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To cite: Quickfall M, Green S, Hesketh K, *et al*. EXamining the feasibility of exerCisE to manage symptoms of Lupus (EXCEL): a protocol for a randomised controlled pilot study. *Lupus Science & Medicine* 2025;**12**:e001382. doi:10.1136/lupus-2024-001382

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/lupus-2024-001382).

Received 6 September 2024
Accepted 30 November 2024

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ABSTRACT

Introduction SLE is a chronic autoimmune disease that results in sustained hyperactivation of innate and adaptive immune cells and widespread inflammatory damage. Regular exercise reduces SLE symptoms including fatigue and joint pain and improves patient quality of life. However, most individuals with SLE are not sufficiently active to achieve these benefits, and guidance on the optimal approach to exercise is limited. EXCEL will examine the feasibility of conducting a large-scale randomised controlled trial comparing the effects of a remotely monitored, home-based, exercise programme with standard of care for individuals with SLE.

Methods and analysis 30 females with SLE will be recruited, and those randomised into Exercise (SLE-Ex) will codesign a progressive training plan with support from the research team. The aim of each 12-week plan will be to complete 150 min of moderate (60–70% heart rate max, HR_{max}) or 90 min of vigorous exercise (>70% HR_{max}) per week. SLE-Ex will be encouraged to exercise independently (without support) from weeks 13–18. Participants with SLE that are randomised into Control (SLE-Con) will maintain habitual activity without support for 18 weeks. Measures of feasibility and acceptability will be reported, and peripheral blood will be collected at weeks 0, 12 and 18 to explore whether the frequency, phenotype and metabolic profile of lymphocyte subsets has changed. Biomarkers of SLE activity, and self-reported measures of fatigue, sleep quality and health-related quality of life will also be monitored at these timepoints. Blood and self-reported measures will be compared with a healthy control (HC) group (n=15, age and body mass index matched) at baseline only.

Ethics and dissemination A favourable ethical opinion was given by South East Scotland Research Ethics Committee (22/SS/0082). Findings will be disseminated at conferences and published in peer-reviewed journals.

Trial registration number ISRCTN72757645.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Emerging evidence demonstrates that regular exercise can help to manage symptoms of SLE and improve health-related quality of life. Despite this, the majority of people with SLE do not meet recommended guidelines for physical activity, which may be attributable to the lack of formal guidance on the optimal methods of exercise for this population. SLE is characterised by a breakdown of immunological tolerance, with aberrations in the frequency and function of differentiated T and B lymphocyte subsets possibly underpinning disease pathology. There is evidence to support beneficial immunomodulatory effects of regular exercise in healthy individuals; however, there is a dearth of evidence in people with SLE.

WHAT THIS STUDY ADDS

⇒ EXCEL is a pilot study that will examine the feasibility of conducting a large, randomised controlled trial (RCT) to investigate the effect of a remotely monitored exercise programme, with standard care, for individuals with SLE. Participants will codesign a progressive, home-based exercise programme and receive regular support from the research team to promote long-term adherence and assist with the transition to independent exercise. Mobile health (mHealth) devices will be used to monitor participant's physical activity and exercise, as they offer a practical alternative to supervised approaches. Peripheral blood samples will also be collected at weeks 0, 12 and 18 to determine whether exercise training changes the frequency, phenotype and metabolic profile of lymphocytes in people with SLE.

INTRODUCTION

SLE is a chronic, multisystem autoimmune disease that predominantly affects females in the period between puberty and menopause. The disease follows an unpredictable flare and remission cycle and is extremely heterogeneous in its clinical presentation. SLE is estimated to affect 4.91 per 100 000 person-years in the UK alone[1] and carries a significant economic and social burden as debilitating symptoms such as chronic fatigue, joint pain and cognitive dysfunction restrict an individual's daily activity and ability to work.[2]

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Findings from this study will inform the design of future, larger- scale exercise intervention studies for individuals with SLE, and contribute to the growing evidence in support of integrating exercise into SLE clinical care. Furthermore, our pioneering immunological data will provide insight into the mechanisms underpinning previously observed clinical benefits of exercise for those with SLE sparking further research in the field.

