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Whole-body photobiomodulation therapy for chronic pain: a protocol for a feasibility trial

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ABSTRACT

Introduction Chronic pain conditions are a leading cause of disease and disability. They are associated with symptoms such as fatigue, sleep and mood disturbances. Minimal evidence is available to support effective treatments and alternatives treatment approaches are called for. Photobiomodulation therapy has been highlighted as one promising option. A whole-body therapy device (NovoTHOR) has recently been developed with a number of potential advantages for people with chronic pain. Research is needed to consider the feasibility of this device.

Methods and analysis A single-centre single-armed (no placebo group) feasibility study with an embedded qualitative component will be conducted. The intervention will comprise 18 treatments over 6 weeks, with 6-month follow-up, in the whole-body photobiomodulation device. A non-probability sample of 20 adult participants with a clinician diagnosis of chronic axial pain, polyarthralgia, myofascial pain or widespread pain will be recruited (self-referral and clinician referral). Outcome measures will focus on acceptability of trial processes with a view to guiding a definitive randomised controlled trial. Analyses will use descriptive statistics for quantitative aspects. The qualitative element will be assessed by means of a participant-reported experience questionnaire postintervention and semistructured audio-recorded interviews at three stages; preintervention, midintervention and postintervention. The latter will be transcribed verbatim and a reflexive thematic analysis will be used to identify emerging themes. Exploratory outcomes (participant-reported and performance-based measures) will be analysed according to data distribution.

Ethics and dissemination The study has received ethical approval from the Leicester Central Research and Ethics Committee. Findings will be disseminated via local chronic pain groups, public register update, submission for presentation at scientific meetings and open-access peer-reviewed journals, and via academic social networks.

Trial registration number NCT05069363.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first study investigating this novel therapy in this population.
⇒ Methods utilised are rigorous and informed with patient and public involvement.
⇒ This is a feasibility trial focusing on acceptability of trial intervention and processes.
⇒ A small sample size will be selected to identify important parameter estimates.
⇒ A single arm trial is proposed and does not include an active or inactive control group such as a placebo intervention for comparison.

INTRODUCTION

The International Association for the Study of Pain define pain as 'an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage'.[1] When pain becomes chronic it is persistent or recurrent, lasting longer than 3 months.[2] It is a multidimensional phenomenon and prognosis is heavily influenced by a diverse array of psychosocial variables including distress levels, coping mechanisms and contextual factors.[3] According to the 11th edition of *International Classification of Diseases* classification, there are two broad groups: (1) 'chronic primary pain' which includes conditions such as non-specific low back pain and fibromyalgia (FM), that is, those conditions where the cause is not known; and (2) 'chronic secondary pain' which encompasses cancer-related pain, neuropathic pain, visceral pain, post-traumatic and postsurgical pain, headache and orofacial pain, and musculoskeletal pain. This revised taxonomy allows for recognition of chronic pain as a health condition in its own right.[4]

Chronic pain carries with it a profound impact on both individuals and society. Internationally, it is the leading cause of disability and disease burden.[5 6] Research suggests a mean prevalence of 30% globally,[7] with estimates of 13%–50% in the UK.[5] Across Europe, chronic pain incurs a cost of €200 billion per annum.[7]

There is no known effective treatment for chronic primary pain conditions like FM, likely owing to their complex nature.[8] It is

commonplace for affected individuals to try a multitude of therapies, often accompanied with side effects despite evidence of limited benefit.[9 10] The most recent National Institute for Health and Care Excellence (NICE) guidance regarding chronic pain management advises against use of the many commonly instituted pain medications.[11] The paucity of strong recommendations in international guidelines[12–14] highlights a need for exploring other therapeutic methods and modalities. NICE has called for further treatment options to be made available to these patients,[15] and have identified photobiomodulation (PBM) therapy as demonstrating positive effects on pain and quality of life, describing it to be a promising therapy and recommending further research in the area.[12]

PBM is a safe and non-invasive low energy light (red and near infrared) therapy that is absorbed by endogenous chromophores to induce cellular changes.[16–18] Focused PBM has demonstrated positive results when treating a multitude of acute and chronic pain conditions.[19–32] The therapy has received recent recognition from national and international healthcare governing bodies in treatment of cancer-related painful oral mucositis.[16] It is traditionally delivered by a trained therapist using a small probe applied to specific painful areas; as such, sessions can take up to 90 min in widespread pain conditions such as FM. Recent studies have called for larger probes and stipulated that novel delivery devices would be advantageous.[19 33]

The development of whole-body devices has allowed participants themselves to operate the device. For example, the NovoTHOR (figure 1) device delivers the treatment to the whole-body in 20 min or less and requiring no specialist skills to deliver the treatment, appearing less labour intensive and time-consuming. Whole-body PBM therapy is a novel mode of treatment with the potential to address multiple aetiological mechanisms in patients experiencing chronic and diffuse pain. Co-existing features commonly include cognitive and emotional impairment and evidence is emerging that PBM therapy can aid in the treatment of these ailments.[34]

We will explore the use of whole-body PBM therapy as a treatment option for chronic widespread pain. To the best of our knowledge, this is the first study using this device in this population. We suggest commencing with a feasibility study to assess acceptability of the therapy and study procedures in our population, with a view to designing a definitive RCT. We want to see if there is a potential to reduce pain and pain-related comorbidities by treating the whole body, rather than localised PBM therapy.

AIM AND OBJECTIVES

Aim

To undertake a feasibility study of whole-body PBM in the management of chronic pain.

Objectives

To determine study procedures with a view to guiding a definitive randomised controlled trial (RCT), specifically:

1. To determine whether eligibility criteria is either too open or too restrictive by estimating eligibility and recruitment rates.
2. To investigate acceptability of the trial device and treatment schedule (including perceptions, values and opinions).
3. To assess the acceptability of outcome measures, including user-friendliness of questionnaires.
4. To investigate the feasibility (and factors influencing this) of the outcome measures as methods to measure efficacy of the interventions within a definitive trial.
5. To assess refusal rates and barriers to uptake.
6. To assess trial retention rates including completion of therapy (6 weeks) and trial follow-up (6 months).
7. To assess potential effectiveness of whole-body PBM therapy using a combination of patient-reported and

Figure 1 NovoTHOR. Reprinted with permission.

