**Additional file 1.**


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

| Section/item | ItemNo | Description | Page no |
|---|---|---|---|
| **Administrative information** | | | |
| Title | 1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | Pg.1 Pg.22 |
| Trial registration | 2a | Trial identifier and registry name. If not yet registered, name of intended registry | Pg.3 |
| | 2b | All items from the World Health Organization Trial Registration Data Set | Not applicable. The manuscript does not contain any data |
| Protocol version | 3 | Date and version identifier | Pg.22 |
| Funding | 4 | Sources and types of financial, material, and other support | Pg.23 |
| Roles and responsibilities | 5a | Names, affiliations, and roles of protocol contributors | Pg.1,22 |
| | 5b | Name and contact information for the trial sponsor | Pg.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 | Pg.23 |
| | 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) | Pg.14 |

**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of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | Pg.3-5 |
| | 6b | Explanation for choice of comparators | Pg.3-5 |
| Objectives | 7 | Specific objectives or hypotheses | Pg.3-5 |
| 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) | Pg.3-5 |

**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 | Pg.6-7 |
| 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) | Pg.7-8 |
| Interventions | 11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | Pg.10-12 |
| | 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) | Pg.10 |
| | 11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) | Pg.10 |
| | 11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | Pg.10 |

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| 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 | Pg.12-13 |
| 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) | (Table 1) |
| 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 | Pg.8-9 |
| Recruitment | 15 | Strategies for achieving adequate participant enrolment to reach target sample size | Pg.7 |
| **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 | Pg.9 |
| 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 | Pg.9 |
| Implementation | 16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | Pg.9 |
| Blinding (masking) | 16a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | Pg.9 |

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| | 16b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | Pg.9 |
| **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 | Pg.13-14 |
| | 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 | Pg.13-14 |
| 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 | Pg.14 |
| 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 | Pg.14-16 |
| | 20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | Pg.14-16 |
| | 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) | Pg.14-16 |
| **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 | Pg.14 |

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| | 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 | Pg.14 |
| 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 | Pg.10 |
| Auditing | 23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | Pg.10 |
| **Ethics and dissemination** | | | |
| Research ethics approval | 24 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval | Pg.3 |
| 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) | N/A, All relevant trial plans have been determined before the trial |
| Consent or assent | 26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | Pg.6 |
| | 26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | N/A, no ancillary studies in this trial |
| 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 | Pg.14 |
| Declaration of interests | 28 | Financial and other competing interests for principal investigators for the overall trial and each study site | Pg.23 |
| 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 | Pg.14 |

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| 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 | Pg.11 |
| 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 | N/A, The protocol has not yet obtained data, if the data is obtained in the future, it will be published in the form of articles |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers | N/A, all works and articles will be completed by the research team members |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | Pg.16 |
| **Appendices** | | | |
| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates | Pg.6 Additional file 2) |
| 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 | N/A, no biological specimens were collected as part of this trial |

*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. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license. Reproduced from SPIRIT. SPIRIT Statement, Publications and Downloads. Available from: https://www.spirit-statement.org/publications-downloads/.[55]

**Additional file 2.**

# Informed consent

Dear patient:

Having confirmed that you have knee osteoarthritis, we invite you to participate in "Effect of acupuncture on the cognitive control network of patients with knee osteoarthritis: a randomized controlled trial".Please read the following as carefully as possible before you decide whether to participate in this study.It can help you understand the study and why it was conducted, the procedures and duration of the study, the benefits, risks and discomfort it may have given you after participating in the study.

## I、 Study setting and purpose

Knee osteoarthritis (knee osteoarthritis,KOA) is a common chronic joint disease characterized by degeneration, destruction, and hyperostosis of knee cartilage, and studies have shown a prevalence of KOA of approximately 6% - 13% in men and 7% - 19% in women over the age of 45 years, with females at a higher risk than males45%, chronic pain is the most common clinical symptom of knee osteoarthritis, which seriously affects the health of the middle-aged and old people, and managing chronic pain and preventing its recurrent attacks is of great clinical importance for the prevention and treatment of this disease.

Acupuncture treatment of knee pain has a long history and significant efficacy, and persistent effects are also an important feature of acupuncture analgesia, and clinical studies have also confirmed that acupuncture treatment of KOA has exact efficacy, can significantly improve patients' symptoms such as pain, unfavorable activity, stiffness, swelling, and improve patients' anxiety and depression status. However, the central mechanism of acupuncture in treating patients with KOA is not clear, which prevents its clinical application and further promotion. Therefore, we will analyze the efficacy of verum acupuncture, sham acupuncture and the waiting-list for knee osteoarthritis and explore the activity of the cognitive control network in three groups of patients by fMRI, so as to reveal the central mechanism of acupuncture in the treatment of knee osteoarthritis.

