayed recall score. The secondary outcome will be the TMT score.

Ethics and dissemination

This study has been approved by the ethical review committee of the Beijing Geriatric Hospital (protocol number: 2015-021). Informed consent will be obtained from all participants or their guardians. The authors intend to submit the findings of the study to peer-reviewed journals or academic conferences to be published.

Trial registration number

ChiCTR-INR-16009872 (http://www.chictr.org.cn)

Strengths and limitations of this study

► The bespoke CPT is specially designed for older people with mild dementia by the research team of multidisciplinary professionals

► The randomized controlled trial design minimizes the risk of selection bias.

► As the sample size is calculated based on the primary outcome, this study may fail to demonstrate statistical differences of secondary outcomes.

► An open-label study design is often viewed as leaning towards bias, however it is not feasible to achieve a blinded intervention for this study.

INTRODUCTION

There are various clinical symptoms of people with dementia, which usually start with cognitive impairments, such as memory loss, and then complaints of inattention, miscalculation, lack of logical reasoning and disorientation[1]. Besides cognitive impairments, people with dementia may also experience some changes psychologically and physically. There might be changes in personality, mood swings, ability to communicate and behaviors. It is often observed that patients with dementia feel anxious, depressed and may become verbally and physically aggressive. As the disease progresses, these symptoms gradually affect their ability in maintaining their activities of daily living, which leads to loss of independence. Current pharmacologic interventions used to maintain cognitive function, such as acetylcholinesterase inhibitors and memantine, have limited efficacy, and there are usually side effects[2-5]. Meanwhile, typical and atypical antipsychotics for dementia have the same or even severe side effects.

According to neuroplasticity theory, the repetition of stimulate-reflect training can help patients with dementia in preservation and restoration of brain functions, even when the brain has pathological damage to some extent[6]. There has been a considerable focus on the non-pharmacological approach to enhancing cognition. Many studies suggest that mind-body exercise can efficiently prevent the onset of

dementia by delaying age-related cognitive decline, and benefit the prognosis of dementia[7-10].

As one of traditional Chinese martial arts, Tai Chi is an aerobic mind-body exercise with mild-to-moderate physical movements that are safe for older people[11]. Tai Chi requires mind concentration and shifting the balance of body in accordance with gentle and smooth movements and steady breathing. In the theory of traditional Chinese medicine, Qi (Qi is one of the fixed technical terms in traditional Chinese medicine, referring to behavioral patterns seen to occur through the spatial extension of a physical medium, which is both activity and active substance) and blood are the two most fundamental materials to maintain human life activities. Qi and blood can both be mobilized coordinately when practicing Tai Chi, which helps maintain the balance of Yin and Yang (the two opposite properties of all natural things in traditional Chinese medicine) and improves harmony of human body[12]. As the nature of Tai Chi exercise strengthens the muscles of lower limbs of the body, it helps improve stability and minimize the risk of falls[11]. Tai Chi is a recommended exercise for fall prevention in older people by the American Geriatrics Society, because it not only improves muscular strength, co-ordination and balance, but also is an enjoyable activity with a potential as a long-term exercise regime[13]. A randomized trial in older Chinese people without dementia carried out by Mortimer, et al in

2012 suggest that Tai Chi increases brain volume and improves cognitive function more effectively than the intervention of social interaction[14]. Evidence has also shown that Tai Chi is an appropriate exercise for individuals with dementia in early stages, which helps improve quality of life, brain function inducing reconstruction of neurons, and Tai Chi could become an emerging alternative therapy for people with dementia[15-17]. Other studies reported that physical exercise like Tai Chi improved mood and alleviated psychiatric problems in early or middle stages of dementia and also significantly reduced caregiver distresses[18]. For example, Sticky Hands Tai Chi, a special Tai Chi training technique practiced with a partner, promoted a comforting intimate interaction between the two persons and improved exercise adherence and mood in older people with dementia[15].

