ISRCTN72757645 https://doi.org/10.1186/ISRCTN72757645

EXCEL: EXamining the feasibility of exerCisE to manage symptoms of Lupus

Submission date
15/11/2023

Recruitment status
No longer recruiting

Registration date
10/01/2024

Overall study status
Completed

Last Edited
28/01/2025

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[X] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Lupus is a disease in which the immune system is over-active resulting in inflammation and damage in different organs. Although regular participation in exercise can support health and wellbeing in people with Lupus we do not know whether exercise can reduce this immune system over-activity. The aim of this study is to measure how immune cells change after a home-based exercise programme and determine whether it can reduce the activity of lupus.

Who can participate?
Women aged over 18 years with lupus who currently don't exercise

What does the study involve?
This is an 18-week study that requires three visits to Sandwell General Birmingham. Each participant will be randomly allocated to one of two groups: control (standard NHS care) or home-based exercise (plus standard NHS care). The researchers will recruit a group of healthy age and activity-matched female participants for baseline comparisons only. Blood samples will be taken from all groups at the start of the study and then 12 and 18 weeks later for patient groups only.
Participants will co-design an exercise programme with the aim of exercising for 150 minutes at a moderate intensity or 90 minutes at a vigorous intensity by the end of the 12 weeks. This can be an exercise type of the participant's choice (e.g. walking or cycling), which will be discussed with an exercise specialist. The researchers are fully aware that there are days where fatigue, joint pain or other symptoms might make this exercise programme unmanageable. As part of the intervention, they will give advice on how to exercise on these challenging days.
A secondary aim of this project is to recruit patients with SLE nationally to complete a brief online survey about lifestyle habits to help with the design of a larger national trial.

What are the possible benefits and risks of participating?
All participants will receive training and experience in designing their own exercise programme that is coordinated using mobile health (mHealth) technology. This will give participants confidence in managing the progression of exercise in their normal life moving forward. Participants' general and clinical health will be measured, for example, blood pressure and heart rate. Once the study has finished, advice will be provided on the best types of exercise to

benefit participants' health and Lupus.
A small needle will be inserted into a vein of the arm on three occasions (visits 1-3). As far as discomfort is concerned, there might be a small sting with insertion but otherwise these procedures are not usually painful. There is a very small risk of infection and bruising at the site of insertion. This risk will be much reduced by using trained staff and good procedures. The amount of blood taken at each of the three visits (54 ml) is equivalent to approximately 3-4 tablespoons. It is safe to lose this amount of blood over 18 weeks (162 ml).
Fatigue will be experienced during the exercise sessions, which is normal and short-lived. However, during exercise there is a very minimal risk of unforeseen heart complications. Although specific figures are not available for people with Lupus, the risk of a cardiac event or complication in adults without existing heart disease ranges from 1 in 400,000 – 800,000 hours of exercise. Even in patients with heart disease, who are recognised as high risk, the risk equates to 1 death every 176,000 hours of exercise. As such, the risk is deemed extremely small. Participants are free to stop exercising at any point if they feel uncomfortable.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
January 2021 to March 2025

Who is funding the study?
LUPUS UK

Who is the main contact?
Dr Alex Wadley, a.j.wadley@bham.ac.uk

Contact information

Type(s)
Public, Scientific

Contact name
Dr Alex Wadley

ORCID ID
https://orcid.org/0000-0002-1820-8446

Contact details
School of Sport, Exercise & Rehabilitation Sciences
University of Birmingham
Edgbaston Park Road
Birmingham
United Kingdom
B15 2TT
+44 (0)121 414 8011
a.j.wadley@bham.ac.uk

Type(s)
Principal investigator

Contact name
Dr John Reynolds

Contact details
University of Birmingham
University of Birmingham Research Labs
1st Floor, Queen Elizabeth Hospital
Birmingham
United Kingdom
B15 2WB
+44 (0)1213713248
j.a.reynolds.1@bham.ac.uk

Type(s)
Scientific

Contact name
Miss Victoria Quickfall

Contact details
Edgbaston Park Road
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 (0)121 414 8011
vmq142@student.bham.ac.uk

Type(s)
Public

Contact name
Miss Megan Quickfall

Contact details
Edgbaston Park Road
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 (0)121 414 8011
excel@contacts.bham.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
311784

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 53944, IRAS 311784

Study information

Scientific Title
Examining the feasibility and acceptability of a remotely monitored exercise intervention on clinical, immunological and psychological aspects of health in patients with systemic lupus erythematosus

Acronym
EXCEL

Study objectives
It is hypothesised that patients in the Exercise group will have greater device-derived physical activity, reduced concentrations of clinical biomarkers, reduced numbers of autoreactive immune cells and improved lupus-specific quality of life and sleep quality compared to patients in the Control group.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/12/2022, South East Scotland Research Ethics Committee 02 (2nd Floor, Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, UK; +44 (0)131 536 9000; ruth.fraser4@nhslothian.scot.nhs.uk), ref: 22/SS/0082

