BMJ Open

Effectiveness of Yijinjing exercise in the treatment of early-stage knee osteoarthritis: a randomized controlled trial protocol

Guangxin Guo [1,2] Yihang Wang [2] Xiruo Xu [2] Kaiqiu Lu [2] Xuanying Zhu [3] Yijia Gu [4] Guangpu Yang [5] Fei Yao,[1,2,6] Min Fang [3,6]

To cite: Guo G, Wang Y, Xu X, *et al*. Effectiveness of Yijinjing exercise in the treatment of early-stage knee osteoarthritis: a randomized controlled trial protocol. *BMJ Open* 2024;**14**:e074508. doi:10.1136/bmjopen-2023-074508

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2023-074508).

GG, YW and XX are joint first authors.

Received 11 April 2023
Accepted 11 January 2024

For numbered affiliations see end of article.

Correspondence to
Min Fang;
fangmin19650510@163.com

ABSTRACT

Introduction Knee osteoarthritis (KOA) is still a challenging degenerative joint disease with high morbidity and disease burden. Early-stage KOA, the focus of this study, could present a Window of Opportunity to arrest the disease process and reduce the disease burden. Yijinjing exercise is an important part of physical and psychological therapies in Traditional Chinese Exercise and may be an effective treatment. However, there is no clinical efficacy assessment of Yijinjing exercise for patients with early-stage KOA. Therefore, we designed a randomised controlled trial to evaluate the effectiveness of Yijinjing exercise on patients with early-stage KOA.

Methods and analysis This is a parallel-design, two-arm, analyst assessor-blinded, randomised controlled trial. In total, 60 patients with early-stage KOA will be recruited and randomly assigned to the Yijinjing exercise group (n=30) and health education group (n=30) at a ratio of 1:1, receiving 12 weeks of Yijinjing exercise or health education accordingly. The primary outcome will be measured with the Western Ontario and McMaster Universities Osteoarthritis Index, and the secondary outcomes will include the Visual Analogue Scale, Short-Form 36 Item Health Survey Questionnaire, Beck Depression Inventory, Perceived Stress Scale, Berg Balance Scale, and Gait Analysis for a comprehensive assessment. Outcome measures are collected at baseline, at 12 week ending intervention and at the 12 week, 24 week and 48 week ending follow-up. The primay time point will be 12 weeks postintervention. Adverse events will be recorded for safety assessment.

Ethics and dissemination This study has been approved by the ethical application of the Shanghai Municipal Hospital of Traditional Chinese Medicine Ethics Committee (2021SHL-KY-78).

Trial registration number ChiCTR2200065178

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ To the best of our knowledge, this study will be the first randomised controlled trial to explore the effectiveness of Yijinjing exercise in the treatment of early-stage knee osteoarthritis (KOA) patients.
⇒ This study will evaluate pain intensity, stiffness, and physical function, life quality, psychological health, and knee function, which will support the clinical efficacy of Yijinjing exercise in early-stage KOA patients.
⇒ This study will use gait analysis to evaluate the kinetic and kinematic function of patients with early-stage KOA.
⇒ Due to the specific nature of exercise interventions, it is difficult to ensure that participants and instructors are blinded.

INTRODUCTION

Knee osteoarthritis (KOA) has become a major public health challenge globally[1] that requires proper disease management for the early stage to arrest the disease process. KOA is characterised by chronic pain and disability with a high global prevalence.[2] The prevalence of KOA is increasing in younger age group of 35–55.[3–5] KOA affects more than 260 million people worldwide,[6] increasing by 9.3% from 1990 to 2017,[1] and the prevalence may continue to increase.[7] Relatively advanced KOA can cause irreversible structural damage to the joints.[8] And KOA ranks as the 11th highest contributor to the global disability, seriously damaging the patient's quality of life.[9 10] Early-stage KOA, as a possible Window of Opportunity to prevent the disease process and improve the quality of life, should be given enough attention.[11 12]

Proper management of early-stage KOA[13 14] could arrest the disease process, restore joint homeostasis, and thereby reduce the burden of disease.[11] Early-stage KOA is a type of KOA that is symptom-focused for diagnosis.[11 15] Patients present primarily with pain and discomfort in the knee joint. The symptoms are episodic and may persist for weeks. Pharmacological treatment can reduce pain and improve physical function in patients with KOA.[16] However, the long-term pharmacological treatment may have adverse

effects,[17–19] causing enormous economic pressure and reducing quality of life.[20–22]

Targeted and appropriate exercise may be an effective treatment for early-stage KOA. Exercise therapy is widely used in KOA treatment to improve muscle strength and functional activity.[8 23 24] Previous studies show that Traditional Chinese Exercise (TCE) can alleviate pain and improve functions.[25–28] Yijinjing exercise, as an important part of physical and psychological therapies in TCE, has been widely used to treat neck pain,[29–33] ankylosing spondylitis[34] and sequelae of stroke,[35–38] which can improve the muscle strength[39 40] and knee function,[41 42] and relieve knee pain and psychological stress.[33 43 44]

However, clinical evidence for the efficacy of Yijinjing exercise in patients with early-stage KOA is still lacking. To the best of our knowledge, this randomised controlled trial is the first study to evaluate the effectiveness in early-stage KOA patients treated by Yijinjing exercise. Furthermore, this study is based on in-depth research from previous studies, as the subjects of this study are limited to early-stage KOA patients and have optimised Yijinjing exercise programme for early-stage KOA patients.[44] For patients with early-stage KOA, we claim that Yijinjing exercise to be superior to health education strategy of the non-surgical management of KOA in pain relief and function improvement after a 12 week intervention.

METHODS AND ANALYSIS

Study design

The study will be a randomised, single-centre, superiority, parallel controlled trial. Only outcome assessors and statisticians will be blinded due to the limitations of the intervention methodology. A total of 60 patients with early-stage KOA will be recruited from the Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine. All patients will be provided with written informed consent at the time of recruitment. The patients will have equal opportunity to be assigned to Yijinjing exercise group and health education group in a 1:1 allocation ratio. Patients in the Yijinjing exercise group and the health education group will receive 12 weeks of Yijinjing exercise and health education, respectively. Data management and statistics will be conducted at the School of Acupuncture-Moxibustion and Tuina, Shanghai University of Traditional Chinese Medicine. The study process is shown in figure 1. The planned start and end dates for the study are 30 February 2024 to 30 February 2026.

The present study is a randomised controlled trial. During the treatment, patients in the Yijinjing exercise group will practice Yijinjing exercise, while the health education group will receive health education. Both the outcome assessments will be performed at five time points, namely the baseline, the end of the treatments at 12 weeks, and 12, 24, and 48 weeks of follow-up subsequently. The schedule of enrolment, interventions, and assessments is shown in table 1.

Study setting

The study will be conducted at the Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, China.

Safety measurements

Safety evaluations will be conducted at screening, throughout the trial, and at follow-up 12, 24, and 48 weeks after the last Yijinjing exercise. The safety evaluations will be initially conducted by the attending physician with more than 5 years of work experience, followed by a final review by a chief physician with more than 15 years of work experience. The initial assessors will receive a series of training on expertise and risk assessment from our research team and pass the training examination before formally implementing the safety assessment during the study. Any adverse events (AEs) will be collated from case report forms and follow-up questionnaires even though Yijinjing exercise and health education are at low risk. Researchers will then analyse whether AEs are directly related to the rehabilitation programme. When sports injuries occur or condition suddenly deteriorates during the trial with serious complications or severe AEs such as breathing difficulties, sports injuries and falls, the trial will be terminated immediately and prompt medical treatment will be administered according to the condition of the subject. Researchers will then analyse whether they are directly related to the rehabilitation programme. Serious AEs will be reported to the Shanghai Municipal Hospital of Traditional Chinese Medicine Ethics Committee in a timely manner.