China has the largest number of older people with dementia[19] and Tai Chi is originated from China. Tai Chi experts in China have developed various programs of Tai Chi, but none is especially designed for older people with cognitive impairments. Therefore, a set of Tai Chi program named “Cognition Protecting Tai Chi” (CPT) has been designed by the research team of multidisciplinary professionals in the first stage of this study. The second stage of this study is to test the effectiveness of the CPT program in improving cognitive function, and to evaluate its effects and impacts on psychological behavior, mood swings, risk of falls and

ability in maintaining activities of daily living for people with mild dementia with comparison to usual care. If results are positive, it would demonstrate the potential to become a routine cost-effective exercise for older people with mild dementia.

METHODS

Settings: This study is designed at Center for Cognitive Disorders of Beijing Geriatric Hospital (BGH). The Case Report Forms will be kept and research data will be analyzed by BGH. This hospital is a tertiary hospital which is the highest rank in China's hospital system in terms of capacity of beds and research capability. BGH has 900 inpatient beds and is located in Haidian District of Beijing. The Center for Cognitive Disorders of BGH is a department serving older people with cognitive impairments. It is also the Guidance Center for Cognitive Rehabilitation of Haidian District. The recruitment, assessment, intervention, and follow-ups of participants will be conducted at three long-term care facilities near BGH at where the participants reside.

Study design

There are two stages in this study design (Figure 1).

The first stage is the development of the CPT program by the research team. The CPT program was specifically designed for cognitively impaired patients by a research team of geriatricians, neurologists,

rehabilitation specialists, experts of sports medicine, and experienced practitioners of traditional Chinese medicine in 2016. The team has modified the traditional Chinese Tai Chi to suit people with mild dementia. Any unsafe and complex actions in the traditional eight style Tai Chi program was removed, and some movements which were thought to be more beneficial for cognitive functions were added based on theories of traditional Chinese medical science. For example, the researchers removed the posture of standing on one foot and added some movements of rotating wrists and fingers in consideration of the suitability and safety aspects of the program for people with dementia. The CPT program contains eight styles of Tai Chi movements and each movement can be divided into three different maneuvers. Between January 2017 and May 2017, the CPT has been performed in five patients with mild dementia who were invited to learn and practice the CPT program for four weeks. The CPT has been further modified where necessary based on the comments and the feedback provided by the participants before the completion of final version of the CPT.

In addition to routine Starting Posture and Closing Form, there are eight styles of Tai Chi movements in the CPT, including Raising Both Hands, Forearm Rolling on Both Sides, Brush Knee and Twist Step on Both sides, Grasp the Bird's Tail-Left Side and then Right Side, Cloud Hands, Single Whip, Work at Shuttles on Both Sides, and Raising

Left and then Right Hand (Figure 2).

The second stage is a randomized controlled trial which will be conducted to test the effectiveness of the CPT program.

Recruitment of participants

Participants will be recruited from long-term care facilities near BGH. These facilities are Wenquan nursing home, Lengquan nursing home, and Hexihui nursing home. There are altogether more than one thousand older residents living in these nursing homes, thus sufficient samples can be provided. Residents who meet the inclusion criteria will be recruited.

Inclusion criteria

Residents aged 60 years or older with mild dementia (diagnosis is based on The Diagnostic and Statistical Manual of Mental Disorders, 4th edition), who have a Clinical Dementia Rating score less than 2 will be enrolled into this study.

Exclusion criteria

Residents who have severe visual or auditory impairment, serious medical conditions in major organs (such as heart, lung, kidney, liver and so on), illnesses affecting mobility, or are unable to accept assessments or interventions which are required in this study for any reasons.

Randomization and allocation sequence

Participants will be enrolled by dementia specialists. The

randomization will be carried out by an independent research assistant who will not be involved in the enrollment, assessment, or intervention of the participants. Random number sequences will be generated using SAS software. Sealed envelopes with the serial number outside and group number inside will be produced and kept in a locked drawer which will be inaccessible to all the researchers. The envelopes will be opened sequentially by the independent research assistant after baseline assessments and participants will be assigned to two groups (i.e. one intervention group and one control group) at a ratio of 1:1 according to the group number printed inside the envelopes. Outcome evaluators and data analysts will be blinded to the group assignment.