In recent years, there have been many updates to European Alliance of Associations for Rheumatology guidelines for managing SLE, to reflect an improving understanding of the condition.[3] Current pharmacological strategies focus on preventing immunological flares and organ damage, and commonly begin with hydroxychloroquine monotherapy or in combination with glucocorticosteroids. As the prolonged use of high-dose steroids is strongly associated with toxicity and adverse effects, with increasing disease severity comes the introduction of immunomodulatory and/or biological agents.[4] Despite advances such as belimumab, development of new pharmaceutical therapies is slow. Moreover, many people with SLE still report low health-related quality of life,[5] are at high risk of comorbidities such as cardiovascular disease[6] and obesity[7] and have a 2.6-fold higher mortality compared with the general population.[8] As a result, non-pharmacological interventions and adjuvant therapies to help manage SLE symptoms and patient health are recommended.[9]

To this end, there is an increasing body of evidence to support the use of exercise as a method of SLE management. Various studies have demonstrated that regular exercise can improve fatigue,[10–12] joint and muscle pain,[13] cardiorespiratory health,[14] metabolic health[15] and quality of life[16] for people with SLE. In spite of this evidence, the majority of individuals with SLE do not meet WHO recommendations for physical activity, with a recent systemic review reporting that just 11% of some cohorts met published guidelines.[17] Disease-specific factors including fatigue and joint pain are commonly cited barriers to physical activity in people with SLE and highlight the need for a personalised approach.[18]

Recommendations relating to physical activity and exercise for those with SLE have recently become available yet focus heavily on supervised training methods.[19] These approaches are highly resource demanding, inaccessible to most and may not be maintained following cessation of the intervention.[20 21] Home-based methods that remove barriers such as travel time, specialised equipment and membership costs[22] should therefore be considered and have demonstrated high acceptability and adherence in previous studies.[23 24] For individuals with SLE, non-randomised trials have demonstrated remotely supported exercise programmes are feasible, well adhered to and can promote health improvements.[25 26] However, more research is needed to ascertain the optimal approach to exercise for this cohort, and to ensure exercise adherence is maintained post-intervention.

While some clinical benefits of exercise have been reported for people with SLE, the immunomodulatory effects remain poorly characterised. SLE aetiology centres around a loss of immunological tolerance and the sustained production of a wide variety of autoantibodies. ANAs are the most noteworthy array in this context and are often used in diagnosis as >95% of individuals with SLE are seropositive.[3] ANAs arise as a result of persistent apoptosis and dysregulated clearance of dead cells. The accumulation of nucleic debris stimulates toll-like receptors (TLR) on innate immune cells and leads to the release of type 1 interferons which strongly promote B cell differentiation and, together with genetic and environment factors, the loss of self-tolerance.[27] Autoantibody secretion leads to the generation of immune complexes in target tissue which promotes complement activation and localised inflammation. Nonetheless, SLE pathology is not restricted to B cell abnormalities. Chronic T cell activation, via autoantigen presentation, further amplifies and expands the inflammatory attack by supporting B cell development and the release of proinflammatory cytokines.[28] Sustaining activation of these innate and adaptive immune components is highly energy demanding and metabolic abnormalities have been reported in SLE.[29 30] Double-negative T cells (CD4–CD8–) are particularly important in this respect, as strong producers of interleukin (IL)-17, and are significantly expanded in SLE cohorts.[31] Perturbations deeper within immune cell lineages are also seen, as individuals with SLE show reduced numbers of both CD4+ and CD8+ T cells, but also a skewed memory phenotype, exemplified by lower frequencies of naïve, but higher memory subsets compared with healthy controls (HC).[32] Similarly, impaired function and reduced frequency of regulatory T cells (Tregs), which are responsible for maintaining immune homeostasis, have been implicated in SLE progression.[33]