Sample size calculation

Power analysis is based on published data regarding to changes in the total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score in an open trial[45] concerning TCE treatment in KOA. The difference in the reduction in WOMAC scores between the TCE treatment group and the control group in previous studies was 4.22. The SD in the TCE treatment and the control group were 5.15 and 3.24, respectively. Suppose α=0.05, a power level of 0.9 and a 20% rate dropout, a total of 60 participants was calculated by the PASS software (PASS 15, NCSS, LLC, Kaysville, UT, USA).

Inclusion and exclusion criteria

Inclusion criteria

1. KOA diagnosis according to criteria listed in the Chinese guideline for the diagnosis and treatment of osteoarthritis (2021 edition).[23]
2. Kellgren–Lawrence score≤2.[46 47]
3. Pain level≥3 on the 10-point Visual Analogue Scale (VAS).
4. Man or woman aged 35–65 years.
5. Ability to perform basic body movements like walking.
6. No communication barriers with researchers to understand the instructions.
7. Body mass index≤36 kg/m^2.

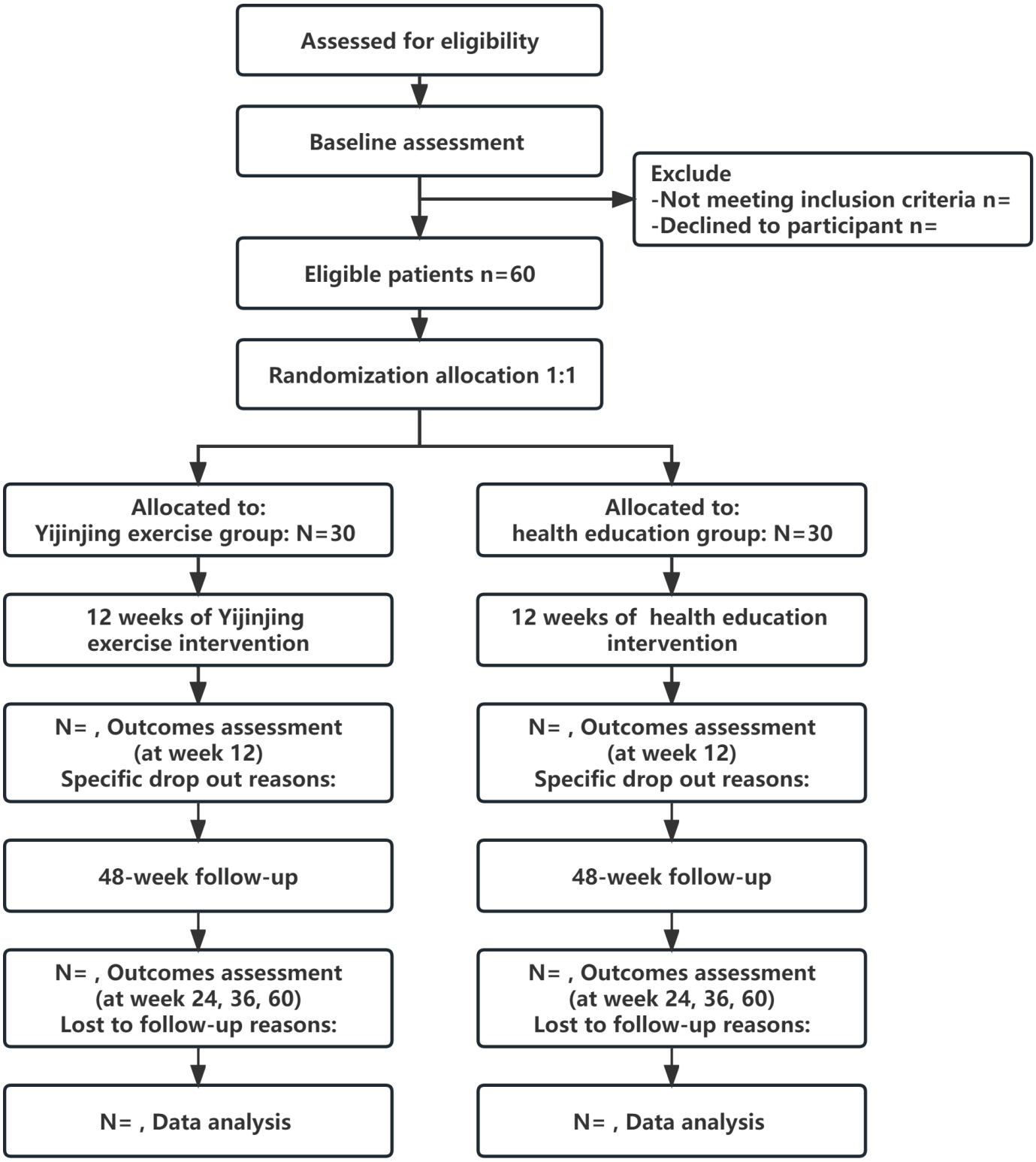

Figure 1 CONSORT flow chart of the study. CONSORT, Consolidated Standards of Reporting Trials.

8. Willingness to participate and sign the informed consent form.

Exclusion criteria

1. Physical or mental illness that seriously interferes with daily life or contraindicates exercise.
2. The Montreal Cognitive Assessment cognitive status evaluation score≤24.[48]
3. Inability to independently complete gait analysis.
4. Knee surgery or intra-articular injections within 3 months.
5. Yijinjing or other clinical exercises in the last 3 months.

Table 1 The schedule of enrolment, interventions, and assessments

	On enrolment	Intervention period	End of intervention	End of follow-up		
Time point	Week 0	Weeks 1–12	Week 12	Week 24	Week 36	Week 60
Inclusion/exclusion criteria	×					
Informed consent	×					
Demographic characteristics	×					
Randomisation and allocation	×					
WOMAC	×		×	×	×	×
VAS	×		×	×	×	×
SF-36	×		×	×	×	×
BDI	×		×	×	×	×
PSS	×		×	×	×	×
BBS	×		×	×	×	×
Gait analysis	×		×	×	×	×
Safety measurement		×	×	×	×	×

BBS, Berg Balance Scale; BDI, Beck Depression Inventory; PSS, Perceived Stress Scale; SF-36, Short-Form 36 Item Health Survey Questionnaire; VAS, Visual Analogue Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

6. Other reasons considered necessary by the researchers, such as communication barrier due to inability to speak Chinese; surgery is planned within the next 12 weeks; inability to commit to the Yijinjing exercise requirements.

Drop-out criteria

1. Inability to continue owing to serious medical conditions.
2. Voluntary withdrawal.

Recruitment

Patients with early-stage KOA will be recruited. In our study, participants will be recruited from Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine. Recruitment methods included WeChat networking, online advertisements, doctor referrals, posters, and leaflets. WeChat is currently considered the most popular social media in China. Both medical staff and patients have their own WeChat accounts for convenient and fast online communication. Shanghai Municipal Hospital of Traditional Chinese Medicine is a tertiary hospital in Shanghai, with an outpatient department for the treatment of Yijinjing exercise. Before the trial, participants will be briefed on the study process and their responsibilities. They will be informed about the examination items and precautions. Participants will be informed that their participation is entirely voluntary, and they could refuse or withdraw at any time without affecting their medical or other benefits. Written informed consent will be obtained prior to the commencement of any study-related treatments. Research assistants will be responsible for obtaining informed consent.

Randomisation and allocation concealment

Sixty eligible subjects will be randomly assigned to Yijinjing exercise group and health education group at a 1:1 equal ratio after baseline assessment. The random list will be generated by a statistician using the computer programme (Strategic Applications Software). An independent assistant will then make sequentially numbered, sealed and opaque random envelopes that will contain the corresponding random numbers and intervention methods. Envelopes will be sealed and stored before use, and then distributed to the patients by researchers to determine patient groupings.