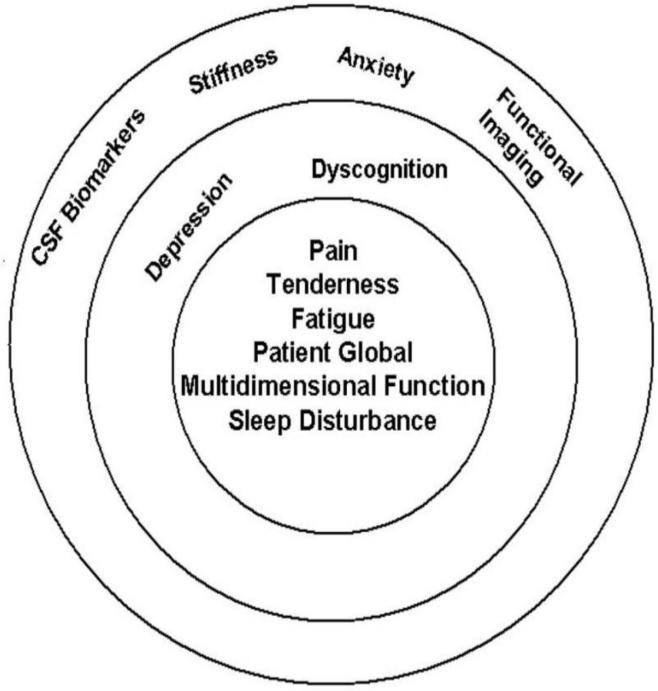

Figure 2 OMERACT hierarchy of domains. Reprinted with permission. The innermost circle contains the core set of domains to be assessed in all clinical trials of FM. The second concentric circle includes the outer core set of domains to be assessed in some but not all FM trials. The outermost circle includes the domains on the research agenda that may or may not be included in FM trials.[35] FM, fibromyalgia.

performance-based outcomes printervention and postintervention.

1. To measure the six core domains (figure 2) set out by OMERACT Working Group for FM,[35] as an example of a chronic pain condition.
2. To assess four of the 'peripheral' OMERACT domains.

8. To synthesise data to inform the sample size of a definitive trial.
9. To assess participants' perceptions and experience:
   1. Regarding their condition.
   2. Regarding the trial device and processes.
   3. Regarding future randomisation, blinding and placebo therapy.

METHODS AND ANALYSIS

The following is laid out in accordance with the Consolidated Standards of Reporting Trials (CONSORT) extension to pilot and feasibility trials guidance.[36]

Trial design

A feasibility study designed as a single-centre and single-armed trial with embedded qualitative component. The following trial procedures are reported in accordance with SPIRIT-PRO extension.[37]

Trial setting

This study will be conducted at Sandwell and West Birmingham (SWB) NHS Trust, West Midlands. The NovoTHOR PBM therapy device will be installed in a designated space at the Clinical Research Facility, Sandwell General Hospital.

Recruitment

Potentially eligible participants will be recruited from two sources:

1. Self-referral/registration of interest of SWB-registered patients to a designated research telephone and email. This will be possible via a trial recruitment poster that will be displayed in pain and rheumatology clinic areas and pain procedures areas.
2. SWB-registered patients identified in pain clinics and procedure lists by the patient's usual pain doctor who is not involved in the research trial.

Trust interpreters and 'Language Line' will be utilised to ensure a representative sample of non-English speaking participants are recruited. Participant Information Sheets (PIS) will be translated into the five most commonly spoken languages at the Trust; Punjabi, Urdu, Polish, Romanian and Bengali.

Eligibility criteria

The following criteria are in keeping with several other studies looking at PBM therapy in chronic pain.[38–42]

Inclusion criteria

1. Currently diagnosed or receiving treatment for a widespread chronic pain condition, including but not limited to:
   1. Axial pain of any origin
   2. Polyathralgia of any origin
   3. Myofascial pain of any origin
   4. A diagnosis of chronic widespread pain or FM
2. Able to provide informed written consent
3. ≥18 years
4. Able to commit time to the trial treatment schedule of 6 weeks
5. Score as low or moderate risk on the COVID-19 risk stratification tool— *applicable for the duration of the pandemic.*

Exclusion criteria

1. Pregnancy
2. Severe skin diseases (eg, skin cancer, severe eczema, dermatitis or psoriasis)
3. Body weight≥136 kg, as per manufacturer instructions.
4. Uncontrolled comorbidities (eg, uncontrolled diabetes defined as HbA1c>69 mmol/mol, decompensated heart failure, major psychiatric disturbance such as acute psychosis or suicidal ideation).
5. Use of systemic corticosteroid therapy including oral prednisolone or corticosteroid injections within the preceding 6 months as recommended by the manufacturer; steroids are thought to inhibit the anti-inflammatory effect of PBM therapy.[43]

Table 1 Template for intervention description and replication checklist

Brief name	► Whole body photobiomodulation therapy—18 sessions
Why	► Eighteen sessions is the currently recommended and widely instituted and accepted practice with the NovoTHOR device. ► This device was developed in 2013, and since then 251 NovoTHOR systems have been developed of which 217 systems are still in regular use, treating at least 4 patients per device per day. This equates to approximately 1.6 million treatments since its inception. No significant adverse events have been reported to date.
What	► All participants entering the trial will receive a course of whole-body PBM therapy. ► The NovoTHOR Whole-Body PBM therapy device consists of a hinged, clamshell design with light-emitting diodes (LEDs) arranged to emit near-infrared and visible red light → PBM light therapy is delivered to the entire body at once. ► A Participant Information Sheet will be provided at least 48 hours before participants are requested to consent to the study. They will be given the opportunity to undertake an experience session. ► Participants will be expected to lie horizontal in the device with the lid as closed as they are comfortable with.
Who provided	► All trial investigators, following a short training session in the use of NovoTHOR.
How	► The LED equipment delivers red and near infrared light therapy to the participant (as per the settings illustrated in table 2).
Where	► Clinical Research Facility, SWB Trust. ► Participants are registered at the Trust and are therefore geographically within the region. ► The device requires a well-ventilated, spacious, temperature-controlled room, with appropriate mains electricity.
When and how much	► Session 1=6 min. ► Session 2=12 min. ► Sessions 3–18=20 min. ► Timescale: 3 treatments/week for 6 weeks. ► The dosage of LED light (also known as 'fluence') will be equivalent to 25 J/cm^2. The device will supply a dual wavelength of red and near-infrared light with a 50:50 ratio; 660 nm and 850 nm, respectively.
Tailoring	► After liaison with experienced clinicians within the field with experience dealing with our population in the NovoTHOR, we decided to slowly uptitrate the treatment times during the first three treatments for all participants.
Modifications	► This will be described at the end of the trial.
How well	► This will be described at the end of the trial.

