ISRCTN51854714 https://doi.org/10.1186/ISRCTN51854714

Pain-LESS Study

Submission date	Recruitment status	[ ] Prospectively registered
18/03/2019	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
19/06/2019	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
01/11/2023	Musculoskeletal Diseases	[ ] Record updated in last year

Plain English summary of protocol

Current plain English summary as of 31/10/2023:
Background and study aims
Fibromyalgia patients commonly experience cognitive issues such as concentration and memory difficulties and sleep disorders. Despite the prevalence of these symptoms, no established treatments currently exist. Traditional in-person Cognitive Behavioural Therapy (CBT), which focuses on modifying unhelpful thoughts and behaviours, is both expensive and challenging to deliver on a broad scale. New digital forms of CBT, specifically for insomnia (CBT-I), have shown promise in improving cognitive symptoms and sleep quality, but their effect on fibromyalgia patients is yet to be explored.

The goal of this clinical trial is to investigate the potential benefits of a digital Cognitive Behavioural Therapy for Insomnia (dCBT-I) platform, Sleepio, in individuals suffering from fibromyalgia.

The main questions this study aims to answer are:
Does the application of Sleepio improve the quality of life in individuals with fibromyalgia?
Does the use of Sleepio improve cognitive function in individuals with fibromyalgia?
Does the use of Sleepio enhance sleep quality in these same individuals?

Who can participate?
This study will focus on patients who have been diagnosed with fibromyalgia.

What does the study involve?
Participants will be asked to complete a series of online questionnaires and home-based online assessments, which will assess their quality of life, cognitive function, sleep quality, and pain levels. They may choose to attend a study visit at the John Radcliffe Hospital in Oxford.

Participants will be randomly assigned to either use the Sleepio platform or standardised health advice, including sleep hygiene material. Those assigned to Sleepio will undergo a series of six 20-minute sessions over 10 weeks with a virtual therapist focusing on cognitive and behavioural strategies for improving sleep. Additionally, a subset of participants will undergo further testing via sleep actigraphy and/or neuroimaging with MRI scans. Further assessments will be requested at 12 weeks, 24 weeks, and one year following enrolment in this component of the study.

Researchers will compare the two groups to determine if the use of Sleepio has a positive effect on quality of life, cognitive function, and sleep quality.

What are the possible benefits and risks of participating?
Participants will not benefit directly from taking part in this study, but we hope that the information we get from this study will help to improve our understanding of the impact of dCBT-I (Sleepio) in a fibromyalgia population and inform sleep treatment options for those with fibromyalgia in future.

Taking part in this study may require participants to attend the hospital for more visits than they would otherwise need. The sensory testing may cause minor, temporary discomfort but participants will be in control of the triggers applied and be free to stop the assessment at any point in time.

MRI is safe and non-invasive and does not involve any ionising radiation (x-rays). However, because they use a large magnet to work, MRI scans are not suitable for everybody. Because of this, participants will be asked pre-screening safety questions to help determine if they are able to take part. Some people scanned in MRI scanners, especially 7 Tesla scanners, may experience a mild dizzy sensation as they are moved into the scanner. This is normal and the sensation starts to go away as soon as you are in the scanner. Occasionally a possible abnormality may be detected. In this case, we would have the scan checked by a doctor. If the doctor felt that the abnormality was medically important, the participant would be contacted directly and recommended to have a hospital (NHS) diagnostic scan arranged. All information is kept strictly confidential.

Where is the study run from?
Oxford University Hospital NHS Trust, Nuffield Orthopaedic Centre, Oxford

When is the study starting and how long is it expected to run for?
May 2019 to April 2025

Who is funding the study?
The University of Oxford

Who is the main contact?
Dr. Anushka Soni, anushka.soni@ndcn.ox.ac.uk

Previous plain English summary:
Background and study aims
Conditions of the musculoskeletal system, which affect joints, muscles ligaments and bones, are common and often painful. It is hugely frustrating for sufferers and can affect many aspects of their lives. We used to think that the pain was directly due to the pain signals from the joints or other tissues where the pain is being experienced. There is now evidence that this is not the only explanation for the pain and it may be related to changes in the chemical transmitters involved in the body’s pain detection system in the brain. Magnetic resonance imaging of the brain can be used to show how patients may have different brain responses to pain, even though their symptoms may be very similar. We will subgroup patients according to information about the symptoms that a patient is experiencing, as well as measurements of their pain thresholds as well as their brain-based responses to pain. In turn, this may help us to predict who will find one type of treatment more helpful than a different one. In the future, we hope that this will help more patients to manage their symptoms better.