Blinding

Due to the specific nature of exercise interventions, it is difficult to blind the participants and researchers. However, outcome assessors and statisticians will be blinded in this study. They will only be responsible for the results analysis and data collection. The recruitment and assignment information will be hidden from the assessors to ensure the accuracy and reliability of the results. There will be no unblinding at any point.

Intervention

Yijinjing exercise group

The participants in Yijinjing exercise group will receive 12 weeks of Yijinjing exercise intervention. They will be taught by experienced professional Yijinjing exercise instructors (clinical experience in Yijinjing exercise therapy≥10 years, with the teacher qualification certificate of higher education). Before conducting trials, the instructor must go through meticulous clinical trial training and cannot implement an intervention until they pass an examination. The course includes the instruction of six movements, involving details such as the breathing

Table 2 Details of the operation of Yijinjing exercise

Sequence of actions	Action details
Action 1 Wei Tuo presenting the pestle 3 routine	Slowly squat and put the palms together in front of the chest. While inhaling, slightly flex the knee joints, and keep the knees not extending beyond toes. Keep eyes on the ground about 3 m in front of the body. Concentrate and maintain the position for 10 s. Exhale while slowly straightening the knee joints. During this process, keep eyes closed tightly, and feel the position of knee joints. The operation at this stage also lasts for 10 s.
Action 2 Plucking a star and exchanging a star cluster	Adopt a posture of standing with one foot forward, with the toes of the front foot on the ground, and the centre of gravity on the back foot. Place one hand 30 cm above the same side of the head, and the other hand on the lumbosacral area, and then perform knee flexion and extension with inhalation and exhalation. The rhythm is the same as in action 1. Keep the eyes on the fingertips when flexing the knees, and close the eyes when extending the knees to feel the position of the knee joint.
Action 3 The black dragon displaying its claws	Adopt a posture of standing with one foot forward, with the toes of the front foot on the ground, and the centre of gravity on the back foot. Place one hand 30 cm above the same side of the head, and the other hand on the lumbosacral area, and then perform knee flexion and extension with inhalation and exhalation. The rhythm is the same as in action 1. Keep the eyes on the fingertips when flexing the knees, and close the eyes when extending the knees to feel the position of the knee joint.
Action 4 Pulling nine cows by their tails	Stand with the lower limbs separated by a distance of 1 m, and extend the upper limbs to the limit in the horizontal direction. Make a lunge with both lower limbs in the left and right directions, with the centre of gravity on the forefoot. While inhaling, stare at the floor 3 m ahead for 8–10s. Externally rotate the hip joint of the front lower limb, extend the knee joint, and flex the knee joint of the rear lower limb. The centre of gravity is on the back foot. Maintain the exhalation for 10s, and finally restore to the initial preparation posture.
Action 5 Three plates falling on the floor	Put the hands in front of the chest, and then flex the knee joint with inhalation (the range of flexion angle is larger than any other movement). Put hands on the outside of the knee joint, holding for 2s, and keep the eyes on the ground 3 m ahead; then exhale, straighten the knee joint, close the eyes, feeling the position of the knee joint.
Action 6 Swinging the tail	Move the hands, with the fingers interlaced, to the top of the head. Turn the palms up, and stretch the arms upwards. Straighten the hips and knees and twist the body to the left. Bend the hips and knees and turn the body to the right. Straighten the hips and knees and twist the body to the right. Bend the hips and knees and turn the body to the left. Put the hands down from both sides.

rate, meditation method, knee flexion, and extension rotation angle. The specific exercise content refers to the health qigong compiled by the General Administration of Sport of China,[49] the specific action characteristics of which are shown in table 2 and figure 2. In the first week, the instructor will lead participants through the entire process and introduce the details of each movement, and encourage them to discuss their feelings and confusions following the exercise to ensure that every participant could practice Yijinjing exercise correctly. After the initial week of exercise, participants will continue with home-based exercises. To ensure adherence to correct exercise methodologies, ongoing support and supervision will be provided by the instructors through video conferences. The intervention frequency will be 30 min twice a week, preceded by a 5 min warm-up and followed by a 5 min relaxation. Training intensity will be assessed using the modified Borg Fatigue Rating Scale (score≥5).[44 50] The scale ranges from 0 to 10, where 0 indicates no exertion at all and 10 represents maximal exertion. This method provides a nuanced understanding of the participant's perceived exertion during the Yijinjing exercises. After Yijinjing exercises, participants are asked to rate their level of fatigue using this scale. The score ≥5 is qualified. Otherwise, the training intensity of Yijinjing exercise will be increased to qualified, and the increased training intensity and training duration will be recorded.

Health education group

The participants in health education group will receive 12 weeks of group-based KOA-related health education by instructors, a non-surgical management strategy recommended by the guideline.[16] The instructors providing the health education are professors from Shanghai University of Traditional Chinese Medicine with over 10 years of experience in treating KOA. The 40 min educational session will be organised twice a week, with face-to-face instruction the first week and then transition to video conferencing. The session will be based on relevant KOA guidelines and results from recent discoveries.[10 23 24 51 52] The session will include the following: (1) the basic concept of KOA, (2) risk factors associated with KOA, (3) KOA prevention and management, (4) self-care strategies, and ways to improve the quality of life (such as lifestyle changes to relieve pain).

The intervention will last for 12 weeks in both groups, and then both groups will be followed up for another 48 weeks. Participants in both group will be reminded weekly not to practice other clinical exercises, and if they do, they will be recorded. To ensure compliance, both

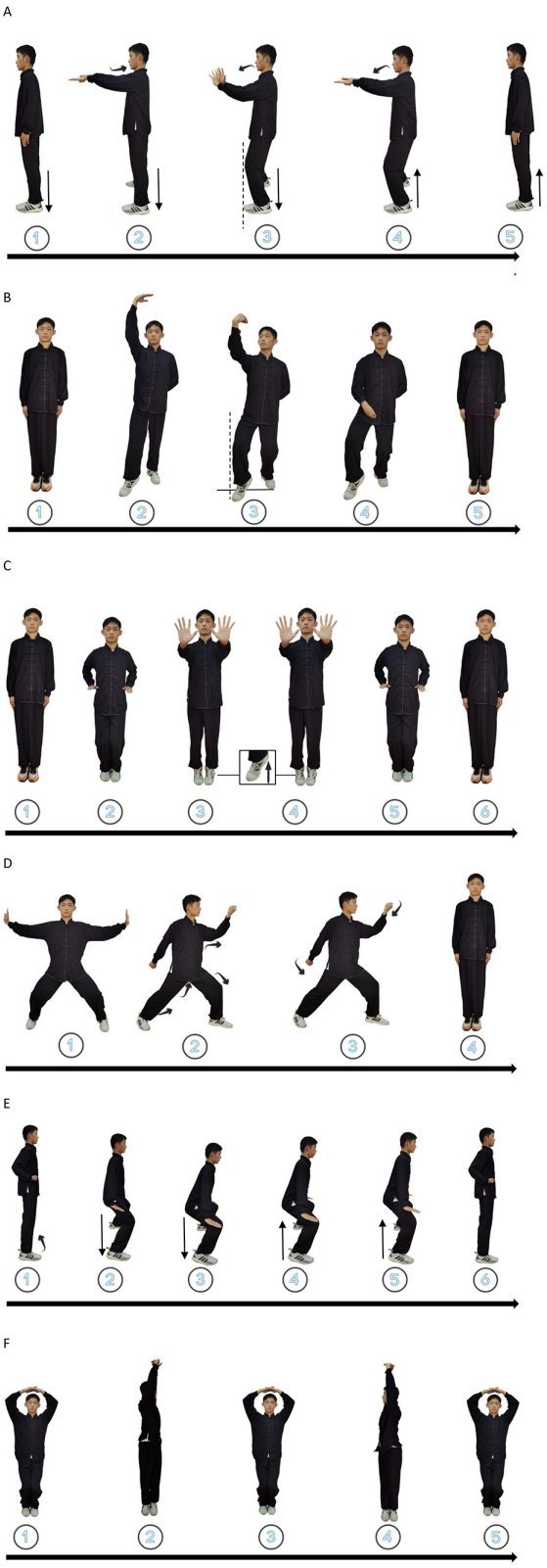

Figure 2 Demonstration of Yijinjing exercise. (A) Action 1, (B) Action 2, (C) Action 3, (D) Action 4, (E) Action 5, and (F) Action 6.

groups will not be prohibited from using medication. However, medication is only allowed when the VAS score is ≥3. Only the prescribed dose of celecoxib capsules will be used. Patients who use medication when the VAS is still ≤3 or overuse the medication will be considered as drop-out. The frequency of medication will be observed and recorded.