PBM, photobiomodulation; SWB, Sandwell and West Birmingham.

6. Known active malignancy
7. Inability to enter the NovoTHOR device or lie flat for 20 min (either due to physical reasons or other for example, claustrophobia).
8. Patients speaking a language for which an interpreter cannot be sought (namely Oromo, Tigranian, Amharic and Greek. Interpreters for all other languages at the Sponsor Trust can be sought)

Intervention

In order that the intervention can be replicated when building on future research, we have utilised the template for intervention description and replication checklist[44] (table 1). NovoTHOR dosage parameters are exhibited in table 2.

Study duration

We envisage the recruitment period should take approximately 3–6 months. Follow-up data will be collected at 6 months. This study schedule is depicted in table 3 and figure 3, including an overview of events at each study visit—in keeping with SPIRIT-PRO (SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials) Extension guidance.[37]

Sample size

The trial will continue until 20 participants are recruited and complete 6 weeks of whole-body PBM therapy. CONSORT guidelines for feasibility studies require a

Table 2 NovoTHOR parameters

NovoTHOR XL parameters		Unit
Wavelengths of red and near-infrared LEDs 50:50 ratio	660 850	nm nm
Number of LEDs	2400	
Power emitted per LED	0.289	W
Beam area per LED (at the lens/skin contact surface)	12.0	cm^2
Total power emitted	694	W
Total area of NovoTHOR emitting surfaces	26 740	cm^2
Treatment time	1200	s
Continuous wave (not pulsed)	CW	
Irradiance	0.028	W/cm^2
Fluence	33.6	J/cm^2

LEDs, light-emitting diodes.

Table 3 Outline of study flow

Procedures	Telephone call	Baseline visit	First visit	Visit 2–visit 17	Final visit	6-month telephone Follow-up
Eligibility	x					
Assessment						
Informed consent		x				
Blood tests						
Full blood count						
Urea and electrolytes						
Liver function tests		x				
HbA1c (if diabetic)						
Demographics						
Age						
Gender						
Marital status						
Employment status						
Educational level		x				
Ethnicity						
Medical history						
Duration of chronic pain symptoms						
Comorbidities						
Medications		x				x
Measurements						
Height						
Weight		x			x	
BMI						
Blood pressure						
Heart rate						
Oxygen saturations						
Participant-reported outcome measures*						
Brief pain inventory		x			x	
Widespread pain index/ symptom		x			x	
Severity score						
Fatigue severity scale		x			x	
Jenkins sleep questionnaire		x			x	
Patient global impression of change					x	x
Revised fibromyalgia impact questionnaire		x			x	x
Hospital anxiety and depression scale		x			x	
Performance-based outcome measures†						
Tender point count						
Stroop test		x			x	
Treatment			x	x	x	
Weekly Numerical Rating Scale (NRS)—applicable for preceding week				x	x	
Participant-reported experience measure (online supplemental file 1)					x	
Audio-recorded qualitative interviews (online supplemental file 2 for topic guide)			x	x	x	

*Please see table 4 for more detail.
†Please see table 5 for more detail.
BMI, body mass index.

