Supplemental Materials:

Contents

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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	9
	2b	All items from the World Health Organization Trial Registration Data Set	9
Protocol version	3	Date and version identifier	19
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	21
	5b	Name and contact information for the trial sponsor	NA
	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	22

	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)	16-17
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of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	6-7
	6b	Explanation for choice of comparators	8
Objectives	7	Specific objectives or hypotheses	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
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)	10
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, 15
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
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	14-15
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)	12, 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	17-18
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	16
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	16
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	16
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	16
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	16
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	15

	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	N/A
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	15
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	18-19
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	19
	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)	18
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	16

	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	16
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	16
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	20
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)	20
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
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	19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	22

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	17
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	N/A
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	20
	31b	Authorship eligibility guidelines and any intended use of professional writers	20
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplementary material III
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

*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.

List of Sites in the Trial

No.	Site
1	West China Hospital of Sichuan University
2	The Second Hospital of Jilin University
3	The Second Affiliated Hospital of Heilongjiang University of Chinese Medicine
4	General Hospital of Ningxia Medical University
5	Shanghai General Hospital
6	Zhongnan Hospital of Wuhan University
7	The First Affiliated Hospital of Xinjiang Medical University
8	Qinghai University Affiliated Hospital
9	The First Hospital of Longquanyi District of Chengdu
10	Mianzhu people's Hospital
11	Ya’an people's Hospital
12	Ganzi People's Hospital
13	Yibin City No. 2 People's Hospital
14	Mianyang Central Hospital
15	Nanjiang people's Hospital
16	Dechang people's Hospital
17	The First Affiliated Hospital of Zhengzhou University

Version：V3.0 Date：29th, April 2021

Patient Consent Form

Dear participant:

You are invited into the “Pulsed Electromagnetic Fields for the Management of Knee Osteoarthritis: Multicentre, Randomised, Controlled, Non-inferiority Trial” which has been approved by the ethics committee on biomedical research of West China Hospital of Sichuan University (#2021-220).

1. Why do we carry out this study?

Knee osteoarthritis (KOA) is the most common cause of pain and disability. Pulsed electromagnetic fields (PEMFs) is an available treatment. Nonetheless, the clinical effects are consistent. Thus, this study aims to determine the effect of PEMFs with specific parameters on pain relief and function improvement by comparing them with the positive control (celecoxib).

2. What do you need to do if you agree to participate in this study?

You will be randomly assigned to the PEMFs or usual care group. Patients in the PEMFs group will receive a 6-week PEMFs therapy, and these in the drug group will receive a 6-week Celebrex treatment. You will be required to complete the visit by telephone at baseline (before randomization), and at weeks 1, 3, 6, 10, 18, and 30 after enrolment.

3. These individuals are not suitable for participating in this trial, who:

a) be diagnosed with fibromyalgia or other arthritis, like rheumatoid arthritis or inflammatory arthritis.

b) have a history of knee surgery or intra-articular injection in the past 6 months.

c) have treatments of steroids, methotrexate, or azathioprine.

d) previously used PEMFs in treating similar symptoms.

e) received any analgesics during one-week preceding inclusion.

f) be with any unstable medical or psychiatric illness.

4. What are the potential risks and possible adverse events of participating in the study?

Potential risks: The treatment options may not alleviate your existing symptoms due to personal emotions, anxiety, and other risk factors, and may aggravate the anxiety symptoms or fear of the disease although they are based on evidence-based medical guidelines and previous research evidence.

Adverse events:

- ✧ Skin allergy symptoms due to personal constitution reasons or using the patch.
- ✧ Gastrointestinal discomfort due to taking pain relief drugs.

Risk prevention and disposal: Researchers and medical workers have medical qualifications and complete the standardized training. During this process, patients will be free of charge and will receive appropriate examination and treatment at belonging site if suffered adverse events.

5. What are benefits you can take from the study?

- ✧ Free visit and treatment.
- ✧ Improvement in symptoms.
- ✧ Reduction dependence on drugs and avoid side effects caused by medicine.

6. Are there any fees need to pay during the study?

Participant in this study is completely free of charge, and patients can receive a transportation subsidy of up to ¥400 with the ticket.

7. Is personal information confidential?

Your research data will be kept in the West China Hospital of Sichuan University, and your medical records will be accessible to researchers, research authorities, and ethics review committees. Any public reports on the findings of this study will not disclose your personal identity.

8. Must I participate in a study?

Participation in this study is completely voluntary, and you may refuse to participate in the study or withdraw from this study at any stage of the trial without discrimination or retaliation, and your medical treatment and rights will not be affected. If you decide to withdraw from this study, please contact your doctor for proper diagnosis and treatment of the disease.

Patient Statement:

I have read the above presentation on this study, and my researchers have fully explained to me the purpose of this study, its operational process, and the possible risks and potential benefits of participating in this study and answered all my relevant questions.

I understand the purpose of this study and I am free to withdraw at any time without medical cares or legal rights being affected. I am voluntary to participate in this study.

I understand that results of my visits may be shared with the research team of West China Hospital of Sichuan University.

I agree to allow any information provided to be medical research upon the understanding that my identity will remain anonymous wherever possible.

Please indicate your wishes in the below scenarios:		
Please tick or initial yes or no:	Please tick ✓ or initial	
	YES	NO
I agree for my details to be shared and used in further research that be running by West China Hospital of Sichuan University	☐	☐

Patient (to be completed by the patient):

Signature: _____

Name (block letters): _____

Date: _____

Phone: _____

Legal representative (block letters, if applicable): _____

Relationship with patient: _____

Witness (block letters, if applicable): _____

Date: _____

Investigator Statement:

I have explained the request to the above-named patient, particularly, the ethical principles, risks, benefits, free, voluntariness and confidentiality that may arise from participating in this study. And he/she has indicated his/her willingness for participating in this study.

Signature: _____

Name (block letters):_____

Date:_____

Ethics Committee on Biomedical Research,

West China Hospital of Sichuan University

Tel: 028-85422654，028-85423237

(1 copy for patient; 1 held in patient notes, original stored in Investigator Site File)