Adherence

Participants will be encouraged and supervised to receive the intervention by telephone each week and will be asked to fill out weekly charts. And participants will be provided with remote video supervision during the intervention and asked to sign a recording form after the intervention. For Yijinjing exercise group, the study will calculate adherence as the percentage of the 24 scheduled Yijinjing exercise sessions completed. For health education group, the study will calculate adherence as the percentage of the 24 scheduled sessions completed.

Outcome measurements and follow-up

This study will test the outcome indicators at five time points: baseline, the end of 12 week intervention, and the end of the 12 week, 24 week, and 48 week follow-up. The primary indicator will be the WOMAC score. The secondary indicators include VAS, Short-Form 36 Item Health Survey Questionnaire (SF-36), Beck Depression Inventory (BDI), Perceived Stress Scale (PSS), Berg Balance Scale (BBS), and Gait Analysis. After the end of the trial, the mean and SD of the two sets of each outcome indicators will be combined with the corresponding formula to test the power of the trial and judge the reliability of the trial results. The primary time point will be 12 weeks postintervention. The secondary time point will be 12, 24, and 48 weeks after follow-up.

Basic information

Participants' sociodemographic data (including age, gender, height, weight, blood pressure, occupation, educational background, employment status, and residential area) and medical history (including the date of diagnosis, duration of KOA, and previous treatments for KOA) will be assessed at baseline.

Primary outcomes

The WOMAC is an internationally recognised lower limb assessment method, widely used in the clinical assessment of KOA symptoms with high reliability and validity in Chinese KOA patients.[53 54] The WOMAC consists of three main areas: pain, stiffness, and joint function, to assess the structural and functional status of the knee.[55] The WOMAC consists of three subscales, including pain (20 points), stiffness (8 points), and daily functional activities (68 points), with a total score of 0–96. A higher total score indicates a higher level of knee dysfunction; a lower total score indicates a better functional status of the knee joint. The total score of the WOMAC scale will be used to assess the clinical efficacy of Yijinjing exercise in patients with KOA.[56] The primary outcome will be assessed in both the Yijinjing exercise group and the health education group.

Secondary outcomes

Secondary outcomes will assess the clinical impact of Yijinjing exercise and health education on the pain level, life quality, psychological health, and knee function in patients with early-stage KOA. Measurements include VAS, SF-36, BDI, PSS, BBS, and Gait Analysis.

Visual Analogue Scale (VAS)

The VAS is a sequence of 10 cm numbers, one of the most commonly used scales to assess pain.[57] The left side corresponds to level 0, indicating no pain, while the right side corresponds to level 10, indicating the most severe pain. Patients can mark their pain level in this segment. From the left side to the right side, the higher the number, the higher the pain score.[58] It will be by paper in using the VAS to avoid adverse effects on the VAS assessment when using different models of tablets.

Short-Form 36 Item Health Survey Questionnaire (SF-36)

The quality of life will be measured by the SF-36. The SF-36 consists of 36 items assessing eight health concepts: basic competence (10 items), physical activity (four items), social activities (two items), physical pain (two items), mental health (five items), daily activities (four items), vitality (four items), and general health status (five items). Each health concept is scored from 0 to 100, with 0 corresponding to the worst health condition and 100 for the best health condition. The higher the score, the better the health status. The SF-36 has high reliability and validity in the Chinese population.[53 59 60]

Beck Depression Inventory (BDI)

The BDI is a self-rating scale to determine the degree of depression. The scale is divided into 21 items, including depression, pessimism, and self-disappointment. Each item is scored on a 0, 1, 2, or 3 scale and the cumulative score for each item is the total score. The total score range for the BDI is 0–39, the higher the score, the more severe the depression.[61] The BDI is one of the most commonly used self-rating scales for depression and a classic tool for depressive state, screening with internal consistency and validity in non-psychiatric patient populations.[59 62 63]

Perceived Stress Scale (PSS)

The PSS is a self-assessment tool for measuring the severity of stress and can detect overall and prevalent stress in life.[64–66] The PSS contains 10 items, each rated on a 5-point Likert scale, with 0 meaning never, 1 meaning occasionally, 2 meaning sometimes, 3 meaning often, and 4 meaning always. The total score is 0 to 40, with higher score associated with higher level of perceived stress, with 0–13 indicating low-pressure levels, 14–19 indicating medium pressure levels, and >19 indicating high-pressure levels.

Berg Balance Scale (BBS)

The BBS is a comprehensive scale that measures balance and assesses a patient's balance function by evaluating performance on 14 functional tasks.[67 68] The balance function is divided into 14 items, from easy to difficult, and each item is divided into 5 levels; 0, 1, 2, 3, and 4. The maximum score is 4, and the minimum score is 0. The maximum total score is 56, and the minimum score is 0. A higher total score indicates a relatively better balance in the patient.

Gait analysis

Gait analysis is an examination method to study walking patterns, which can be used in the kinematics and kinetics of the lower limbs of patients with KOA, guiding rehabilitation assessment and treatment, contributing to clinical diagnosis, efficacy assessment, and mechanistic studies.[69 70] The test procedures are as follows: (1) participants will be asked to walk on a 10 m pavement with three one-way walking tasks per test. (2) 3D marker trajectories will be recorded at 100 Hz using a Vicon16 camera MX13+motion system (Vicon, Oxford Indicators, UK). (3) A total of 28 marker points will be affixed for body surface marking based on the anatomical locations specified by the pyCGM2-LowerLimbCGM23 model. (4) 3D kinematic data will be collected with two force platforms (1200 Hz, Advanced 130 Mechanical Technologies, Watertown, MA, USA) using the Vicon Nexus software (Vicon Motion Analysis, Oxford, UK).[71 72]

Data collection and management

Each researcher will receive unified training, such as study requirements, standardised measurements of height, weight, and blood pressure, ensuring that they can collect indicators in a uniform, standard manner. All indicators will be collected peer-to-peer by members in charge of recruitment, the members will inform all participants and obtain their support during recruitment. Participants will be followed throughout intervention to prevent shedding.

All researchers will maintain the confidentiality of all participants' personal information and indicator results. Two members accountable for data will enter all collected data into the computer using a double-data entry method. Data cleaning will be performed before data analysis to prevent discrepancies or coding errors. The electronic data will be checked against the paper records of the original data. Furthermore, the data entered will then be double-checked for accuracy by two other members. Finally, all electronic data will be stored in a zip folder using a password-protected access system, and hard copies of all material will be stored in a specific cabinet.[73] Data will be periodically audited and verified internally. Data monitoring will be conducted by the Science and Technology Department of Acupuncture and Tuina Institute, Shanghai University of Traditional Chinese Medicine. The monitors will verify that all AEs are recorded in the correct format and as defined by the protocol. The monitors will verify the following variables for all participants: initials, date of birth, gender, signed informed consent, eligibility criteria, date of randomisation, treatment assignment, AEs, and endpoints. The administrators will

be required to report weekly data monitoring progress to the Steering Committee regularly, including the accuracy and reliability of data.