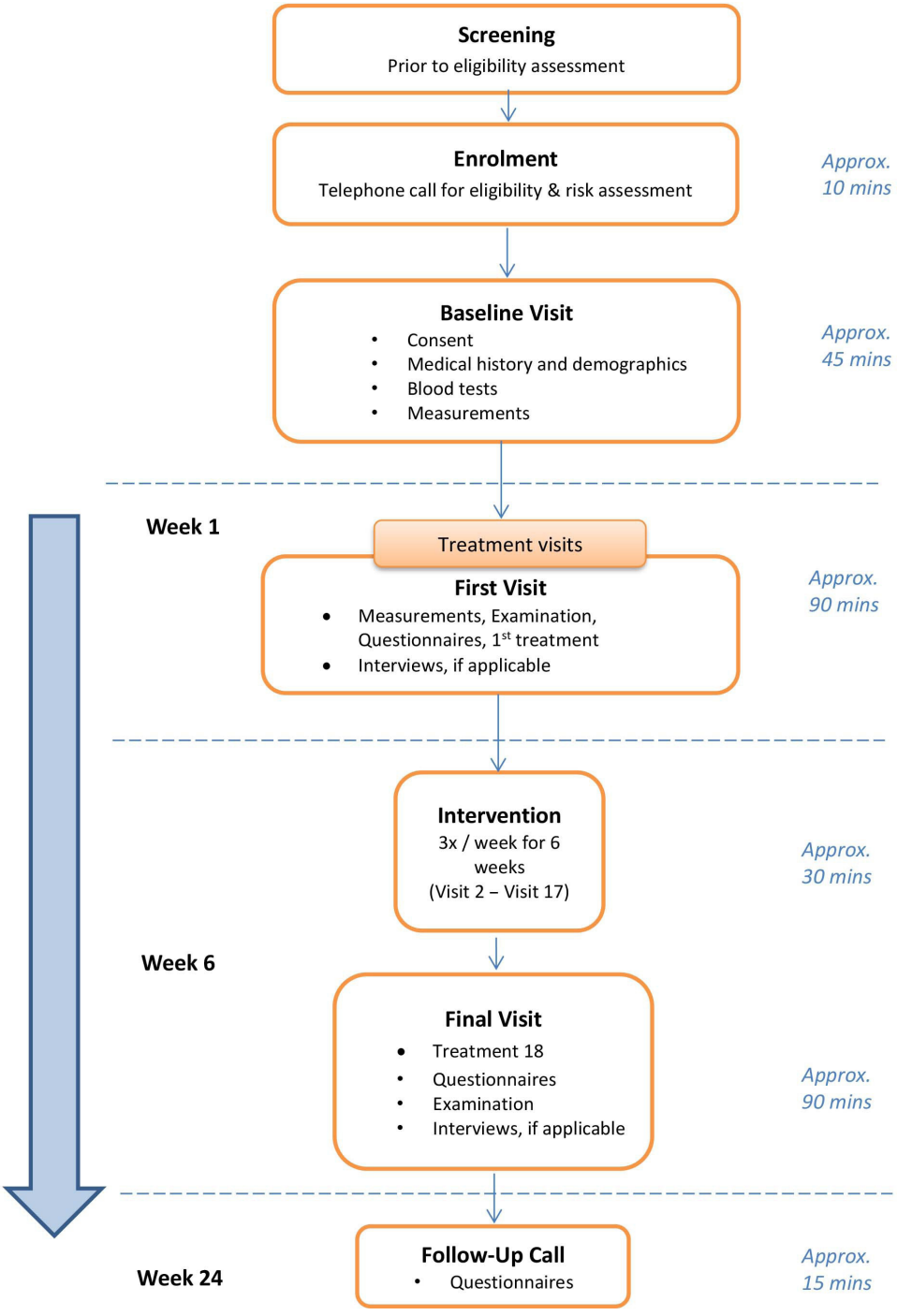

Figure 3 CONSORT study flow diagram. CONSORT, Consolidated Standards of Reporting Trials.

primary evaluation that focuses on descriptive analysis of feasibility/process outcomes (eg, recruitment, adherence and treatment fidelity).[36] In order to gauge our sample size, we took data from a 2019 meta-analysis on focused PBM therapy in fibromyalgia,[45] as best proxy of the widespread chronic pain and included all of the symptoms under observation in this study. Our chosen sample size takes into account the study population's number of visits at our clinics, objectives of the study and recommendations for the sample size calculations in pilot and feasibility trials by Moore *et al*[46] Lancaster and Thabane,[47] Lewis *et al*[48] as well as the 'rules of thumb' for feasibility trials as set out by Kieser and Wassmer.[49]

Sample size for the qualitative component will be guided by the concept of information power.[50] Information power uses specific principles which will guide numbers including the sample specificity, the aim of the study, the use of established theory, quality of dialogue and analysis strategy. We will seek to establish data saturation of themes.[51] Considering past research[52] looking at experiences of an intervention, we will attempt to interview all participants.

Table 4 Patient-reported outcome measures

OMERACT domain	Assessment tool	Brief tool description (taken into account when considering participant burden)
Core domains		
Pain	Brief Pain Inventory Short Form (BPI-SF)	Time to complete: 3 min Number of administrations: 2 (first visit, final visit) Description: 12×11-point NRS
	Widespread Pain Index (WPI) and Symptom Severity Score (SSS)	Time to complete: 4 min Number of administrations: 2 (first visit, final visit) Description: required to tick pain sites (0–19); three questions on symptom severity, 0=no problem, 3=severe; three questions on other symptoms, 0=no problem, 1=problem
Fatigue	Fatigue Severity Scale (FSS)	Time to complete: 1.5 min Number of administrations: 2 (first visit, final visit) Description: 9×7-point Likert scale; 1=strongly disagree, 7=strongly agree
Sleep disturbance	Jenkins Sleep Questionnaire (JSQ)	Time to complete: 1 min Number of administrations: 2 (first visit, final visit) Description: 4×6-point questions; 0=not at all, 5=22–28 days
Patient Global	Patient Global Impression of Change (PGIC)	Time to complete: 1 min Number of administrations: 2 (final visit, follow-up telephone call) Description: 2 questions; first: change post-treatment, 0=no change, 7=considerable improvement. Second: 11-point NRS, 0=much better, 10=much worse.
Multidimensional function	Revised Fibromyalgia Impact Questionnaire (FIQR)*	Time to complete: 3.5 min Number of administrations: 3 (first visit, final visit, follow-up telephone call) Description: 21×11—point numerical rating scale (NRS); 0=no difficulty, 10=very difficult; total maximal score=100
Peripheral domains		
Anxiety	HADS-A *Subsection of Hospital Anxiety and Depression Scale assessment*	Time to complete: 1 min Number of administrations: 2 (first visit, final visit) Description: 7×4-point questions, 'not at all' → 'most of the time'
Depression	HADS-D *Subsection of Hospital Anxiety and Depression Scale assessment*	Time to complete: 1 min Number of administrations: 2 (first visit, final visit) Description: 7×4-point questions, 'not at all' → 'most of the time'
Stiffness	–	Time to complete: N/A (subsection of FIQR) Number of administrations: 3 (first visit, final visit, follow-up telephone call)
Dyscognition	–	Time to complete: N/A (subsection of FIQR) Number of administrations: 3 (first visit, final visit, follow-up telephone call)

Total completion time: 16 min.
*The rationale for inclusion of FM questionnaires is fourfold; (1) a proportion of participants included in the study will have widespread pain symptoms secondary to FM, (2) multifaceted subjective scores, encompassing all aspects of chronic pain in a comprehensive manner, (3) FM is the best proxy for widespread chronic pain symptoms, (4) the FIQR can be utilised for any chronic condition—when it is known as Symptom Impact Questionnaire or SIQR.
FM, fibromyalgia; N/A, not applicable; NRS, Numerical Rating Scale.

Data collection methods

Eligibility criteria will be explored by means of analysing eligibility rates (objective 1). Acceptability will be assessed quantitatively in terms of refusal and retention rates (objectives 5 and 6). Qualitative interviews and patient-reported experience questionnaires will help guide the qualitative aspect of acceptability and practicability of the device (objective 2), treatment schedule (objective 2), trial design and appropriateness of outcome measures (objectives 3 and 4). The eligibility rates, recruitment rates, refusal rates and retention rates will be measured and expressed in proportions. The results will guide design and methods of the future definitive RCT.