It is well established that regular exercise induces anti-inflammatory effects, and, in the context of autoimmune disease, this immunomodulation may help lower disease activity.[34 35] For example, exercise can decrease expression of TLRs on immune cell subsets[36] and increase circulating numbers of Tregs in healthy individuals.[37] However, when considering the impact of exercise on individuals with SLE, immunological research is limited and conflicting.[38] For example, some studies report reductions in cytokines such as IL-6 and tumour necrosis factor alpha in response to regular exercise,[39] while others report no change.[40] As a result, it would be insightful to study the feasibility of remotely supervised exercise interventions for people with SLE and explore its impact on the peripheral blood composition and immunometabolic profile of T and B cell subsets associated with SLE pathology.

Aims

Primary: To examine the feasibility of conducting a subsequent randomised controlled trial (RCT) investigating

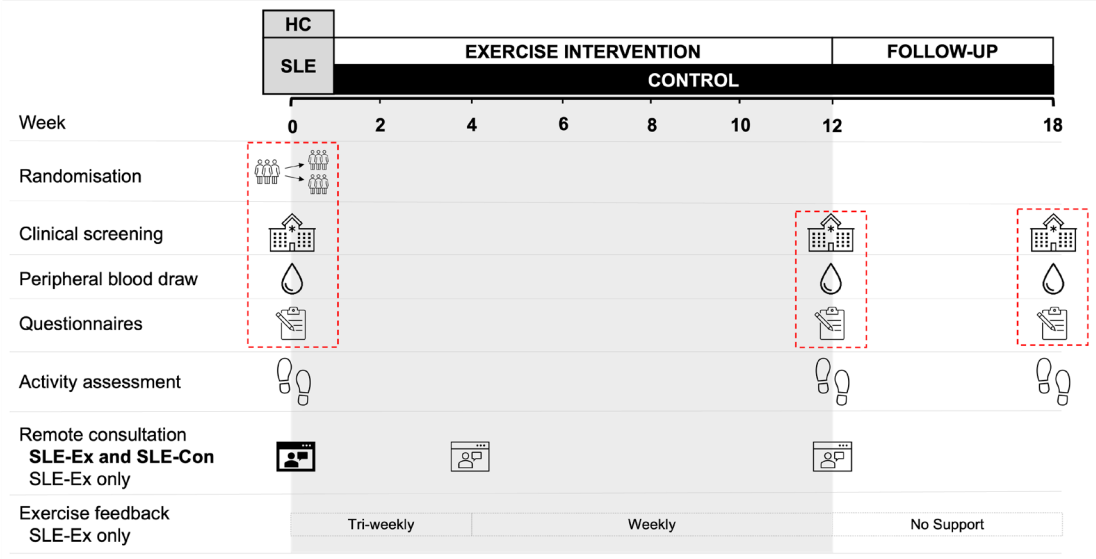

Figure 1 EXamining the feasibility of exerCisE to manage symptoms of Lupus (EXCEL) study design. HC, healthy control; SLE-Con, participants with SLE in the control group; SLE-Ex, participants with SLE in the exercise intervention group.

the effects of a 12-week, remotely monitored, home-based exercise intervention in individuals with SLE.

Secondary: EXamining the feasibility of exerCisE to manage symptoms of Lupus (EXCEL) will also explore whether 12 weeks of exercise training changes the frequency, phenotype and/or the metabolic profile of immune cell subsets in people with SLE. Clinical markers of disease activity and aspects of lifestyle and quality of life will also be determined.

METHODS AND ANALYSIS

Trial design

EXCEL is a prospective single-centre pilot RCT. People with SLE will be randomised into Exercise (SLE-Ex) or Control (SLE-Con) groups. SLE-Ex will complete a 12-week exercise programme, followed by a 6-week independent continuation period, and SLE-Con will continue with their habitual diet and activity levels for 18 weeks. Both groups will attend three research visits (at weeks 0, 12 and 18) during which measurements of general health, objective physical activity and lifestyle will be recorded. Blood samples will also be collected for exploratory analysis of clinical health and immunological outcomes. Age and body mass index (BMI)-matched individuals without SLE (HC) will also complete all procedures at week 0 for a baseline comparison (figure 1).