**This trial will be conducted from October 2020 to December 2022,** and we will enroll 108 subjects.

## II、 Who should not be included in the study

Those with unclear consciousness and inability to express subjective malaise symptoms and those with psychosis;

Progressive malignancy or other severe wasting disease, those with predisposition to co infection and bleeding;

Those with severe primary disease involving the cardiovascular, hepatic, renal, digestive, and hematopoietic systems;

For pregnant, lactating women and those with an intention to conceive in the previous trimester;

Patients who were participating in other clinical trials;

Researchers considered other reasons unsuitable for clinical trialists.

## III、 What will need to be done if enrolled in the study?

1. If you are screening patients with KOA who meet the inclusion criteria, the study will be conducted as follows:

Your doctor will first decide what needle therapy and scanning you receive, based on the random numbers provided by your computer. You will have 1/3 chance to be assigned to 3 different groups for verum acupuncture, sham acupuncture and the waiting-list treatment.

Your medical doctor will rate your clinical symptoms and emotional condition, and please faithfully reflect the change in your condition to your doctor.

2. Other things that you need to cooperate with

You cannot use any medications that improve your pain symptoms and mood conditions during the study.If you do need other treatment, contact your doctor beforehand.

**IV、 Possible benefits of participating in the study**

If you complete the trial as planned, you will be offered free health counseling by the project team in the next 6 months. Sham acupuncture group and waiting-list group at the end of the study, we provide subjects in this group with 20 days of verum acupuncture along with heartfelt thanks to you for your participation in this project study.

Although there is already evidence suggesting a therapeutic effect of the acupuncture regimen employed in this study on KOA, this is not a guarantee that it will definitely be effective for you.The methodology employed in this study is also not the only method for KOA treatment.You can ask your doctor about alternative treatments that may be available.

**V、 Possible adverse effects, risks and discomfort during participation in the study inconvenient**

Fainting, pin site pain, bleeding, hematoma, or infection may occur during the needle procedure.When an adverse event occurs, whether or not it is related to this study treatment, your doctor should be promptly notified, to which he / she will exercise judgment and give appropriate medical attention.At the same time, the investigator will take a detailed record, including: the occurrence time, discontinuation time and duration (can be recorded in days or H), the severity and frequency, the treatment method and outcome, the analysis of the causal relationship between the adverse event and the test treatment method, the tracking of the adverse event and the serious adverse event, and so on.All clinical data regarding adverse events such as inspection offprints, prescriptions, etc. should be kept in the original files.

**VI、 There is a voluntary option to participate in the study and withdraw from the study halfway**

Whether to participate in the study depends entirely on your will.You may decline to participate in this study, or withdraw from this study at any time during the course of the study, which does not affect your and inter physician relationships, nor the loss of benefit to your medical treatment or otherwise.

In your best interest consideration, your doctor or investigator may discontinue your continued participation in this study at any time during the course of the study.

**VII、 What should be done now?**

Whether to participate in this study was decided by yourself (and your family).

Thank you for reading the above material.If you decide to participate in this study, please let your doctor know that he / she will schedule everything for you regarding the study.

# Informed consent signature page

**Clinical research project name:**Effect of acupuncture on the cognitive control network of patients with knee osteoarthritis: a randomized controlled trial

**Subject acceptance unit:** the First Affiliated Hospital of Henan University of traditional Chinese Medicine

**Consent statement**

I have read the above introduction to this study and have had the opportunity to talk to and raise questions with physicians about this study.All questions I asked were answered satisfactorily.

I know of the possible risks and benefits of participating in this study.I know that participation in the study is voluntary and I confirm that there has been ample time to consider this, and understand:

I can always ask my doctor for more information.

I can withdraw from this study at any time without discrimination or reprisal, and medical treatment and equity will not be affected.

I am equally clear that if I withdraw from the study halfway, I would be a great advantage to the whole study if I tell the doctor about the changes in my condition and complete the corresponding physical examination and physicochemical examination.

If I need to take any other medication because of the change in condition, I will ask the doctor in advance or truthfully tell the doctor in hindsight.

I agree with the health administration, the ethics committee, or the sponsor to consult my research materials on behalf of the sponsor.

I will be given a signed and dated copy of informed consent.

Finally, I decided to agree to participate in this study and guaranteed to comply with medical advice as much as possible.

**Patient signatures:_____Date：_**

**Contact number: _____**

I confirm that details of this trial, including its power and possible benefits and risks, have been explained to patients and give them a signed copy of their informed consent.

**Patient signatures:_____Date：_**

**Contact number**: **_____**

Ethics Committee of the First Affiliated Hospital of Henan University of traditional Chinese medicine Telephone number: 0371-66285929