A combination of patient-reported (table 4) and performance-based (table 5) measures will be employed (objectives 7–9). The following patient-reported outcome measures have all demonstrated reliability and validity in the assessment of pain conditions.[53–61] Additionally, these tools are recognised as the recommended standardised assessment tools for FM domains by an international consortium of experts in the field (2012).[62] Out of the following seven questionnaires, five are less than a single page. The remaining two are less than three pages. All encompass simple tick box answers. Participants will complete paper questionnaires in the clinic room. For non-English speaking participants, an interpreter will be present. After testing with layperson representatives, it is estimated that the time taken to complete all outcome measures will be less than 20 min. Not all questionnaires will be asked each time (see brief tool description in

Table 5 Performance-based outcome measures

OMERACT domain	Assessment tool	Brief tool description (taken into account when considering participant burden)
Core domains		
Tenderness	Tender point count using a dolorimeter set to apply 4 kg/cm^2 of pressure—18 tender points as described by American College of Rheumatology	Time to complete: 2 min Number of administrations: 2 (first visit, final visit) The Manual Tender Point Survey/Fibromyalgia Intensity Score (MTPS/FIS) method will be used where the participant rates pain severity on application of the dolorimeter at each tender point on a verbal NRS. NRS≥2 is required to count a tender point as positive. A tender point about the size of a penny, located in clusters in soft tissues around the neck, chest, shoulders, elbows, hips and knees. These 18 specific tender points were identified by the American College of Rheumatology in 1990,[71] and are often painful in FM patients. For a tender spot to be considered positive, the participant will experience temporary pain when a small amount of pressure is applied to the specific area. Positive tender points are no longer required to make a diagnosis of FM, but clinicians may still choose to examine these areas in routine practice to strengthen the probability of diagnosis and/or monitor response to treatment. Reliability and reproducibility will be ensured with the use of a dolorimeter set to apply a prespecified pressure at each of the tender points. Pain with 4 kg/cm^2 pressure or less (taken to be equivalent to application of digital pressure until the pulp of the thumb nail becomes white) is considered to be a positive tender point.[72]
Peripheral domains		
Dyscognition	Stroop Test (to assess inhibitory control and processing speed)	Time to complete: 1 min Number of administrations: 2 (first visit, final visit) This is a computer-based test. A series of colours are spelt out on the screen; blue, red, yellow, green. Each time the word appears, it is presented in a different colour; blue, red, yellow or green. The participant must select the correct *colour* of the word. This is a timed task for 60 s. If the answer is selected incorrectly, the next word will appear. The test is scored by number of correct answers in this time period. No marks are lost for incorrect answers.
Total completion time: 3 min.		

FM, fibromyalgia; NRS, Numerical Rating Scale.

table 4 for further information regarding individual questionnaires).

Data management

All data manipulation will be consistent with the Office for National Statistics recommendations as stated in the 'Review of the Dissemination of Health Statistics: Confidentiality Guidance', 2006.[63] Compliance with the UK General Data Protection Regulation 2018[64] will be demonstrated throughout. Once enrolled, the participant will be allocated a unique study number—data will be pseudoanonymised by this coding method. The database that contains participant identifiable data will be separate to the research data. Only study numbers will be used for recording research data. The study delegation log with outlined duties will be kept, as well as a standard operating procedure (SOP) for device operation. All research records will be archived as per the Trust Research and Development (R&D) Archiving SOP and the end of study will be reported to the HRA and the Research Ethics Committee.

Quantitative data analysis

The primary feasibility outcome data (objectives 2–4) will be summarised using descriptive statistics, including narrative descriptions. Primary statistical analyses will be non-parametric, but if the data distribution allows, we will use also parametric statistics. Categorical data will be presented as frequencies and percentages, while continuous data will be presented as means, SD, median, mode and IQR, depending on the data distribution. Data will be assessed for normality both visually and with Shapiro-Wilk test. Recruitment, participation and retention rates (objectives 1, 5 and 6) will be reported and presented in a CONSORT flow diagram.

Both patient-reported and performance-based outcomes will be analysed (objective 7). Estimates of effect will be reported as 95% CI without p values, and will be used to generate CIs for a future RCT (objective 8).

Table 6 Data analysis

Data type	Statistical test
Normally distributed continuous variables for example, FIQR	Student's paired t test
Non-parametric ordinal data for example, tender point count	Wilcoxon signed-rank test (will be used to compare pretreatment and post-treatment scores)
Categorical data for example, marital and employment status	Fisher's exact test
Paired continuous data for example, comparison of mean scores pretreatment and post-treatment	Student's paired t test
Subgroup analysis for example, gender and ethnicity comparisons	One-way analysis of variance
Non-parametric data (if assumptions of normality not met)	Wilcoxon signed-rank test Mann-Whitney test Kruskal-Wallis analysis

FIQR, Fibromyalgia Impact Questionnaire.

Table 6 provides a summary for the intended utilisation of statistical tests according to the type of data produced. Data will be analysed using SPSS or an equivalent statistical package.

Qualitative data analysis

A reflexive thematic analysis[65] will be undertaken within six stages. Two independent researchers will examine the first five interviews in order to establish agreed focus and initial thematic content from open coding, initially participant by participant to maintain uniqueness. These two reviewers will then discuss and identify common themes across participants. All further stages will be undertaken by the lead researcher where supervising authors will act as a critical friend. The lead researcher will present a defendable case to the steering group for the later stages. For the purpose of the study, this analysis will be undertaken separately and inductively (objective 9). Depending on study results, the analysis will be presented separately as themes, or integrated at the stage of presentation to explain quantitative results if possible.

Data monitoring

Simple mean imputation for missing data will be employed where applicable.[66] Additionally, missing data will be reported with reasons given where possible in order to assess the feasibility of methodology. This will be valuable when informing outcome measures for the definitive trial.

Risk assessment

A summary of hazard and risks will be kept in the Investigator Site File. There are exemptions for certain expected events relating to chronic pain patients and/or treatment that do not need reporting (other than in the Case Report Form). For this population, these include: flare ups or pain and increase in medication dosages, increased unscheduled healthcare usage including GP and Emergency Department visits for a flare, time off work/college/University due to flare. In addition, recognised minor expected side effects such as sensations of localised warmth and tingling will not be recorded as adverse events. See table 7 for definitions and action plan.

Auditing

The R&D department of SWB Trust are the trial Sponsor. The Trial Steering Committee will meet at allocated trial points including prior to recruitment, or if AEs occur. The trial committee comprised academics from the University of Birmingham (AS and NRH) and a chronic pain patient representative who is not a participant in the trial (NG). They will meet at least 6 monthly or more frequently if required.

Patient Public Involvement (PPI)

We have followed the NIHR INVOLVE collaborative guidance described in the 'UK Standards *for* Public Involvement in Research' (2019)[67] and have utilised the GRIPP2 short form template[68] when gaining PPI with regard to our aims and methods. Patients have been central towards the development of our methodology, particularly in relation to symptom domains to be investigated.

The proposed research has been designed in conjunction with patients diagnosed with FM at SWB Trust, as a predominant example of a chronic pain population experiencing symptoms of widespread pain. Patients have been involved in decision-making from the start. We have been informally liaising with approximately 30 patients over 12 months, including the use a focus group. One patient has taken on the role of liaison member—checking over detailed aspects of the trial design, PIS, user-friendliness of questionnaires and will participate in the Trial Steering Committee.

Limitations of this study

There are some limitations to this study. There is no control or placebo group and the sample size is not powered; hence, efficacy of the trial intervention cannot be established. For this reason, participants are able to continue to receive their usual care (with the exception of steroids) which has the potential to introduce bias. There is a possibility of treatment being non-uniform between participants in that they can receive treatment without the lid being fully close if they were to feel claustrophobic. For the purposes of this feasibility trial, this will be noted and be used to help guide study procedures for a definitive RCT.

ETHICS AND DISSEMINATION

Ethical considerations

The study has Leicester Central Research Ethics Committee (21/EM/0231) and Health Research Authority (project ID 278452) approvals, granted on 13 October 2021. Local approval was obtained from SWB

Table 7 Event definitions and action plan

Adverse events (AE)	► Any unfavourable or unintended symptom or sign associated with the intervention during the trial. ► Any AE considered to be of clinical significance by the local chief investigator as causing harm to the participant will be recorded and rated in severity. ► Data to be recorded: onset, resolution outcome, severity. ► Causality will be assessed by site investigators and reported as none, unlikely, possible, probable or definite.
Serious adverse events (SAE)	► Defined as persistent or significant, requiring intervention or hospitalisation. Participants affected by SAEs will undergo risk assessment as to whether it is safe to continue in the trial.
Adverse device events and serious adverse device events	► AEs and SAEs that have a reasonable possibility of being attributable to the device.

NHS Trust Research and Development department (20PAIN01). Recruitment of participants will be consecutive. Each participant will receive written study information and be required to provide written inform consent before any study procedure is undertaken.

Protocol amendments

Protocol amendments will be communicated with relevant parties such as the trial investigators, Sponsor, university, trial registries, and if required, trial participants.

Dissemination policy

Findings of the trial will be widely disseminated to patients, healthcare professionals, commissioners and the general public. Research findings will be published within 1 year of the study's completion, and the results section in the public register to which the study is registered will be updated, as per best practice guidance.[69] Participants' involvement in the trial will be acknowledged by providing them with a summary of the findings. The importance of this has been confirmed by our patients following discussions at focus groups.

We wish to disseminate findings in a user-friendly way which is accessible to multiple audiences. Our patient public involvement members will play a key role here. There are specific focus groups at our Trust, such as Pain Management Programmes. In particular, our patient liaison representative has regular access to community chronic pain groups. We will make our results locally available to both patients and staff via the Trust Intranet, and nationally via Pain Charity websites such as Fibromyalgia Action UK. Subsequent to TSC approvals, findings will be submitted for presentation at local, national and international meetings (regional Pain Consultant Forums, British Pain Society, International Association for the Study of Pain). Data will be submitted to international peer-reviewed scientific journals (eg, *PlosOne, British Journal of Pain, European Journal of Pain, Pain Medicine*). We recognise that use of social media and academic social networks (eg, LinkedIn, Twitter) are becoming widely used dissemination tools,[70] which we intend to use to ensure our research is visible.

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REFERENCES

1 Raja SN, Carr DB, Cohen M, *et al*. The revised international association for the study of pain definition of pain: concepts, challenges, and compromises. *Pain* 2020;161:1976–82.
2 Treede R-D, Rief W, Barke A, *et al*. A classification of chronic pain for ICD-11. *Pain* 2015;156:1003–7.
3 Meints SM, Edwards RR. Evaluating psychosocial contributions to chronic pain outcomes. *Prog Neuropsychopharmacol Biol Psychiatry* 2018;87:168–82.
4 Treede R-D, Rief W, Barke A, *et al*. Chronic pain as a symptom or a disease: the IASP classification of chronic pain for the International classification of diseases (ICD-11). *Pain* 2019;160:19–27.
5 Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *Br J Anaesth* 2019;123:e273–83.
6 GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. *Lancet* 2020;396:1204–22.
7 El-Metwally A, Shaikh Q, Aldiab A, *et al*. The prevalence of chronic pain and its associated factors among Saudi Al-Kharj population; a cross sectional study. *BMC Musculoskelet Disord* 2019;20:177.
8 Kia S, Choy E. Update on treatment guideline in fibromyalgia syndrome with focus on pharmacology. *Biomedicines* 2017;5:20.
9 Taylor R, Pergolizzi JV, Puenpatom RA, *et al*. Economic implications of potential drug–drug interactions in chronic pain patients. *Expert Rev Pharmacoeconomics Outcomes Res* 2013;13:725–34.
10 Kisselev SB, Moskvin SV. The use of laser therapy for patients with fibromyalgia: a critical literary review. *J Lasers Med Sci* 2019;10:12–20.
11 National Institute for Health and Care Excellence. Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain NICE guideline [NG193], 2021. Available: https://www.nice.org.uk/guidance/ng193 [Accessed 24 May 2021].
12 Taulaniemi A, Kankaanpää M, Rinne M, *et al*. Fear-avoidance beliefs are associated with exercise adherence: secondary analysis of a randomised controlled trial (RCT) among female healthcare workers with recurrent low back pain. *BMC Sports Sci Med Rehabil* 2020;12:28.
13 Mc Veigh JG, Lucas A, Hurley DA, *et al*. Patients' perceptions of exercise therapy in the treatment of fibromyalgia syndrome: a survey. *Musculoskeletal Care* 2003;1:98–107.
14 Jack K, McLean SM, Moffett JK, *et al*. Barriers to treatment adherence in physiotherapy outpatient clinics: a systematic review. *Man Ther* 2010;15:220–8.
15 National Institute for Health and Care Excellence. Commonly used treatments for chronic pain can do more harm than good and should