Setting and recruitment

The EXCEL study will be coordinated between the University of Birmingham and Sandwell and West Birmingham NHS Trust. Recruitment of 30 individuals with SLE will primarily be through NHS clinic lists within the trust; however, campaigns on the Lupus UK and EXCEL study websites, and social media platforms, will also be used. 15 healthy, age and BMI-matched control participants (HC) will be enroled towards the end of the recruitment window from the Birmingham community using social media campaigns.

Participant selection

To reduce the risk of biological sex-related differences confounding results, and to reflect the global prevalence characteristics, EXCEL will only recruit females with SLE. NHS trust staff will identify eligible individuals from secondary care records and make initial contact. Individuals expressing an interest in the study will be provided with a participant information sheet and given the opportunity to contact the medical team at Sandwell General Hospital for further information. Those wishing to take part will be invited to Sandwell General Hospital for a screening assessment by medical staff. Prior to this appointment, individuals will be asked to refrain from doing any strenuous exercise for 48 hours and to fast from midnight. Provided the criteria outlined in table 1 are met, informed consent will be obtained by medical staff (see online supplemental materials 1 and 2) and the participant will be enrolled and immediately complete baseline research visit procedures.

Randomisation

Participants with SLE will be assigned to a study arm (SLE-Ex or SLE-Con) using a balanced random permutated block method, and the online tool Sealed Envelope,[41] stratifying by age (<40 or ≥40) and BMI (<30 or ≥30). Although disease severity will be scored during screening, participants will not be stratified by these values before analysis. Allocations will be held by the University of Birmingham research team. The nature of the trial prevents participant, researcher or staff blinding.

Table 1 EXCEL inclusion and exclusion criteria

Inclusion criteria (all participants)	Aged 18 years or older.
	Female.
Inclusion criteria (SLE only)	Clinically stable disease activity as assessed by a member of the medical team (deemed eligible for inclusion if they have no A or B scores in the BILAG 2004 index).
	Participant and consultant feel they are able to exercise safely (PAR-Q screening, see online supplemental file 4).
Exclusion criteria	Increase to the dosage of current lupus-specific medications (eg, steroids, antimalarial medications and/or immunosuppressants) within the last 3 months.
	Addition of new lupus-specific medications (eg, steroids, antimalarial medications and/or immunosuppressants) within the last 3 months.
	Patients with inactive SLE but in whom there is a planned change in medication.
	Pregnant or planning pregnancy.
	Currently engaging in ≥60 min of moderate-intensity exercise or ≥30 min of vigorous-intensity exercise per week.
	Have uncontrolled blood pressure.
	Additional health conditions that might incur risk.
	Not owning a smart device or having no access to Wi-Fi or mobile data.

BILAG, British Isles Lupus Assessment Group; EXCEL, EXamining the feasibility of exerCisE to manage symptoms of Lupus; PAR-Q, Physical Activity Readiness Questionnaire.

Outcome measures

Feasibility and acceptability assessment

Primary outcome measures for the EXCEL study are outlined in table 1. Medical staff will record the total number of patients who were approached, were eligible and consented to take part in the study. Where possible, feedback from individuals that expressed interest but subsequently declined to participate will be recorded. The research team will calculate recruitment as the percentage of the target (30 individuals) met at the end of the recruitment period. Adherence to the exercise intervention will be monitored using data from mobile health (mHealth) technology and is defined by the number of exercise sessions completed as a total of the number of sessions prescribed. Compliance to moderate and vigorous-intensity prescriptions for each session will be based on the achievement of the minimum prescribed Heart Rate Physical Activity Score, as previously described.[42 43] Compliance to lower intensity exercise will alternatively be defined as completing the prescribed duration of the session. Completion will be measured as the number of participants (as a percentage of those recruited) that attend research visit 3, and the total number of dropouts will also be reported, with reasoning if provided.