Who can participate?
This study will focus on patients who have been diagnosed with either fibromyalgia or inflammatory arthritis and have been advised to start a new treatment by the doctors looking after them.

What does the study involve?
The study will follow patients for a period of 12 months after starting a new treatment (this may be a standard medication used for arthritis, or a programme of exercise combined with talking therapies). Many of the visits will be conducted alongside planned appointments at the hospital for their routine clinical care, but some extra research visits will take place in the research centre at the John Radcliffe Hospital where brain scans are done for research purposes.

What are the possible benefits and risks of participating?
Participants will not benefit directly from taking part in this study, but we hope that the information we get from this study will help to improve the treatment of musculoskeletal pain in the future.

Taking part in this study will require participants to attend the hospital for more visits than they would otherwise need. The sensory testing may cause minor, temporary discomfort but participants will be in control of the triggers applied and be free to stop the assessment at any point in time.

MRI is safe and non-invasive and does not involve any ionising radiation (x-rays). However, because they use a large magnet to work, MRI scans are not suitable for everybody. Because of this, participants will be asked pre-screening safety questions to help determine if they are able to take part. Some people scanned in MRI scanners, especially 7 Tesla scanners, may experience a mild dizzy sensation as they are moved into the scanner. This is normal and the sensation starts to go away as soon as you are in the scanner. Occasionally a possible abnormality may be detected. In this case, we would have the scan checked by a doctor. If the doctor felt that the abnormality was medically important, the participant would be contacted directly and recommended to have a hospital (NHS) diagnostic scan arranged. All information is kept strictly confidential.

Where is the study run from?
Oxford University Hospital NHS Trust, Nuffield Orthopaedic Centre, Oxford

When is the study starting and how long is it expected to run for?
May 2019 to September 2024

Who is funding the study?
The University of Oxford

Who is the main contact?
Dr. Anushka Soni, anushka.soni@ndcn.ox.ac.uk

Contact information

Type(s)
Public

Contact name

Dr Anushka Soni

ORCID ID
http://orcid.org/0000-0002-7831-4208

Contact details
Botnar Research Centre
Windmill Road
Oxford
United Kingdom
OX3 7LD
01865 227374
anushka.soni@ndorms.ox.ac.uk

Type(s)
Scientific

Contact name
Dr Anushka Soni

Contact details
Botnar Research Centre
Windmill Road
Oxford
United Kingdom
OX3 7LD
01865 227374
anushka.soni@ndorms.ox.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
252762

ClinicalTrials.gov number
NCT05962138

Secondary identifying numbers
IRAS Project ID 252762

Study information

Scientific Title
Characterisation of Pain in patients with musculoskeletal disease: a prospective, Longitudinal, observational study with an Embedded feasibility window of opportunity Sleep Study

Acronym

Pain-LESS

Study objectives
1. To investigate whether patients with inflammatory arthritis and features of centrally driven pain have reduced chance of responding to treatment.
2. To investigate the features of centrally driven pain, detected through multi-modal assessment, in patients with a range of musculoskeletal conditions

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/04/2019, NHS HRA South Central - Oxford B REC (The Deanery, Christ Church, St Aldate's, Oxford, OX1 1DP, United Kingdom; +44 (0)2071048046; nrescommittee.southcentral-oxfordb@nhs.net), ref: 19/SC/0168

Study design
Prospective observational longitudinal study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Fibromyalgia

Interventions
Current interventions as of 31/10/2023:
Digital Cognitive Behavioural Therapy for Insomnia
6-10 weeks of digital cognitive behavioural therapy for insomnia (Sleepio) delivered online. In addition, participants will receive a booklet published by Versus Arthritis designed for patients with fibromyalgia with general advice, including sleep hygiene. Assessments will include clinical history, questionnaire-based assessment of pain, cognition, mood, sleep and related features, quantitative sensory testing, blood test and neuroimaging.

Previous interventions:
Observational study of treatment as usual for up to 12 months after initiation of treatment. Assessments will include clinical history, disease activity score measures, questionnaire-based assessment of pain and related features, quantitative sensory testing and neuroimaging.