not be used, says NICE in draft guidance, 2020. Available: https://www.nice.org.uk/news/article/commonly-used-treatments-for-chronic-pain-can-do-more-harm-than-good-and-should-not-be-used-says-nice-in-draft-guidance [Accessed 2 Aug 2021].
16 National Institute for Health and Care Excellence. Low-level laser therapy for preventing or treating oral mucositis caused by radiotherapy or chemotherapy (Interventional procedures guidance [IPG615]), 2018. Available: https://www.nice.org.uk/guidance/ipg615 [Accessed 18 Jul 2020].
17 Chung H, Dai T, Sharma SK, *et al*. The nuts and bolts of low-level laser (light) therapy. *Ann Biomed Eng* 2012;40:516–33.
18 Farivar S, Malekshahabi T, Shiari R. Biological effects of low level laser therapy. *J Lasers Med Sci* 2014;5:58–62.
19 Clijsen R, Brunner A, Barbero M, *et al*. Effects of low-level laser therapy on pain in patients with musculoskeletal disorders: a systematic review and meta-analysis. *Eur J Phys Rehabil Med* 2017;53:603–10.
20 International Association for the Study of Pain. Myofascial pain [fact sheet] (revised 2017), 2010. Available: https://s3.amazonaws.com/rdcmsiasp/files/production/public/Content/ContentFolders/GlobalYearAgainstPain2/20092010MusculoskeletalPain/14.%20Myofascial%20Pain%20Fact%20Sheet%20Revised%202017.pdf [Accessed 5 Jul 2020].
21 Chow RT, Johnson MI, Lopes-Martins RAB, *et al*. Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. *Lancet* 2009;374:1897–908.
22 Haldeman S, Carroll L, Cassidy JD, *et al*. The bone and joint decade 2000–2010 Task force on neck pain and its associated disorders. *Spine*2008;33:S5–7.
23 Maia MLdeM, Bonjardim LR, Quintans JdeSS, *et al*. Effect of low-level laser therapy on pain levels in patients with temporomandibular disorders: a systematic review. *J Appl Oral Sci* 2012;20:594–602.
24 Bisset L, Coombes B, Vicenzino B. Tennis elbow. *BMJ Clin Evid* 2011;2011:1117.
25 Favejee MM, Huisstede BMA, Koes BW. Frozen shoulder: the effectiveness of conservative and surgical interventions-systematic review. *Br J Sports Med* 2011;45:49–56.
26 Glazov G, Yelland M, Emery J. Low-level laser therapy for chronic non-specific low back pain: a meta-analysis of randomised controlled trials. *Acupunct Med* 2016;34:328–41.
27 Qaseem A, Wilt TJ, McLean RM, *et al*. Noninvasive treatments for acute, subacute, and chronic low back pain: a clinical practice guideline from the American College of physicians. *Ann Intern Med* 2017;166:514–30.
28 Rayegani SM, Raeissadat SA, Heidari S, *et al*. Safety and effectiveness of low-level laser therapy in patients with knee osteoarthritis: a systematic review and meta-analysis. *J Lasers Med Sci* 2017;8:S12–19.
29 Deana NF, Zaror C, Sandoval P, *et al*. Effectiveness of low-level laser therapy in reducing orthodontic pain: a systematic review and meta-analysis. *Pain Res Manag* 2017;2017:8560652.
30 de Andrade ALM, Bossini PS, Parizotto NA. Use of low level laser therapy to control neuropathic pain: a systematic review. *J Photochem Photobiol B* 2016;164:36–42.
31 Huisstede BM, Hoogvliet P, Franke TP, *et al*. Carpal tunnel syndrome: effectiveness of physical therapy and Electrophysical modalities. An updated systematic review of randomized controlled trials. *Arch Phys Med Rehabil* 2018;99:1623–34.
32 Carcia CR, Martin RL, Houck J, *et al*. Achilles pain, stiffness, and muscle power deficits: Achilles tendinitis. *J Orthop Sports Phys Ther* 2010;40:A1–26.
33 Zadik Y, Arany PR, Fregnani ER, *et al*. Systematic review of photobiomodulation for the management of oral mucositis in cancer patients and clinical practice guidelines. *Support Care Cancer* 2019;27:3969–39.
34 Gonzalez-Lima F, Barrett DW. Augmentation of cognitive brain functions with transcranial lasers. *Front Syst Neurosci* 2014;8:36.
35 Mease P, Arnold LM, Choy EH, *et al*. Fibromyalgia syndrome module at OMERACT 9: domain construct. *J Rheumatol* 2009;36:2318–29.
36 Eldridge SM, Chan CL, Campbell MJ, *et al*. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ* 2016;355:i5239.
37 Calvert M, King M, Mercieca-Bebber R, *et al*. SPIRIT-PRO Extension explanation and elaboration: guidelines for inclusion of patient-reported outcomes in protocols of clinical trials. *BMJ Open* 2021;11:e045105.
38 Ruaro JA, Fréz AR, Ruaro MB, *et al*. Low-level laser therapy to treat fibromyalgia. *Lasers Med Sci* 2014;29:1815–9.
39 Gür A, Karakoc M, Nas K, *et al*. Effects of low power laser and low dose amitriptyline therapy on clinical symptoms and quality of life in fibromyalgia: a single-blind, placebo-controlled trial. *Rheumatol Int* 2002;22:188–93.
40 Tomazoni SS, Costa LdaCM, Guimarães LdeS, *et al*. Effects of photobiomodulation therapy in patients with chronic non-specific low back pain: protocol for a randomised placebo-controlled trial. *BMJ Open* 2017;7:e017202.
41 de Carvalho PdeTC, Leal-Junior ECP, Alves ACA, *et al*. Effect of low-level laser therapy on pain, quality of life and sleep in patients with fibromyalgia: study protocol for a double-blinded randomized controlled trial. *Trials* 2012;13:221.
42 da Silva MM, Albertini R, de Tarso Camillo de Carvalho P, *et al*. Randomized, blinded, controlled trial on effectiveness of photobiomodulation therapy and exercise training in the fibromyalgia treatment. *Lasers Med Sci* 2018;33:343–51.
43 Lopes-Martins RAB, Albertini R, Lopes-Martins PSL. Steroids block the anti-inflammatory effects of low level laser therapy. In: Hamblin MR, Waynant RW, Anders J, eds. *Mechanisms for low-light therapy*, 2006: 98–103.
44 Hoffmann TC, Glasziou PP, Boutron I, *et al*. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ* 2014;348:g1687.
45 Yeh S-W, Hong C-H, Shih M-C, *et al*. Low-level laser therapy for fibromyalgia: a systematic review and meta-analysis. *Pain Physician* 2019;22:241–54.
46 Moore CG, Carter RE, Nietert PJ, *et al*. Recommendations for planning pilot studies in clinical and translational research. *Clin Transl Sci* 2011;4:332–7.
47 Lancaster GA, Thabane L. Guidelines for reporting non-randomised pilot and feasibility studies. *Pilot Feasibility Stud* 2019;5:114.
48 Lewis M, Bromley K, Sutton CJ, *et al*. Determining sample size for progression criteria for pragmatic pilot RCTs: the hypothesis test strikes back! *Pilot Feasibility Stud* 2021;7:40.
49 Kieser M, Wassmer G. On the use of the upper confidence limit for the variance from a pilot sample for sample size determination. *Biometrics* 1996;38:941–9.
50 Malterud K, Siersma VD, Guassora AD. Sample size in qualitative interview studies: guided by information power. *Qual Health Res* 2016;26:1753–60.
51 Saunders B, Sim J, Kingstone T, *et al*. Saturation in qualitative research: exploring its conceptualization and operationalization. *Qual Quant* 2018;52:1893–907.
52 Soundy A, Lee RT, Kingstone T, *et al*. Experiences of healing therapy in patients with irritable bowel syndrome and inflammatory bowel disease. *BMC Complement Altern Med* 2015;15:106.
53 Mendoza T, Mayne T, Rublee D, *et al*. Reliability and validity of a modified brief pain inventory short form in patients with osteoarthritis. *Eur J Pain* 2006;10:353–61.
54 Galvez-Sánchez CM, de la Coba P, Duschek S, *et al*. Reliability, factor structure and predictive validity of the widespread pain index and symptom severity scales of the 2010 American College of rheumatology criteria of fibromyalgia. *J Clin Med* 2020;9:2460.
55 Takasaki H, Treleaven J. Construct validity and test-retest reliability of the fatigue severity scale in people with chronic neck pain. *Arch Phys Med Rehabil* 2013;94:1328–34.
56 Duruoz MT, Ulutatar F, Ozturk EC, *et al*. Assessment of the validity and reliability of the Jenkins sleep scale in ankylosing spondylitis. *Int J Rheum Dis* 2019;22:275–9.
57 et alBaranidharan G, Williams A, Wilson S. 2019 outcome measures. 1st edn, faculty of pain medicine of the Royal College of Anaesthetists. Available: https://www.britishpainsociety.org/static/uploads/resources/files/Outcome_Measures_January_2019.pdf [Accessed 6 Aug 2021].
58 Chang K-V, Hung C-H, Sun W-Z, *et al*. Evaluating soreness symptoms of fibromyalgia: establishment and validation of the revised fibromyalgia impact questionnaire with integration of soreness assessment. *J Formos Med Assoc* 2020;119:1211–8.
59 Jensen OK, Callesen J, Nielsen MG, *et al*. Reproducibility of tender point examination in chronic low back pain patients as measured by intrarater and inter-rater reliability and agreement: a validation study. *BMJ Open* 2013;3:e002532.
60 Bell T, Trost Z, Buelow MT, *et al*. Meta-analysis of cognitive performance in fibromyalgia. *J Clin Exp Neuropsychol* 2018;40:698–714.
61 Din NC, Meng ECT. Computerized Stroop tests: a review. *J Psychol Psychother* 2019;9:1.
62 Sim J, Lewis M. The size of a pilot study for a clinical trial should be calculated in relation to considerations of precision and efficiency. *J Clin Epidemiol* 2012;65:301–8.
63 Office for National Statistics. Review of the dissemination of health statistics: confidentiality guidance 2006 [online]. Available: https://www.ons.gov.uk/file?uri=/methodology/methodologytopicsandstat

isticalconcepts/disclosurecontrol/healthstatistics/confidentialityguidancctcm77181864.pdf [Accessed 2 Jul 2021].
64 Data Protection Act. Data protection act 2018 [online], 2018. Available: https://www.gov.uk/government/collections/data-protection-act-2018 [Accessed 15 Jul 2021].
65 Braun V, Clarke V. Reflecting on reflexive thematic analysis. *Qual Res Sport Exerc Health* 2019;11:589–97.
66 Jakobsen JC, Gluud C, Wetterslev J, *et al*. When and how should multiple imputation be used for handling missing data in randomised clinical trials – a practical guide with flowcharts. *BMC Med Res Methodol* 2017;17.
67 UK Standards for Public Involvement. Better public involvement for better health and social care research, 2019. Available: https://www.invo.org.uk/wp-content/uploads/2019/11/UK-standards-for-public-involvement-v6.pdf [Accessed 5 Mar 2020].
68 Staniszewska S, Brett J, Simera I, *et al*. GRIPP2 reporting checklists: tools to improve reporting of patient and public involvement in research. *BMJ* 2017;358:j3453.
69 Health Research Authority. Publication and dissemination of research findings [online], 2021. Available: https://www.hra.nhs.uk/planning-and-improving-research/best-practice/publication-and-dissemination-research-findings/ [Accessed 2nd Aug 2021].
70 Ross-Hellauer T, Tennant JP, Banelytė V, *et al*. Ten simple rules for innovative dissemination of research. *PLoS Comput Biol* 2020;16:e1007704.
71 Wolfe F, Smythe HA, Yunus MB. The American College of rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria Committee. *Arthritis Rheum* 1990;33:160–72.
72 Tastekin N, Uzunca K, Sut N, *et al*. Discriminative value of tender points in fibromyalgia syndrome. *Pain Med* 2010;11:466–71.