Intervention

This study is designed as a 10 month-randomized controlled trial. In addition to their routine treatment and usual care for ADL, the intervention group will perform the CPT exercise three times a week for 20 minutes each time under the guidance of the professional therapists at where the participants reside. The intervention will be practiced in groups with one therapist to five to eight participants. The control group will only receive routine treatments and usual care for ADL. The intervention to the participant should be discontinued if any complication that could affect the outcomes of the CPT occurs. The participants will be encouraged to complete follow-ups. The participants

and their representatives have access to the research team anytime if they need to discuss any issues or concerns during the study period. The participants will be explained that they can discontinue with the intervention at any time during the period of the study. Demographic information of participants who withdraw from the study after randomization and the reasons for their withdrawal will be collected.

Assessment

The trial will utilize the most commonly used tools (see below) that have been carefully selected to assess the efficacy of CPT. The Chinese version of Mini Mental State Examination (MMSE)[20] is a 30-point questionnaire which is used to measure cognitive impairments. It examines functions of attention, calculation, recall, language, ability to follow simple commands and orientation.

The Montreal Cognitive Assessment (MoCA) Beijing version (www.mocatest.org) is also a 30-point test for assessing cognitive function. MoCA includes cognitive domains for short-term memory recall, visuospatial abilities, multiple aspects of executive functions, attention, concentration and working memory, language and orientation to time and place. Because there are more difficult and multiple tasks in MoCA, MoCA is more sensitive to detect mild cognitive changes than MMSE does[21].

The World Health Organization–University of California Los Angeles

Auditory Verbal Learning test (WHO-UCLA-AVL)[22] is a tool to assess immediate recall and delayed recall with 15 words independent in meaning. Immediate recall is performed by asking the participants to remember and recall those 15 words just after each auditory learning, and this learning-recall process is repeated for three times to generate an average performance score. An average performance is recorded. Delayed recall is performed by asking the participants to recall those 15 words 30-45 minutes after the immediate recall has been completed.

The study utilizes the method of the Trail Making Test (TMT) which is a neuropsychological test of visual attention and task switching. It can provide information on visual search speed, scanning, speed of processing, mental flexibility, as well as executive functioning. A Chinese version of Shape TMT was used in this study. This Shape TMT shows numbers from 1 to 25 twice, once in a circle and once in a square. The participants are asked to connect them in sequential order alternately between circles and squares (circle 1, square 1, circle 2, square 2, etc.) [23]. This Shape TMT has been proved to be a sensitive test of visual search and sequencing[24].

The Geriatric Depression Scale (GDS)[25] is a 30-item self-report assessment used to identify depression in the elderly, of which questions are answered in a "yes" or "no" format. It is appropriate to test older individuals with mild or moderate cognitive impairment using GDS.

The Neuropsychiatric Inventory (NPI)[26] assesses common psychiatric and behavioral symptoms in dementia. Its items include hallucinations, delusions, agitation/aggression, dysphoria/depression, anxiety, irritability, disinhibition, euphoria, apathy, aberrant motor behavior, sleep and night-time behavior disturbance, appetite and eating disorders. Information can be obtained from caregivers who have in-depth knowledge of the patients' performance. The caregivers will also be asked to rate their own distress level associated with daily care and support provided by them to the patients.

The Barthel Idex (BI)[27] is an ordinal scale used to measure performance in ADL. The ten variables describing ADL and mobility addressed in the Barthel scale are: presence or absence of fecal incontinence, urinary incontinence, grooming, toileting, feeding, transferring (e.g. from chair to bed), walking, dressing, climbing stairs and bathing. The scoring is based on information provided by the participant's informant, who can be his/her family members or caregivers.

All participants will undergo all above assessments at 0 (baseline), five and ten months within the current study period. Fall incident will also be recorded. Fall will be defined as the experience of a sudden, involuntary, unintentional change of position, down on the ground or on a lower plane. When assessing a definite fall, the team will try to get an

eyewitness account or records of security cameras (all the areas of the nursing homes where participants live will be monitored by 24-hour security cameras).

Outcomes

The psychometric tools used in this study will be analyzed to assess the efficacy of the CPT. The primary outcome is the WHO-UCLA-AVLT delayed recall score. The secondary outcome is the score of the TMT. The fall incident will be analyzed to assess the safety of this Tai Chi program. Complaints of medical symptoms related to the intervention will be documented and treated when necessary, including fatigue, pain, dizziness, and so on.