Data analysis

All data processing and statistical analyses will be performed by SPSS statistical software V.26.0 (IBM), conducted by independent data assessors who are unaware of the group allocation. Missing data will be replaced according to the principle of the last observation carried forward. For the missing data, several sensitivity analyses will be conducted to evaluate their effects on the results of the experiment. An intention-to-treat analysis will be applied to all the outcomes. For example, non-adherent participants will be included for intention-to-treat analysis. A sensitivity will be then conducted to test if it alters the results. The Shapiro–Wilk test will be used to determine the normality of the primary outcome and all other secondary outcomes data, and then to obtain means, SD, maxima, minima, medians, CIs, and frequencies (composition ratios). For continuous outcome measures, analysis of variance will be used to adjust baseline outcome values to compare the difference in mean change between the two groups (follow-up minus baseline).[59] The results will be expressed as estimated differences with 95% CI. Log-binomial regression will be used to compare the likelihood of improvement in pain and function between the two groups. Results will be expressed as a relative risk at 95% CI. Multifactorial analysis will be used to adjust for confounders. Statistical significance is demonstrated by a p-value (bilateral) of less than 0.05. For participants with bilaterally KOA, we will use multiple statistical analysis strategies. For example, we will record the number of left or right knees in all participants who meet the inclusion criteria, and statistically analyse the changes in VAS pain for all knee joints by Yijinjing exercise. At the same time, we will conduct subgroup analysis of participants with single knee pain to explore the changes of VAS pain of participants with single knee pain induced by Yijinjing exercise. In addition, we will conduct a subgroup analysis of participants with bilateral knee pain to explore the changes of VAS pain in participants with bilateral knee pain by Yijinjing exercise.

DISCUSSION

Increasing attention is paid to the early-stage KOA[14 74–76] because articular cartilage can still regenerate, while articular cartilage may be permanently lost in the advanced stage.[15 77] Due to the limited benefits of pharmacologic therapy and surgery, non-pharmacologic therapy has gradually gained attention in managing KOA.[78] Non-pharmacological approaches, such as exercise, weight loss, and healthy diet are strongly recommended in managing KOA.[21] Exercise has the benefits of muscle strengthening and hypertrophy, weight management, and potential disease-modifying effects.[79–81] Traditional exercise training focuses on improving muscle strength, which is critical to the mobility of KOA patients. Recently, growing evidences have advocated the potential benefits of TCE on symptomatic improvement of KOA.[82] We have previously launched the clinical application of Taiji in elderly people with KOA.[45 83 84] Yijinjing exercise, a kind of TCE that combines physical activity, mental focus, and controlled breathing, is easier to learn and promote than Taijiquan studies.[85 86] However, the evidence and mechanism for the effect of Yijinjing exercise on early-stage KOA are still insufficient.[87]

To the best of our knowledge, this is the first study that explores the effects of Yijinjing exercise for early-stage KOA. Previous studies on Yijinjing exercise for KOA have been published, but the effectiveness of early-stage KOA patients is still unclear.[41 88–91] The prior research of our group[44] has confirmed that Yijinjing exercise therapy could improve the walking speed and restore the trend of normal gait of KOA and appeared be associated with improvements in psychological well-being including reduced stress, anxiety, depression, and mood disturbance to manage KOA. In contrast to end-stage KOA, structural alterations in joint tissues at an earlier stage may be more susceptible to disease-modifying interventions, potentially slowing or preventing progressive change.[92]

Our study has some strengths. First, this trial will explore the effectiveness of Yijinjing exercise in the treatment of early-stage KOA in a comprehensive scale. Regardless of structural changes, multiple patient-reported outcomes must be evaluated to reflect clinically meaningful changes better. This study will evaluate pain intensity, stiffness, and physical function, life quality, psychological health, and knee function, which will support the clinical efficacy of Yijinjing exercise in early-stage KOA patients. The pathological changes are usually presented throughout the gait motion and are often difficult or incomplete to induce symptoms on static examination.[93 94] Gait analysis can allow the discrimination of KOA patients from asymptomatic participants and can also differentiate KOA patients with low KL grade (KL 1–2) from high KL grade (KL 3–4) with a high success rate.[95] Besides, the follow-up time for early-stage KOA patients after Yijinjing exercise is long. Researches have shown that a 48 week follow-up period will be sufficient to investigate the persistence of intervention effects on KOA.[24 52 96]

However, the study also has some limitations. First, the patients and therapist will not be blinded to the treatment. Second, the participants will come from the same geographic area, which limits the generalisability of the results. In addition, multi-centre efforts are needed in the future.

In summary, given the notable impact and implications of pain and dysfunction among patients with early-stage KOA, we hope this trial will provide more options for medical practitioners to control the course of KOA, and to address symptoms with as little burden as possible. Yijinjing exercise has showed potential clinical effect on the various dimensions of KOA which may improve patients' quality of life, help them get back to normal life,

and thus reduce the healthcare and economic burden on the society. This study can also provide evidence-based medicine evidence on the Yijinjing exercise treatment of KOA, which will contribute to the development of international expert consensus and play an important role in the treatment of the early-stage KOA through traditional Chinese physiotherapy.

Patient and public involvement

Before the recruitment phase, a subset of eligible KOA patients will be invited to investigate the feasibility of the study design and intervention. Their comments will then be used to make appropriate adjustments and to add health education components of interest to them. No patients or members of the public will be involved in the study design or any other parts of this protocol (including the recruitment as well as the statistical phase of the results).

Author affiliations
[1]Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, China
[2]School of Acupuncture-Moxibustion and Tuina, Shanghai University of Traditional Chinese Medicine, Shanghai, China
[3]Shuguang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, Shanghai, China
[4]School of Rehabilitation Science, Shanghai University of Traditional Chinese Medicine, Shanghai, China
[5]School of Basic Medical Sciences, Shanghai University of Traditional Chinese Medicine, Shanghai, China
[6]Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai, China

Acknowledgements Thanks to all the doctors of Shanghai Municipal Hospital of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine for their help in the trial design. Thanks to Rongqian Cao and Yuanhao Shen from School of Acupuncture-Moxibustion and Tuina, Shanghai University of Traditional Chinese Medicine for the demonstration of Yijinjing exercise movements and picture making. Thanks to Natchapol Opatprapai, William Lau, QUEK SUE PHIE, Adele Lim En Thong, Lye Heng Ze, Teh Yong Jia, Sebastian Chrisandy Anggaswara from Shanghai University of Traditional Chinese Medicine for the help in language simplification and grammar correction.

Contributors GG planned the study protocol and drafted the manuscript. GG, YHW, XX, KL, XZ, YG, GY, FY, and MF planned the study protocol and revised the manuscript. GG will carry out the Yijinjing exercise intervention of patients. YHW will be responsible for generating and distributing the random numbers. FY will carry out the health education of patients. XX will recruit and screen eligible participants in the outpatient department and the inpatient department. KL, XZ, YG, and GY will participate in designing the outcome measurements and assessing the outcomes. MF was the study coordinator and managed the study. All authors read and approved the final manuscript.

Funding This study is supported by Future Plan for Traditional Chinese Medicine development of Science and Technology of Shanghai Municipal Hospital of Traditional Chinese Medicine (WL-JXXK-2021001K); Future Plan for Traditional Chinese Medicine Inheritance and Development of Shanghai Municipal Hospital of Traditional Chinese Medicine (WLJH2021ZY-GZS007; WLJH2021ZY-ZYY011); National Natural Science Foundation of China (no. 82105042); Postdoctoral Science Foundation of China (no. 2021M692156); Shanghai Postdoctoral Excellence Programme (no. 2020371); 'Three Year Action Plan for Promoting Clinical Skills and Clinical Innovation in Municipal Hospitals' Training Programme for Innovative Translational Skills of Research Physicians of Shanghai Development Centre (SHDC2022CRT018). The funding sponsors had no role in the study design, analysis, collection, and interpretation of the data, or the writing and decision for publication.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Guangxin Guo http://orcid.org/0000-0002-2081-5229
Yihang Wang http://orcid.org/0009-0007-3254-2655
Xiruo Xu http://orcid.org/0000-0002-2532-3901
Kaiqiu Lu http://orcid.org/0009-0003-7618-2293
Xuanying Zhu http://orcid.org/0009-0001-0875-1306
Yijia Gu http://orcid.org/0009-0009-0476-727X
Guangpu Yang http://orcid.org/0009-0008-9609-625X
Min Fang http://orcid.org/0000-0001-6688-437X

REFERENCES

1 Safiri S, Kolahi A-A, Smith E, *et al*. Global, regional and national burden of osteoarthritis 1990-2017: a systematic analysis of the Global Burden of Disease Study 2017. *Ann Rheum Dis* 2020;79:819–28.
2 Culvenor AG, Øiestad BE, Hart HF, *et al*. Prevalence of knee osteoarthritis features on magnetic resonance imaging in asymptomatic uninjured adults: a systematic review and meta-analysis. *Br J Sports Med* 2019;53:1268–78.
3 Ackerman IN, Bucknill A, Page RS, *et al*. The substantial personal burden experienced by younger people with hip or knee osteoarthritis. *Osteoarthritis and Cartilage* 2015;23:1276–84.
4 Deshpande BR, Katz JN, Solomon DH, *et al*. Number of Persons With Symptomatic Knee Osteoarthritis in the US: Impact of Race and Ethnicity, Age, Sex, and Obesity. *Arthritis Care & Research* 2016;68:1743–50. 10.1002/acr.22897 Available: https://acrjournals.onlinelibrary.wiley.com/toc/21514658/68/12
5 Ackerman IN, Kemp JL, Crossley KM, *et al*. Hip and Knee Osteoarthritis Affects Younger People, Too. *J Orthop Sports Phys Ther* 2017;47:67–79.
6 Hunter DJ, March L, Chew M. Osteoarthritis in 2020 and beyond: a Lancet Commission. *Lancet* 2020;396:1711–2.
7 Jang S, Lee K, Ju JH. Recent Updates of Diagnosis, Pathophysiology, and Treatment on Osteoarthritis of the Knee. *Int J Mol Sci* 2021;22:22.
8 Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis. *JAMA* 2021;325:568.
9 Nevitt MC, Tolstykh I, Shakoor N, *et al*. Symptoms of Knee Instability as Risk Factors for Recurrent Falls. *Arthritis Care & Research* 2016;68:1089–97. 10.1002/acr.22811 Available: https://acrjournals.onlinelibrary.wiley.com/toc/21514658/68/8
10 Ren X, Lutter C, Kebbach M, *et al*. Compensatory Responses During Slip-Induced Perturbation in Patients With Knee Osteoarthritis Compared With Healthy Older Adults: An Increased Risk of Falls? *Front Bioeng Biotechnol* 2022;10:893840.
11 Mahmoudian A, Lohmander LS, Mobasheri A, *et al*. Early-stage symptomatic osteoarthritis of the knee - time for action. *Nat Rev Rheumatol* 2021;17:621–32.
12 Ogawa A, Iijima H, Takahashi M. Identification of Early Knee Osteoarthritis Based on Knee Joint Trajectory during Stair Climbing. *IJERPH* 2022;19:15023.
13 Zhang X, He B, Wang H, *et al*. Auricular acupressure for treating early stage of knee osteoarthritis: a randomized, sham-controlled prospective study. *QJM* 2022;115:525–9.
14 Wang Q, Runhaar J, Kloppenburg M, *et al*. Diagnosis for early stage knee osteoarthritis: probability stratification, internal and external validation; data from the CHECK and OAI cohorts. *Seminars in Arthritis and Rheumatism* 2022;55:152007.
15 Shimizu H, Shimoura K, Iijima H, *et al*. Functional manifestations of early knee osteoarthritis: a systematic review and meta-analysis. *Clin Rheumatol* 2022;41:2625–34.
16 Arden NK, Perry TA, Bannuru RR, *et al*. Non-surgical management of knee osteoarthritis: comparison of ESCEO and OARSI 2019 guidelines. *Nat Rev Rheumatol* 2021;17:59–66.