Study design
Randomized; Interventional; Design type: Treatment, Device, Physical

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Systemic lupus erythematosus

Interventions
This study will involve two groups of people with SLE and a third group of healthy female volunteers. For the SLE groups, there will be an intervention group (standard NHS care plus mHealth intervention, n = 15) and a control group (standard NHS care only, n = 15). Patients will be required to visit Sandwell General Hospital Clinical Research Facility on three occasions over 18 weeks: week 1 (baseline), 12 (end intervention) and 18 (6 weeks post intervention). A group of healthy female controls will be recruited for a baseline comparison of immune measures only (n = 15), matched for age and levels of physical activity.

Initial Phone or Video Meeting and Informed Consent (30-minute time commitment)
The researchers will arrange an initial meeting, via telephone or video call (depending on preference), so that the participant can ask any questions they may have about the study. They will also assess the participants' eligibility for the study by asking a few questions. They will then arrange the first in-person visit at the Clinical Research Facility.

In-Person Visit 1 (all three groups, 1 week before the start of intervention: 120-minute time commitment)
The participant will be asked to visit the Clinical Research Facility at Sandwell General Hospital for the procedures outlined below. For all visits, the participant must be fasted (consume only water, no food from midnight the night before). The participant will also be asked to refrain from any strenuous exercise for a 48-hour period before each study visit.

1. Informed Consent
Once participants have been given sufficient time to consider their participation in the trial and ask any questions, they will be asked to sign a consent form. A letter will be sent to the patient's GP to confirm study participation.
2. Screening
The researchers will ask the participant to fill out two questionnaires to assess their suitability to take part in the study
3. Medical Assessment
The participant will have an appointment with a member of the clinical team to check that they’ re physically ready to commence the study.
4. General Health Assessment
The researchers will measure the participant's height, weight, waist circumference, resting heart rate, blood pressure and pulse.
5. Blood Sampling
The researchers will take a single blood sample. This is equivalent to approximately 3-4 tablespoons. These blood samples will be used for our primary analysis of patients’ white blood cells and routine clinical measures of their lupus disease activity.
6. Questionnaires
The researchers will ask the participants to fill out some questionnaires relating to their health-related quality of life, sleep quality and levels of fatigue.
7. Activity Assessment 1
The researchers will give the participant an activity monitor to wear over a 7-day period. The participant doesn’t need to do anything else during this period. The participant can post the activity monitor back to us in a pre-addressed large letter box that we will give them.
8. Group Allocation
The researchers will then randomise the participants into either the exercise intervention or control group.
9. Equipment
People in the Exercise Group will be given a Polar Ignite watch, heart rate monitor (Polar Verity Sense) and free access to an online training App (Polar Flow). People in the control group will be given just the heart rate monitor.

The next 13 weeks of the study will then be managed remotely by the research team.

Patient and Public Involvement
Prior to submitting the funding application to Lupus UK, the researchers engaged in Patient and Public Involvement (PPI) and will continue to do so during and beyond this study. There is evidence to indicate that regular exercise improves fatigue and quality of life in patients with

SLE. However, understandably, evidence indicates that patients with SLE are substantially less active than the general population. In planning our funding application, we aimed to understand the views of patients with SLE on how manageable this level of exercise was and hear their perspectives on delivering an intervention remotely. We therefore discussed our ideas with patients attending the SLE clinic at City Hospital Birmingham. Feedback was positive, particularly regarding the home-based element. Some patients had concerns about both the frequency and duration of the proposed exercise over 12 weeks, as well as questions regarding their capability in using the associated mHealth technology. This information was crucial in informing the study design and particularly, the coaching sessions detailed below:

Exercise Coaching Session 1 (Exercise group only, 6-7 days before start of intervention: 60-minute time commitment)
The researchers will arrange a meeting via telephone or video call (depending on preference) to design a personalised and progressive exercise program for each participant with the research team. In this first session, they will explore exercise preferences and develop a personalised exercise programme. Between sessions 1 and 2, the research team will design the intervention and provide the participant with a training booklet.

The intervention can be any exercise type (e.g., walking, cycling or body weight exercises) and mode (gym, outdoor, home-based or commuting) of the participant's choice. The intervention programme will increase exercise intensity and duration during the 12 weeks; aiming for a minimum of 150 minutes of moderate-intensity exercise (60-70% HRMAX) or 90 minutes of vigorous exercise (>70% HRMAX) per week by week 12. The researchers are fully aware that there are days where fatigue, joint pain or other symptoms might make this exercise programme unmanageable. As part of the intervention, they will give advice on how to exercise on these challenging days. The researchers will use a 5-level exercise programme that Lupus Europe have recently recommended. The participant can choose an exercise level, which involves progressively more intense exercises, performed either lying down, sitting or standing. All this information and contact with the research team can be carried out via the mobile phone application.