Intervention Type
Behavioural

Primary outcome measure
Current primary outcome measure as of 01/11/2023:
Overall impact of fibromyalgia on patients' lives, capturing domains such as physical impairment, overall well-being, and the intensity of symptoms like pain, fatigue, stiffness, sleep disturbances, and cognitive problems, measured using the Revised Fibromyalgia Impact Questionnaire (FIQR) at baseline and 12, 24 and 52 weeks

Previous primary outcome measure:
Percentage achieving Disease Activity Score <2.6, assessed using a combination of the patient report and clinical assessment, 3 and 6 months after commencing treatment respectively.

Secondary outcome measures
Current secondary outcome measure as of 01/11/2023:
1. Cognitive difficulty, measured using the British Columbia Cognitive Complaints Inventory, at baseline and 12, 24 and 52 weeks
2. Kinesiophobia, measured using the Tampa Scale of Kinesiophobia, at baseline and 12, 24 and 52 weeks
3. Cost-effectiveness of Sleepio, measured using the EQ-5D-5L, at baseline and 12 and 24 weeks
4. Sleep quality, measured using actigraphy, at baseline and 12 weeks
5. Changes in brain structure, measured using brain grey matter volume on structural MRI, at baseline and 12 weeks
6. Changes in brain functional connectivity, measured using brain resting state functional connectivity on resting-state functional MRI, at baseline and 12 weeks
7. Changes in neurotransmitter concentration in the insular, measured using neurotransmitter concentration in the insular on magnetic resonance spectroscopy, at baseline and 12 weeks
8. Changes in brain function, measured using brain resting state activity on arterial spin labelling (ASL) on brain MRI, at baseline and 12 weeks

Previous secondary outcome measure:
Scoring according to: Central Sensitivity Inventory, Fibromyalgia survey criteria, PainDETECT questionnaire alongside neuroimaging findings, collected over a 12-month period.

Overall study start date
08/08/2018

Completion date
30/04/2025

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 31/10/2023:
1. Participant is willing and able to give informed consent for participation in the study.
2. Clinical diagnosis of fibromyalgia/chronic widespread pain
3. For feasibility study

3.1. Concomitant insomnia, frequent waking in the night or early morning waking
3.2. Self-reported difficulties with concentration or memory
3.3. Reliable Internet access

Previous participant inclusion criteria:
1. Participant is willing and able to give informed consent for participation in the study.
2. Clinical diagnosis of either inflammatory arthritis or fibromyalgia/chronic widespread pain

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
490

Key exclusion criteria
Current participant exclusion criteria as of 31/10/2023:
1. Patients from vulnerable groups
2. Patients with a poor understanding of English
3. Patients with known neurological or psychiatric conditions (other than depression or anxiety) likely to independently affect the results of pain assessment, for example, peripheral diabetic neuropathy in the opinion of the research team.
4. For feasibility study
4.1. Major neuropsychiatric disorder (bipolar disorder, schizophrenia or psychotic spectrum disorders), however, participants with depression and anxiety will be eligible
4.2. Epilepsy
4.3. Cognitive impairment, dementia or neurodegenerative disorder
4.4. Recent or planned surgery
4.5. Current or planned night-time shift work
4.6. Sleep disorders such as sleep apnoea, restless leg syndrome, circadian rhythm disorder, or parasomnia
4.7. Taking prescribed sleep medications on more than 2 nights in past 2 weeks
4.8. Currently receiving other psychological therapy for insomnia
4.9. Pregnant or lactating

Previous participant exclusion criteria:
1. Patients from vulnerable groups
2. Patients with a poor understanding of English
3. Patients with known neurological or psychiatric conditions (other than depression or anxiety) likely to independently affect the results of pain assessment, for example peripheral diabetic neuropathy in the opinion of the research team.

Date of first enrolment

01/05/2019

Date of final enrolment
01/07/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Oxford University Hospital NHS Trust
Nuffield Orthopaedic Centre
Windmill Rd
Headington
Oxford
United Kingdom
OX3 7HE

Sponsor information

Organisation
University of Oxford

Sponsor details
Research Services, Clinical Trials and Research Governance
Joint Research Office
Boundary Brook House
Churchill Drive
Headington
Oxford
England
United Kingdom
OX3 7LQ
000000000
ctrg@admin.ox.ac.uk

Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
University/education

Funder Name
University of Oxford

Alternative Name(s)
University in Oxford, Oxford University, , Universitas Oxoniensis

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
We plan to publish the results in peer-reviewed journals and will also disseminate information directly to our study participants on completion of the analysis of the data collected. In addition, we will share the results of the study with the wider public through patient and public involvement initiatives organised by the University of Oxford.

Intention to publish date
01/01/2026

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No