17 Li K, Yan G, Huang H, *et al*. Anti-inflammatory and immunomodulatory effects of the extracellular vesicles derived from human umbilical cord mesenchymal stem cells on osteoarthritis via M2 macrophages. *J Nanobiotechnol* 2022;20:38.
18 Bichsel D, Liechti FD, Schlapbach JM, *et al*. Cross-sectional Analysis of Recommendations for the Treatment of Hip and Knee Osteoarthritis in Clinical Guidelines. *Archives of Physical Medicine and Rehabilitation* 2022;103:559–569.
19 Bindu S, Mazumder S, Bandyopadhyay U. Non-steroidal anti-inflammatory drugs (NSAIDs) and organ damage: A current perspective. *Biochem Pharmacol* 2020;180:114147.
20 Bedard NA, Dowdle SB, Anthony CA, *et al*. The AAHKS Clinical Research Award: What Are the Costs of Knee Osteoarthritis in the Year Prior to Total Knee Arthroplasty? *J Arthroplasty* 2017;32:S8–10.
21 Bruyère O, Honvo G, Veronese N, *et al*. An updated algorithm recommendation for the management of knee osteoarthritis from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). *Seminars in Arthritis and Rheumatism* 2019;49:337–50.
22 Silverman SL, Schepman P, Rice JB, *et al*. Drug utilization, clinical and economic outcomes of patients with osteoarthritis of the hip and/or knee treated with long-term use of traditional NSAIDs, topical NSAIDs, and COX-2 inhibitors. *Curr Med Res Opin* 2022;38:1153–66.
23 Surgeons O, *et al*, Association TJSB, The Subspecialty Group Of Osteoarthritis CAO. Chinese guideline for diagnosis and treatment of osteoarthritis (2021 edition). *Chinese Journal of Orthopaedics* 2021;41:1291–314.
24 Brophy RH, Fillingham YA. AAOS Clinical Practice Guideline Summary: Management of Osteoarthritis of the Knee (Nonarthroplasty), Third Edition. *J Am Acad Orthop Surg* 2022;30:e721–9.
25 Li R, Chen H, Feng J, *et al*. Effectiveness of Traditional Chinese Exercise for Symptoms of Knee Osteoarthritis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *IJERPH* 2020;17:7873.
26 Xiao C, Zhuang Y, Kang Y. Effects of Wu Qin xi Qigong exercise on physical functioning in elderly people with knee osteoarthritis: A randomized controlled trial. *Geriatr Gerontol Int* 2020;20:899–903.
27 Ye J, Simpson MW, Liu Y, *et al*. The Effects of Baduanjin Qigong on Postural Stability, Proprioception, and Symptoms of Patients With Knee Osteoarthritis: A Randomized Controlled Trial. *Front Med (Lausanne)* 2019;6:307.
28 Zhang Y, Huang L, Su Y, *et al*. The Effects of Traditional Chinese Exercise in Treating Knee Osteoarthritis: A Systematic Review and Meta-Analysis. *PLoS ONE* 2017;12:e0170237.
29 Li ZR, Chen LY, Huang NY, *et al*. Based on finite element analysis to observe the clinical effect of Yijinjing excercise supporting day pile on cervical spondylosis. *Fujian Journal of Traditional Chinese Medicine* 2020;51:22–4.
30 Cheng Z, Chen Z, Xie F, *et al*. Efficacy of Yijinjing combined with Tuina for patients with non-specific chronic neck pain: study protocol for a randomized controlled trial. *Trials* 2021;22:586.
31 Cheng Z-J, Zhang S-P, Gu Y-J, *et al*. Effectiveness of Tuina Therapy Combined With Yijinjing Exercise in the Treatment of Nonspecific Chronic Neck Pain: A Randomized Clinical Trial. *JAMA Netw Open* 2022;5:e2246538.
32 Xu RX, Dou SD, Wu NQ. On the mechanism of Yijinjing excercise “supporting day pile” prevention and treatment of cervical spondylosis. *Chinese Manipulation and Rehabilitation Medicine* 2015;6:11–2.
33 Kong L, Ren J, Fang S, *et al*. Traditional Chinese Exercises on Pain and Disability in Middle-Aged and Elderly Patients With Neck Pain: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Front Aging Neurosci* 2022;14:912945.
34 Chen XQ, Pan HL. Clinical observation on improving back stiffness of patients with spinal arthralgia by moxibustion combined with Yijinjing excercise. *Hubei Journal of Traditional Chinese Medicine* 2018;40:42–4.
35 Zhang GD, Liang GQ, Hui RH. Acupuncture combined with muscle-bone strengthening exercise training on hemiplegia after stroke patients with motor function and psychological impact. *Journal of Changchun University of Chinese Medicine* 2016;32:967–9.
36 Chen C-H, Hung K-S, Chung Y-C, *et al*. Mind-body interactive qigong improves physical and mental aspects of quality of life in inpatients with stroke: A randomized control study. *Eur J Cardiovasc Nurs* 2019;18:658–66.
37 Cong HZ. Effect of yijinjing meridian on upper limbmotor function in convalescent stroke patients. *Heilongjiang University Of Chinese Medicine* 2022:60.
38 Zou L, Yeung A, Zeng N, *et al*. Effects of Mind-Body Exercises for Mood and Functional Capabilities in Patients with Stroke: An Analytical Review of Randomized Controlled Trials. *Int J Environ Res Public Health* 2018;15:15.
39 Fang L, Li ZR, Tao XC, *et al*. Effects of Yi Jin Jing on the risk of falling of sarcopenia and disequilibrium elderly. *Chinese Journal of Rehabilitation Medicine* 2020;35:319–23.
40 Zhu G, Shen Z, Shen Q, *et al*. Effect of Yi Jin Jing (Sinew-transforming Qigong Exercises) on skeletal muscle strength in the elderly. *J Acupunct Tuina Sci* 2017;15:434–9.
41 Ye YY, Niu XM, Qiu ZW, *et al*. Effect of Yijinjing on knee joint function in patients with knee osteoarthritis. *Rheumatism and Arthritis* 2019;8:19–23.
42 Zhang Y-P, Hu R-X, Han M, *et al*. Evidence Base of Clinical Studies on Qi Gong: A Bibliometric Analysis. *Complement Ther Med* 2020;50:102392.
43 Chen D, Zhao G, Fu J, *et al*. Effects of Traditional Chinese Exercise on Oxidative Stress in Middle-Aged and Older Adults: A Network Meta-Analysis. *IJERPH* 2022;19:8276.
44 Zhang S, Guo G, Li X, *et al*. The Effectiveness of Traditional Chinese Yijinjing Qigong Exercise for the Patients With Knee Osteoarthritis on the Pain, Dysfunction, and Mood Disorder: A Pilot Randomized Controlled Trial. *Front Med* 2021;8:792436.
45 Zhu Q, Huang L, Wu X, *et al*. Effects of Tai Ji Quan training on gait kinematics in older Chinese women with knee osteoarthritis: A randomized controlled trial. *J Sport Health Sci* 2016;5:297–303.
46 Iijima H, Eguchi R, Shimoura K, *et al*. Transcutaneous Electrical Nerve Stimulation Improves Stair Climbing Capacity in People with Knee Osteoarthritis. *Sci Rep* 2020;10:7294.
47 Iijima H, Shimoura K, Eguchi R, *et al*. Concurrent validity and measurement error of stair climb test in people with pre-radiographic to mild knee osteoarthritis. *Gait Posture* 2019;68:335–9.
48 Jia X, Wang Z, Huang F, *et al*. A comparison of the Mini-Mental State Examination (MMSE) with the Montreal Cognitive Assessment (MoCA) for mild cognitive impairment screening in Chinese middle-aged and older population: A cross-sectional study. *BMC Psychiatry* 2021;21:485.
49 俞越. Analysis of Exercise Prescription for Relieving Symptoms of Type 2 Diabetes Mellitus Patients with Health Qigong. *APS* 2021;09:286–92.
50 Hareendran A, Leidy NK, Monz BU, *et al*. Proposing a standardized method for evaluating patient report of the intensity of dyspnea during exercise testing in COPD. *Int J Chron Obstruct Pulmon Dis* 2012;7:345–55.
51 Oh S-L, Kim D-Y, Bae J-H, *et al*. Effects of rural community-based integrated exercise and health education programs on the mobility function of older adults with knee osteoarthritis. *Aging Clin Exp Res* 2021;33:3005–14.
52 Bell EC, Wallis JA, Goff AJ, *et al*. Does land-based exercise-therapy improve physical activity in people with knee osteoarthritis? A systematic review with meta-analyses. *Osteoarthritis and Cartilage* 2022;30:1420–33.
53 Symonds T, Hughes B, Liao S, *et al*. Validation of the Chinese Western Ontario and McMaster Universities Osteoarthritis Index in Patients From Mainland China With Osteoarthritis of the Knee. *Arthritis Care & Research* 2015;67:1553–60. 10.1002/acr.22631 Available: https://acrjournals.onlinelibrary.wiley.com/toc/21514658/67/11
54 Zeng Z-P, Liu Y-B, Fang J, *et al*. Effects of Baduanjin exercise for knee osteoarthritis: A systematic review and meta-analysis. *Complement Ther Med* 2020;48:102279.
55 Chang T-T, Zhu Y-C, Li Z, *et al*. Modulation in the Stiffness of Specific Muscles of the Quadriceps in Patients With Knee Osteoarthritis and Their Relationship With Functional Ability. *Front Bioeng Biotechnol* 2021;9:781672.
56 Bellamy N. WOMAC: a 20-year experiential review of a patient-centered self-reported health status questionnaire. *J Rheumatol* 2002;29:2473–6.
57 Reed MD, Van Nostran W. Assessing pain intensity with the visual analog scale: a plea for uniformity. *J Clin Pharmacol* 2014;54:241–4.
58 Faiz KW. VAS--visual analog scale. *Tidsskr Nor Laegeforen* 2014;134:323.
59 Kim T-H, Kim KH, Kang JW, *et al*. Moxibustion treatment for knee osteoarthritis: a multi-centre, non-blinded, randomised controlled trial on the effectiveness and safety of the moxibustion treatment versus usual care in knee osteoarthritis patients. *PLoS One* 2014;9:e101973.
60 Atalay SG, Durmus A, Gezginaslan Ö. The Effect of Acupuncture and Physiotherapy on Patients with Knee Osteoarthritis: A Randomized Controlled Study. *Pain Physician* 2021;24:E269–78.
61 Beck AT. An Inventory for Measuring Depression. *Arch Gen Psychiatry* 1961;4:561.