Sample size

The sample size was calculated by Power Analysis and Sample Size Calculation Statistical Software V13.0 based on the results of pre-experiment of this study. Using a type I error of 0.05 and a power of 80%, a mean difference of 2 points is expected between two groups after 10 months. The results show a sample size of 34 per groups is adequate for testing the primary outcome (WHO-UCLA-AVLT delayed recall score). Considering a 15% dropout rate, a total number of 80 participants will be recruited.

Quality control and quality assurance

At least three dementia specialists will work together to examine the

participants and provide diagnosis for each participant. All data will be monitored and reviewed by the PI or research coordinators. Training will be provided to all researchers. Consistency coefficients in scoring assessment scales between researchers should be no less than 0.85. Data entry will be verified by a second researcher in the team. To protect participants' confidentiality, only supervisors, researchers of this study and the ethics committee will be authorized to have access to the personal information and medical records of the participants.

Statistical method

All analyses will be carried out using SPSS version 16.0. The variations of scores of psychometric assessments over time between two groups will be examined using repeated measurement of variance analysis. The association between intervention and incidence of falls will be analyzed using Chi-Square test.

Ethics and dissemination

This study has been approved by the ethical review committee of the Beijing Geriatric Hospital (protocol number: 2015-021). Information leaflets of the study will be available at the three long-term care facilities. The leaflets explain in full detail the aims and objectives of the study, selection criteria and the processes that the study will be adhering to. The research team will provide an individual face to face consultation to all applicants or their guardian to answer any questions they may have.

The applicants can then discuss this with their family if they wish and make a decision to opt in or opt out the study prior to signing the consent form. Informed consent will be obtained from all participants or their guardians. The authors intend to submit the findings of the study to peer-reviewed journals or academic conferences to be published.

Patient and Public Involvement

The original research question and outcome measures were conceived by the authors and were modified based on the face to face screening interview with patients and their guardians by a research assistant. Five patients with mild dementia were invited to learn and practice the CPT program prior to designing the RCT. The CPT was modified based on the comments and the feedback provided by the participants in order to ensure the safety and the applicability of the intervention. Both the burden and the potential benefit of the intervention will be assessed by patients and their advisors before the consent forms are signed. The findings of this study will be made available to the participants and their guardians.

CONCLUSION

This protocol outlined the objectives of the study and explained the CPT exercise developed by the research team including geriatricians, neurologists, rehabilitation specialists, experts of sports medicine, and experienced practitioners of in traditional Chinese medicine. The study is

designed as a randomized controlled trial in order to evaluate the effects of this especially designed CPT on the participants with mild dementia.

Contributors

Jihui Lyu conceived the idea and supervised this study and is the guarantor. Jihui Lyu, Xiangjiang Rong, Xueli Chen, Fangling Li, Wenjie Li and Lian Wei were involved in the design. Wenjie Li, Nayan Huang and Xiangjiang Rong prepared draft manuscript. Jihui Lyu, Mei Champ, and Qian Xiong revised the manuscript. Wenjie Li, Mo Li and Xiangjiang Rong carried out the statistical calculation. All authors approved submission of this manuscript.

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Competing interests

None declared.

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Figure legends:

Figure 1 Trail Flow Chart.

Figure 2 Main movements of the "Cognition Protecting Tai Chi" (CPT).

A1-3: Raising Both Hands

B1-3: Forearm Rolling on Both Sides

C1-3: Brush Knee and Twist Step on Both sides

D1-3: Grasp the Bird's Tail-Left Side and then Right Side, Cloud Hands

E1-3: Cloud Hands

F1-3: Single Whip

G1-3: Work at Shuttles on Both Sides

H1-3: Raising Left and then Right Hand

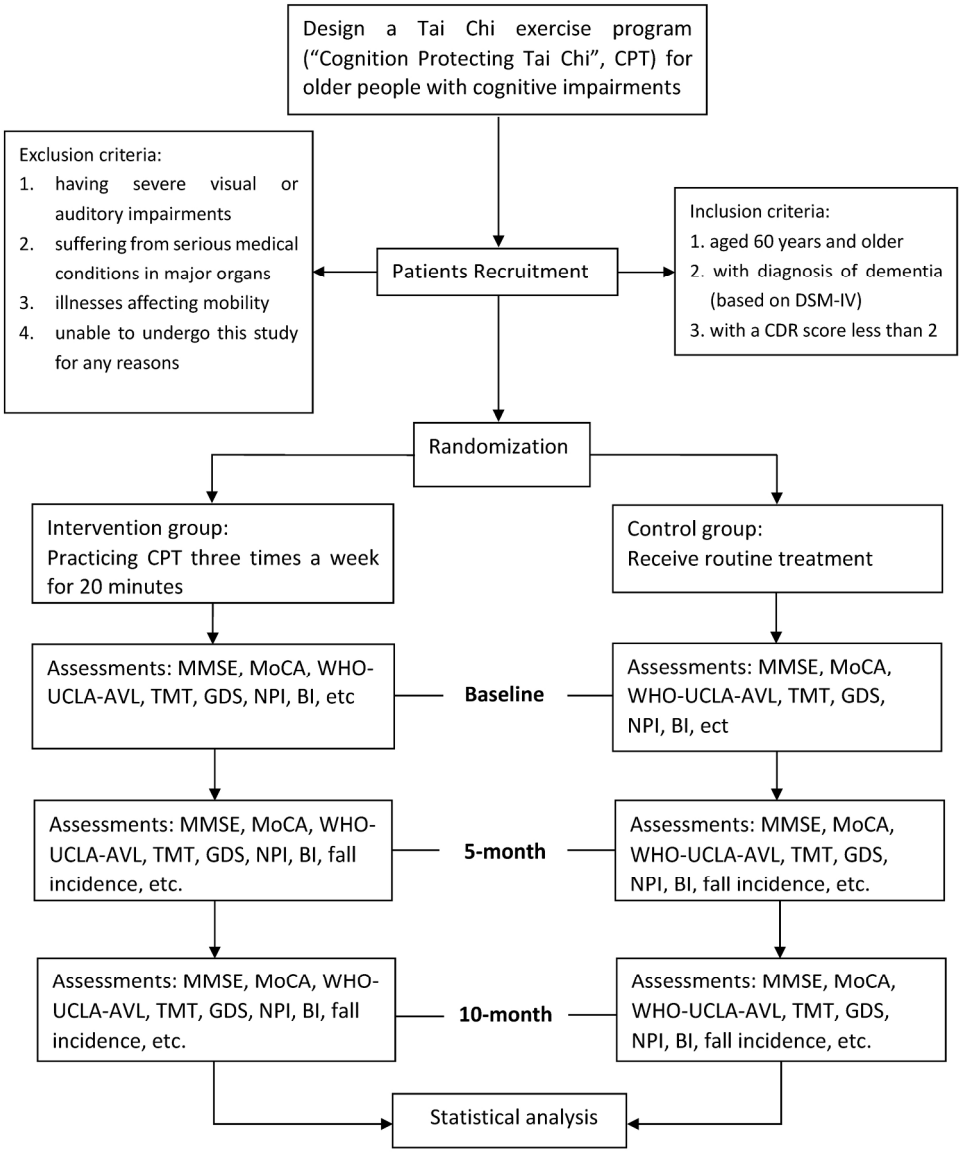

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Figure 2 Main movements of the "Cognition Protecting Tai Chi" (CPT).
A1-3: Raising Both Hands
B1-3: Forearm Rolling on Both Sides
C1-3: Brush Knee and Twist Step on Both sides
D1-3: Grasp the Bird's Tail-Left Side and then Right Side, Cloud Hands
E1-3: Cloud Hands
F1-3: Single Whip
G1-3: Work at Shuttles on Both Sides
H1-3: Raising Left and then Right Hand

292x223mm (300 x 300 DPI)

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	19
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	19
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	6-9
	6b	Explanation for choice of comparators	9
Objectives	7	Specific objectives or hypotheses	8, 9
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	9, 10, 11
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	9
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	11
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	12, 13
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	12, 13
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	12, 13
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	12
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	16
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1. Trail flow chart

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	16
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	11
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	11, 12
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	12
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	12
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	12
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	13-16
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	12, 13

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	16, 17
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	NA
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	17
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	4, 17, 18
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	NA

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	4, 17, 18
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17, 18
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	NA
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	4, 17, 18
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.