Anthropometrics and blood pressure

At each research visit, trained medical staff with relevant research experience will record the following general health measurements; height, weight, waist circumference (taken in the area between the ribs and iliac crest), hip circumference (at the level of maximum width of the buttocks), blood pressure and pulse rate.

Blood sampling

A 40 mL venous blood sample will be collected at each visit; 30 mL collected in sodium heparin vacutainers, 6 mL in EDTA vacutainers and 4 mL serum-activated vacutainers. For SLE-Ex and SLE-Con participants, additional blood samples (14 mL) for standard-of-care tests (biochemistry, autoimmune serology and complete blood cell count) will also be collected at each research visit and processed at Sandwell General Hospital. Research samples will be transported to the University of Birmingham for processing. Isolated plasma and serum will be stored at −80°C, and peripheral blood mononuclear cells (PBMCs) isolated from heparinised blood will be stored overnight at −80°C and then transferred to liquid nitrogen storage at the Human Biomaterials Resource Centre, University of Birmingham.

Participant questionnaires

On visit 1, all participants will complete two questionnaires—Multidimensional Fatigue Inventory[44] and Pittsburgh Sleep Quality Index[45]—to capture perceptions of lifestyle habits and quality of life. A third questionnaire, the Lupus Quality of Life (Lupus QoL),[46] will be completed by SLE-Ex and SLE-Con. All three questionnaires will be repeated on week 12 and week 18, as part of research visit procedures, for SLE-Ex and SLE-Con only. An additional open-ended feedback questionnaire will be completed by the SLE-Ex group at the end of the study to assess the acceptability of the intervention (see online supplemental material 3, 5, 6, 7).

Activity assessment

At research visit 1, all participants will be provided with a wrist-worn triaxial accelerometer (GENEActiv,

Table 2 Details of remote consultation and counselling sessions provided throughout the EXCEL study

Date	Details	Applicable group		
		SLE-Ex	SLE-Con	HC
Week 0	Discuss benefits of exercise, assess preferences and concerns and agree on a SMART exercise plan.	✓	X	X
Week 0	Explain how to use mHealth equipment.	✓	✓	X
Weeks 3–4	Review of progress and, if necessary, adjust exercise plan.	✓	X	X
Week 12	Review of progress, participant feedback and discussion on strategies for maintaining exercise.		X	X

EXCEL, EXamining the feasibility of exerCisE to manage symptoms of Lupus; HC, healthy control; mHealth, mobile health; SMART, Specific, Measurable, Achievable, Relevant and Time-bound.

Activinsights, Kimbolton, Cambridge, UK). Accelerometers will be initialised by the research team beforehand to set start and end recording time. Participants will be asked to wear the monitor for the proceeding 7 days ensuring a minimum wear time of 16 hours/day for four weekdays and one weekend day. SLE-Ex and SLE-Con participants will wear an accelerometer on two further occasions (weeks 11–12 and 18–19). Associated data will be downloaded using the manufacturers' software and processed in R (R Core Team, Vienna, Austria) using the manufacturers' analysis tool (https://activinsights.com/support/geneactiv-support/).

Intervention methods

SLE-Ex: exercise programme

On week 0, SLE-Ex will attend their first exercise consultation (via video call) to discuss the benefits of regular exercise and assess individual preferences and concerns related to exercise (table 2). A Specific, Measurable, Achievable, Relevant and Time-bound physical activity plan will then be codesigned with support from the research team. The type of activities included in each plan will differ based on participant feedback, previous experience and access to equipment; however, all programmes will aim to gradually increase exercise intensity and duration over 12 weeks, with the ultimate goal of achieving 150 min of moderate-intensity or 90 min of vigorous-intensity exercise per week. Participants will have access to three example exercise programmes (www.motivateljmu.com/excel-videos) focused on cardio, strength and high-intensity interval training, which include example exercise videos for each training session. A fourth series containing light-intensity exercise videos created by Lupus Europe (www.lupus-europe.org/videos-on-demand/) will also be included for participants to use when disease symptoms prevent moderate to vigorous-intensity training.

SLE-Ex: mHealth equipment

SLE-Ex will be provided with a Polar Verity Sense heart rate monitor and a Polar Ignite 2 fitness watch (Polar Electro, Finland). Both devices will be linked via Bluetooth to the Polar Flow mobile app where participants will be able to access their exercise programme. The fitness watch will be worn as much as possible and provides access to exercise sessions preset by the research team. Haptic and visual feedback on prescribed intensity (via heart rate) and duration of sessions will also be provided through the fitness watch. Due to the reduced accuracy of wrist-worn heart rate monitors,[47 48] participants will also be asked to wear the Verity Sense monitor during structured exercise sessions. SLE-Ex will learn how to use mHealth equipment during a second exercise consultation session on week 0 (table 2).

SLE-Ex: exercise counselling

Participants will be encouraged to leave comments via the Polar Flow app after each exercise session they complete. These data, along with metrics from heart rate monitoring equipment, will be used to generate personalised feedback sent via text after each session up to week 4. This communication will also be used during a third consultation on weeks 3–4, to review progress and refine the physical activity plan ensuring that each programme fits with participants' needs and lifestyle. Beyond this point, participants will receive weekly feedback on their progress. At the end of the intervention (week 12), SLE-Ex will have a fourth consultation to review progress and discuss strategies for maintaining exercise in the future (table 2).

SLE-Ex: follow-up period

From weeks 13–18, SLE-Ex will be encouraged to continue exercising independently. Participants will remain in possession of mHealth technology, and moderate to vigorous exercise data will be collected; however, feedback and support from the research team will stop.

Control group methods

SLE-Con

SLE-Con will be encouraged to maintain their usual diet and habitual activity throughout the 18-week study. Participants will be provided with Polar Verity Sense optical heart rate monitor (Polar Electro), linked via Bluetooth to the Polar Flow mobile app, and attend a consultation session to learn how to use the device on week 0 (table 2). SLE-Con will be asked to record any structured exercise

Table 3 Parameters measured and tests conducted throughout EXCEL

Measured	Measurement strategy	Outcome
Primary		
Feasibility of the intervention	Ongoing measurements throughout the study	► Number of patients approached, eligible and consented ► Recruitment ► Adherence and compliance to exercise ► Completion ► Number of dropouts (with reasoning)
Acceptability of the intervention	Open-ended feedback questionnaire	Affective attitude and perceived effectiveness
Secondary		
Exercise adherence and compliance	mHealth equipment (heart rate monitor and fitness watch)	► Number of planned sessions completed ► Duration of session ► Exercise intensity by heart rate measurement
Habitual exercise	mHealth equipment (heart rate monitor only)	► Number of exercise sessions completed ► Exercise intensity via heart rate measurement
Activity assessment	GENEActiv accelerometer	Number of steps, minutes of MVPA, minutes of sedentary activity and minutes of non-wear
Anthropometrics	Site staff at research visits	Height, weight, body mass index, hip circumference and waist circumference
Blood pressure	Site staff measure at research visits	Systolic and diastolic blood pressure and pulse rate
Standard-of-care haematological measures	Fasting blood collection at research visits	► Full blood count (eg, total white blood cells, lymphocytes, monocytes and neutrophils) ► Lipid profile (LDL, HDL and triglycerides) ► Liver function (ALT, ALP, albumin and bilirubin) ► Kidney function (potassium, sodium, urea, creatinine, eGFR) ► Disease biomarkers (complement protein 3 and protein 4, DNA antibodies) ► Inflammatory markers (CRP and ESR) ► HbA1c
Immunology	Fasting blood collection at research visits	1. Immunophenotyping of the following lymphocyte subsets: ► CD8+ naïve/memory T lymphocytes ► CD4+ naïve/memory T lymphocytes ► Th17 and CD25+ Treg ► DN T lymphocytes ► CD19+ naïve/memory B lymphocytes 2. PlasmablastsBioenergetic profiling of PBMCs: ► Basal respiration ► Proton leak ► ATP production ► Maximal respiration ► Spare respiratory capacity 3. Glycolytic fluxImmunoassays of plasma/serum cytokine concentration: ► IL-6 ► IL-10

ALP, alkaline phosphatase; ALT, alanine transferase; CRP, C reactive protein; DN, double-negative; eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; EXCEL, EXamining the feasibility of exerCisE to manage symptoms of Lupus; HDL, high-density lipoprotein; IL, interleukin; LDL, low-density lipoprotein; mHealth, mobile health; MVPA, moderate to vigorous physical activity; PBMC, peripheral blood mononuclear cell.

but will not receive any feedback on recorded activity. At the end of the 18-week study period, SLE-Con will be given the opportunity to trial the exercise intervention, with reduced mHealth equipment (fitness watch only) and reduced support from the research team; data will not be included in analyses.

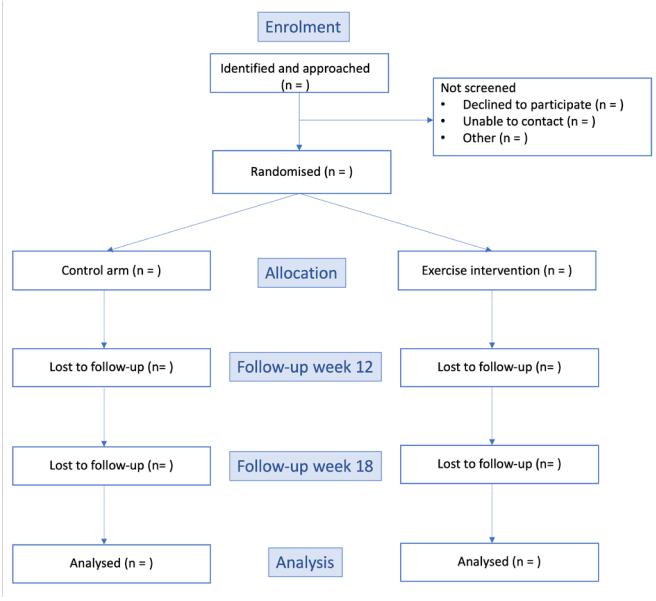

Figure 2 Consolidated Standards of Reporting Trials (CONSORT) diagram reflecting the flow of participants throughout the EXamining the feasibility of exerCisE to manage symptoms of Lupus (EXCEL) study.

Healthy Control

HC participants will not be supplied with mHealth technology and will not receive any feedback or exercise counselling.

Biological analysis

PBMC samples will be thawed and analysed by multicolour flow cytometry for immunophenotyping and bioenergetic profiles determined using the Seahorse XFe96 extracellular flux analyser (Agilent Technologies, USA). Immunoassays will be used to quantify concentrations of inflammatory cytokines in sera and plasma. Results from routine blood tests will also be shared with the research team to assess haematological parameters, blood lipid profiles, liver function, kidney function and biomarkers of SLE disease status (ie, autoantibody titres and complement protein concentrations). Full details of these outcome measures can be found in table 3.

STUDY MONITORING AND DATA COLLECTION

Medical management and safety

All participants will receive NHS standard of care alongside study procedures. The study team will be in regular contact with participants to minimise injuries and address any concerns. Any adverse events will be logged and reviewed by the research team and then referred to the local medical team.

Ancillary care

Participants suffering harm due to their trial participation will be covered. If any issues are raised that impact participants' mental health and well-being, we will signpost them to relevant mental health services (eg, Samaritans or MIND) and recommend discussing these matters with their general practitioner or secondary care consultant.

Data management

Data management with respect to the collection, storage, processing and disclosure of personal information will comply with the General Data Protection Regulation and Data Protection Act 2018. Data will be stored in line with the University of Birmingham's policy at the termination of the project and will be kept securely for 10 years following completion. Full details of these procedures can be found in Protocol version 4.0.

Study monitoring

Any monitoring activities will be reported to the Study Sponsor and Clinical Research Compliance Team at the University of Birmingham and any issues noted will be followed up to resolution. Additional internal quality checks may be triggered, for example, poor data quality, low protocol deviations or an excessive number of participant withdrawals or deviations. If an internal quality check is required, the Clinical Research Compliance Team at the University of Birmingham will contact the site to arrange a date for the proposed visit and will provide the site with written confirmation. The principal investigator will permit trial-related monitoring, quality checks, audits, ethical reviews and regulatory inspection(s) at their site, providing direct access to source data/documents. The principal investigator will comply with these visits and any required follow-up. Sites are also requested to notify the Trials Office of any Medicines and Healthcare products Regulatory Agency (MHRA) inspections.

Data analysis plan

Feasibility data relating to recruitment, dropout and completion will be presented in a Consolidated Standards of Reporting Trials diagram (figure 2). Qualitative data from acceptability questionnaires will be analysed to identify common positive and negative themes and illustrated with quotes. Secondary outcome measures will be reported using descriptive statistics and may be normality tested and subject to transformation. Differences between group means and within participants will be assessed with analysis of variance; p values <0.05 will be considered statistically significant.

Sample size

As the primary aim of this study is to assess feasibility, formal power calculations are not appropriate. Sample size has been estimated based on previous exercise interventions in patients with SLE,[25 26 49] accounting for typical dropout rates and patients undergoing SLE flares. We aim to recruit 15 individuals per study arm and 15 HCs.

Ethics and dissemination

A favourable ethical opinion was given by South East Scotland Research Ethics Committee (22/SS/0082). Guidelines from the International Conference on

Harmonization of Good Clinical Practice as well as the Declaration of Helsinki will be conformed to. The findings of this study will be disseminated at conferences and published in peer-reviewed journals.

Patient and public involvement

Individuals with SLE were invited to provide feedback on the study design prior to receiving funding. Patients' views on exercise manageability, the home-based approach and remote support elements were positive and helped inform the protocol design. Patient-facing documents (ie, Participant Information Sheet) were also reviewed and received good feedback. Patients will be included in the management group to help advise with recruitment, conduct and disseminate the results (eg, present to Lupus UK, to write for patient magazines and speak on local media). Any expenses associated with their help with be covered.

DISCUSSION

To the author's knowledge, EXCEL is the first study to assess the feasibility of conducting an RCT to investigate the effects of a remotely monitored, home-based exercise training programme on clinical, immunological and psychological aspects of health for individuals with stable SLE. A target of 30 individuals will be enrolled on the study, along with 15 age and BMI-matched HC participants for baseline comparisons. As a single-centre study with a limited sample size, the enrolled population will not be balanced by disease severity and/or current physical function; however, data from screening and questionnaire responses at week 0 may provide insight into such demographics. Individuals that do not have access to a smartphone or Wi-Fi will not be included in the study due to the use of mHealth technology. The authors acknowledge these criteria may prevent underprivileged populations from participating; however, remotely supervised exercise programmes reduce many other barriers to exercise participation (eg, membership costs, time efficiency and transport difficulty), are more economically viable for healthcare professionals and are well accepted by individuals with SLE.[25] Findings from this study will inform the design of future, larger scale interventions and contribute to the growing body of evidence supporting the inclusion of regular exercise into clinical care. Immunological analyses will also provide novel insight into the biological mechanisms by which exercise invokes clinical health benefits for individuals with SLE.

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Contributors AJW conceived the study, and together with JR, JVVZ and MC designed the protocol. KH, MC and SG provided resources and support with exercise procedures. MQ will coordinate the project and collect and analyse the data. MQ and AJW are equal guarantors and drafted the current manuscript using Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines (see online supplemental materials). All authors approved the final version.

Funding This work was supported by a grant from Lupus UK awarded to AJW (principal investigator), JR, MC and JVVZ.

Disclaimer The funder will have no role in the study design, data analysis/interpretation, manuscript writing or dissemination of results. The trial will be sponsored by the University of Birmingham who will oversee but will not have authority over study design; collection, management, analysis and interpretation of data; or writing of publications.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the South East Scotland Research Ethics Committee (22/SS/0082). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. No unpublished data are available for sharing.

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