Exercise Coaching Session 2 (Exercise group only, 2-3 days before start of intervention: 60-minute time commitment)
In this second phone or video call, the researchers will go through the specifics of the personalised exercise plan in depth. They will outline which exercise the participant will do, when to do them, how often and how to use the Polar Ignite Watch, Polar Flow App and the coaching website. They will also show the participants the official study website, which will have videos that the participant can follow whilst exercising at home. Finally, the researchers will outline some important safety measures to be aware of whilst exercising.

The fitness watch will act as a personal trainer on your wrist, giving guidance and feedback during exercise on how to complete the planned sessions. The training App will allow participants to see the entire training programme and monitor their progress. Data recorded by the fitness watch will also be available to the research team to help them provide personalised feedback throughout the programme.

Exercise Intervention (Weeks 1-12)
The research team will provide regular feedback on the exercise sessions via the training App, particularly during the first 4 weeks. The research team will send a message based on what the participants did in each session and ask for their feedback. A telephone and/or video call will be arranged between weeks 2-4 to clarify anything that is not clear or discuss the programme in more depth (Exercise Coaching session 3). If necessary, the exercise programme will be modified

based on these conversations. The researchers will then send the participants weekly messages, but the research team will be available at any time for support or to discuss changes to the programme.

If the participants are undertaking the exercise intervention, they will be asked to download the training App, Polar Flow.
The research team do not own the data recorded on the Polar Flow mobile apps or downloaded to the Polar Flow website.
The data is owned by POLAR Electro. However, no personal data will be provided to the company as a unique login and password will be created for the participants using a study code.
The Polar Ignite watch has an in-built GPS tracking function, but this can be disabled at the participant's discretion so that no information regarding their location will be known at any time.
The researchers will provide all participants with a copy of the privacy policies before consenting to the study. They will then ask for the participant's permission to use the mobile App and website.

The Polar Flow App requires information to be downloaded from the participant's phone to cloud storage. This will use mobile phone data and as such could cost money which the research team will not reimburse. The researchers recommend that this is done using Wi-Fi.

Control Group (Weeks 1-12)
In the control group, the participants will not be given any structured advice on the exercise they undertake, but continue any normal physical activity that they routinely undertake (e.g. walking to work or shops, or any physical activity or exercises you usually do). All participants will be given a Polar Verity Sense Heart Rate Sensor to wear during any structured exercise sessions. The participants will receive no feedback from these sessions from the research team.

Activity Assessment 2 (Exercise and Control Groups: Week 11)
For the last week of the intervention, the researchers will send the participants an activity monitor (as before) to wear over a 7-day period. This can be brought back can to the research team during 'In Person Visit 2' below.

In-Person Visit 2 (Exercise and Control Groups, Week 12: 120-minute time commitment)
Participants will be asked to visit the Clinical Research Facility at Sandwell General Hospital for a repeat of some of the procedures on visit 1:
1. Medical Assessment
2. General Health Assessment (height, weight, waist circumference, resting heart rate and blood pressure)
3. Blood Sampling
4. Questionnaires (quality of life, sleep and fatigue)
The researchers will ask that participants return the activity monitor at this visit.

Exercise Coaching Session 4 (Exercise Group Only, 1-2 days after In-Person Visit 2: 30-minute time commitment)
A telephone and/or video call can be arranged to discuss the progress of the training programme and how participants could continue exercising.
During the next 6 weeks, participants will remain in possession of the Polar technology, but support from the research team in the Exercise group will be stopped.

In-Person Visit 3 (Exercise and Control Groups, Week 18: 120-minute time commitment)
Participants will be asked to visit the Clinical Research Facility at Sandwell General Hospital for a repeat of some of the procedures on visits 1 and 2:

1. Medical Assessment
2. General Health Assessment (height, weight, waist circumference, resting heart rate and blood pressure)
3. Blood Sampling
4. Questionnaires (intervention questionnaire (exercise group), quality of life, sleep and fatigue)
5. Activity assessment 3: we will give participants an activity monitor to wear over a 7-day period. This can be posted back to the research team in a pre-addressed large letter box that we will give to each participant.

We will ask that participants return the heart rate monitor and Polar Ignite watch to us at this visit.

Exercise Coaching Session 5 (Control Group Only: 60-minute time commitment)
People in the control group will then be offered a first exercise coaching session and be given the opportunity to trial the exercise intervention under our guidance.

The national online survey is based on previous successful online survey platforms used by members of the research team in clinical populations (PMID: 34512516).