62 Sun XY, Li YX, Yu CQ, *et al*. Reliability and validity of depression scales of Chinese version: a systematic review. *Zhonghua Liu Xing Bing Xue Za Zhi* 2017;38:110–6.
63 Tavares DRB, Moça Trevisani VF, Frazao Okazaki JE, *et al*. Risk factors of pain, physical function, and health-related quality of life in elderly people with knee osteoarthritis: A cross-sectional study. *Heliyon* 2020;6:e05723.
64 Wang Z, Chen J, Boyd JE, *et al*. Psychometric Properties of the Chinese Version of the Perceived Stress Scale in Policewomen. *PLoS ONE* 2011;6:e28610.
65 Liu X, Zhao Y, Li J, *et al*. Factor Structure of the 10-Item Perceived Stress Scale and Measurement Invariance Across Genders Among Chinese Adolescents. *Front Psychol* 2020;11:537.
66 Cheung DST, Deng W, Tsao S-W, *et al*. Effect of A Qigong Intervention on Telomerase Activity and Mental Health in Chinese Women Survivors of Intimate Partner Violence: A Randomized Clinical Trial. *JAMA Netw Open* 2019;2:e186967.
67 Downs S, Marquez J, Chiarelli P. The Berg Balance Scale has high intra- and inter-rater reliability but absolute reliability varies across the scale: a systematic review. *J Physiother* 2013;59:93–9.
68 Meseguer-Henarejos A-B, Rubio-Aparicio M, López-Pina J-A, *et al*. Characteristics that affect score reliability in the Berg Balance Scale: a meta-analytic reliability generalization study. *Eur J Phys Rehabil Med* 2019;55:570–84.
69 Ornetti P, Maillefert J-F, Laroche D, *et al*. Gait analysis as a quantifiable outcome measure in hip or knee osteoarthritis: a systematic review. *Joint Bone Spine* 2010;77:421–5.
70 Kwon SB, Ro DH, Song MK, *et al*. Identifying key gait features associated with the radiological grade of knee osteoarthritis. *Osteoarthritis and Cartilage* 2019;27:1755–60.
71 Birmingham TB, Moyer R, Leitch K, *et al*. Changes in biomechanical risk factors for knee osteoarthritis and their association with 5-year clinically important improvement after limb realignment surgery. *Osteoarthritis and Cartilage* 2017;25:1999–2006.
72 Du M, Sun J, Liu Y, *et al*. Tibio-Femoral Contact Force Distribution of Knee Before and After Total Knee Arthroplasty: Combined Finite Element and Gait Analysis. *Orthop Surg* 2022;14:1836–45.
73 Sit RWS, Chan KKW, Yip BHK, *et al*. Clinical effectiveness of patella mobilisation therapy versus a waiting list control for knee osteoarthritis: a protocol for a pragmatic randomised clinical trial. *BMJ Open* 2018;8:e019103e019103.
74 Shi W, Kanamoto T, Aihara M, *et al*. Articular surface integrity assessed by ultrasound is associated with biological characteristics of articular cartilage in early-stage degeneration. *Sci Rep* 2022;12:11970.
75 Huo J, Ouyang X, Si L, *et al*. Automatic Grading Assessments for Knee MRI Cartilage Defects via Self-ensembling Semi-supervised Learning with Dual-Consistency. *Med Image Anal* 2022;80:S1361-8415(22)00155-4:102508.:.
76 Lewis E, Merghani K, Robertson I, *et al*. The effectiveness of leucocyte-poor platelet-rich plasma injections on symptomatic early osteoarthritis of the knee: the PEAK randomized controlled trial. *Bone Joint J* 2022;104-B:663–71.
77 Szwedowski D, Szczepanek J, Paczesny Ł, *et al*. The Effect of Platelet-Rich Plasma on the Intra-Articular Microenvironment in Knee Osteoarthritis. *Int J Mol Sci* 2021;22:5492:22.:.
78 Sharma L. Osteoarthritis of the Knee. *N Engl J Med* 2021;384:51–9.
79 Lim WB, Al-Dadah O. Conservative treatment of knee osteoarthritis: A review of the literature. *World J Orthop* 2022;13:212–29.
80 Tayfur B, Charuphongsa C, Morrissey D, *et al*. Neuromuscular joint function in knee osteoarthritis: A systematic review and meta-analysis. *Ann Phys Rehabil Med* 2023;66:S1877-0657(22)00035-5:101662.:.
81 Jurado-Castro JM, Muñoz-López M, Ledesma AS-T, *et al*. Effectiveness of Exercise in Patients with Overweight or Obesity Suffering from Knee Osteoarthritis: A Systematic Review and Meta-Analysis. *IJERPH* 2022;19:10510.
82 Bannuru RR, Osani MC, Vaysbrot EE, *et al*. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis and Cartilage* 2019;27:1578–89.
83 Zhu Q, Zhou X, Zhang S, *et al*. Joint Angles and Joint Moments of the Lower Limbs in Four Typical Tai Chi Movements: Consideration for Management of Knee Osteoarthritis. *Res Sports Med* 2021;29:586–92.
84 Zhu Q, Huang L, Wu X, *et al*. Effect of Taijiquan practice versus wellness education on knee proprioception in patients with knee osteoarthritis: a randomized controlled trial. *J Tradit Chin Med* 2017;37:774–81.
85 Wen Y-R, Shi J, Wang Y-F, *et al*. Are Mind-Body Exercise Beneficial for Treating Pain, Function, and Quality of Life in Middle-Aged and Old People With Chronic Pain? A Systematic Review and Meta-Analysis. *Front Aging Neurosci* 2022;14:921069.
86 Fan Y, Wu Y, Wang J, *et al*. Effect of Tuina exercise on quadriceps femoris muscle strength of patients with knee osteoarthritis. *J Acupunct Tuina Sci* 2012;10:321–8.
87 Guo X, Zhao P, Zhou X, *et al*. A recommended exercise program appropriate for patients with knee osteoarthritis: A systematic review and meta-analysis. *Front Physiol* 2022;13:934511.
88 Zhao YY, Fu YQ, Gang JH, *et al*. Clinical Study on YiJin Jing Exercises Combined with Articular Injection for Early-to-Mid Osteoarthritis. *New Chinese Medicine* 2020;52:72–5.
89 Ding J, Ju Z, Zhu Y, *et al*. Clinical observation on electroacupuncture plus Yi Jin Jing (Sinew-transforming Qigong Exercises) for knee osteoarthritis. *J Acupunct Tuina Sci* 2020;18:396–402.
90 Li YT, Ye YY, Niu XM, *et al*. Effects of Yi Jin Jing exercise on the coordination activation ability of lower limb muscles of knee osteoarthritis. *China Journal of Traditional Chinese Medicine and Pharmacy* 2022;37:2380–5.
91 Lv BS, Tai DX. Research Progress of Yijin jing in the Treatment of Orthopedic Diseases. *Journal of Practical Traditional Chinese Internal Medicine* 2022;36:94–6.
92 Landsmeer MLA, de Vos BC, van der Plas P, *et al*. Effect of weight change on progression of knee OA structural features assessed by MRI in overweight and obese women. *Osteoarthritis Cartilage* 2018;26:1666–74.
93 Martinez L, Noé N, Beldame J, *et al*. Quantitative gait analysis after total hip arthroplasty through A minimally invasive direct anterior approach: A case control study. *Orthop Traumatol Surg Res* 2022;108:103214.
94 Wang S, Hase K, Kita S, *et al*. Biomechanical effects of medial meniscus radial tears on the knee joint during gait: A concurrent finite element musculoskeletal framework investigation. *Front Bioeng Biotechnol* 2022;10:957435.
95 Mezghani N, Ouakrim Y, Fuentes A, *et al*. Knee osteoarthritis severity assessment using knee kinematic data classification. *Osteoarthritis and Cartilage* 2012;20:S97.
96 Lai Z, Lee S, Chen Y, *et al*. Comparison of whole-body vibration training and quadriceps strength training on physical function and neuromuscular function of individuals with knee osteoarthritis: A randomised clinical trial. *J Exerc Sci Fit* 2021;19:150–7.
97 Krishnamurthy A, Lang AE, Pangarkar S, *et al*. Synopsis of the 2020 US Department of Veterans Affairs/US Department of Defense Clinical Practice Guideline: The Non-Surgical Management of Hip and Knee Osteoarthritis. *Mayo Clin Proc* 2021;96:2435–47.