Intervention Type
Behavioural

Primary outcome(s)
1. Feasibility of the personalised exercise plan will be evaluated by quantifying recruitment, adherence, and completion rates throughout the 12-week intervention (patient exercise group only)
2. Acceptability of the personalised exercise plan will be evaluated using a questionnaire after completion (patient exercise group only)

Key secondary outcome(s))
Clinical Health:
1. The incidence and severity of disease flares will be assessed using The British Isles Lupus Assessment Group (BILAG)-2004 Index at baseline, week 12, and week 18 (patient groups only)
2. Blood pressure and heart rate will be measured using a sphygmomanometer at baseline, week 12, and week 18 (baseline only for the healthy control group)
3. Anthropometric measures (e.g., height, weight, waist circumference, and hip circumference) will be determined at baseline, week 12, and week 18 (baseline only for the healthy control group)
4. Clinical haematology (full blood count), biochemistry (e.g., lipid Panel, complement proteins, c-reactive protein) and autoimmune serology profiles (e.g., quantitative DNA antibodies) will be obtained at baseline, week 12, and week 18 (baseline only for the healthy control group)

Immune Cell Profiling:
1. The number of autoreactive immune cells (T and B cells) will be quantified using flow cytometry at baseline, week 12, and week 18 (baseline only for the healthy control group)
2. The metabolic profile of immune cells will be quantified using extracellular flux analysis at baseline, week 12, and week 18 (baseline only for the healthy control group)

Lifestyle and Well-Being:
1. Objective physical activity will be evaluated for 7 days at baseline (week prior to intervention), week 11-12 (last week of intervention), and week 18 by using wrist-worn accelerometery

(baseline only for the healthy control group)
2. Self-reported physical activity will be measured using the General practice physical activity questionnaire (GPPAQ) at baseline, week 12, and week 18 (baseline only for the healthy control group)
3. Health-related quality of life will be determined by using the lupus-specific quality of life (LupusQoL) questionnaire at baseline, week 12, and week 18 (baseline only for the healthy control group)
4. Fatigue will be determined by using the Multidimensional Fatigue Index (MFI) questionnaire at baseline, week 12, and week 18 (baseline only for the healthy control group)
5. Sleep quality will be determined by using the Pittsburgh Sleep Quality Index (PSQI) questionnaire at baseline, week 12, and week 18 (baseline only for the healthy control group)

Completion date
31/03/2025

Eligibility

Key inclusion criteria
Patients:
1. Age >18 years old
2. Female patients with SLE (fulfilling classification criteria [1997 ACR, 2012 SLICC or 2019 EULAR /ACR). Note: approximately 90% of people suffering with SLE are female, hence this inclusion criteria
3. Clinically stable disease activity as assessed by a member of the medical team and deemed eligible for inclusion if they have no A or B scores in the BILAG-2004 index
4. Both participant and physician feel that they are able to exercise safely (PAR-Q screening)
5. Consent: demonstrates an understanding of the study and willingness to participate, as evidenced by voluntary written informed consent

Healthy controls:
1. Age: >18 years old
2. Female

National online survey:
1. Age: >18 years old
2. Female patients with SLE (fulfilling classification criteria [1997 ACR, 2012 SLICC or 2019 EULAR /ACR). Note: approximately 90% of people suffering with SLE are female, hence this inclusion criteria
3. Clinically stable disease activity as assessed by a member of the medical team and deemed eligible for inclusion if they have no A or B scores in the BILAG-2004 index
4. Both participant and physician feel that they are able to exercise safely (PAR-Q screening)
5. Consent: demonstrates an understanding of the study and willingness to participate, as evidenced by voluntary written informed consent

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
Exclusion criteria for exercise intervention:
1. Increase in the dosage of current lupus-specific medications (e.g., steroids, anti-malarial medications and/or immunosuppressants) within the last 3 months
2. Addition of new lupus-specific medications (e.g., steroids, anti-malarial medications and/or immunosuppressants) within the last 3 months
3. Patients with inactive disease but in whom there is a planned change in medication
4. Uncontrolled blood pressure
5. Pregnancy or planning pregnancy
6. Undertaking over 60 minutes of structured exercise per week
7. Additional health conditions or medication that might put the participant at risk or interfere with a participant's capacity to exercise will be at the PI's discretion, e.g., kidney or heart complications
8. Not owning a smart device or having no data plan or access to WiFi
9. Unable to provide full informed consent

Date of first enrolment
31/05/2023

Date of final enrolment
18/11/2024

Locations

Countries of recruitment
United Kingdom

Study participating centre
Birmingham City Hospital
Dudley Road
Birmingham
United Kingdom
B18 7QH

Sponsor information

Organisation

University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
LUPUS UK

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made 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?
Protocol article		16/01/2025	28/01/2025	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes