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ActiLup: is it feasible? High-intensity interval training in systemic lupus erythematosus patients with fatigue: protocol for a prospective, monocentric proof-of-concept study

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ABSTRACT

The symptoms of active systemic lupus erythematosus (SLE) potentially lead to inactivity, muscle loss and social isolation. In addition to medical treatment, the current EULAR recommendations describe the relevance of physical activity, exercise and training as a non-pharmacological management option in patients with SLE. A positive interaction between fatigue and the basic health-promoting effects of exercise is well established. Still unclear is what kind of training, setting, and intensity show optimal objective and subjective outcomes. The study will include 40 adult SLE patients with moderate to severe fatigue. The study lasts 28 weeks and is divided into a 12-week "real-world" monitoring phase before rehabilitation, a 4-week inpatient rehabilitation phase, and a 12-week maintenance activity and training phase after the rehabilitation. The parameters consisted of physical performance parameters, laboratory parameters, physician and patient-related questionnaires and activity data based on a fitness watch. During rehabilitation, patients receive individual high-intensity interval training (HIIT), basic endurance training and functional interval training. This proof-of-concept trial aims to investigate if high-intensity interval training is feasible and how VO2peak is increased. Additionally, the effect of the severity of fatigue measured by patient-related outcomes and the number of anti-NR2 antibodies is focussed. This study was approved by the Ethics Committee of the Medical Association of Rhineland-Palatinate and complies with the standards of the Declaration of Helsinki. All participants will sign a written informed consent. Trial registration number: DRKS00022933.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Physical activity and exercise's positive physical and psychological effects are well known and recommended in various guidelines. A positive interaction with fatigue is also described. In general, exercise has a dose-dependent effect on health, and high-intensity interval training (HIIT) seems more time-efficient and shows higher cardiorespiratory outcomes than low-intensity interventions.

WHAT THIS STUDY ADDS

⇒ In this proof-of-concept trial, day-to-day physical activity is tracked for 12 weeks in advance of the intervention, to provide a general overview of the activity level in patients with systemic lupus erythematosus (SLE). While moderate activity intensities are recommended, the study focuses on HIIT, which is not established and is regularly performed in rheumatic diseases, especially SLE. The main question is whether five additional training sessions per week during inpatient rehabilitation are feasible and how cardiorespiratory fitness is affected in patients with fatigue.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Based on the results, further studies will compare the effectiveness and feasibility of different types of training to provide the optimal objective and subjective outcomes of defining training and exercise as the important adjuvant treatment in SLE management in accordance with the current European Alliance of Associations for Rheumatology recommendations.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a relapsing, chronic inflammatory disease of unknown aetiology that can affect almost any organ.

Current data for Germany estimates a prevalence of 79.8/100 000 in women and 13.8/100 000 in men, respectively, within a range of 0.037%–0.14%.[1 2] Despite the improvement in overall survival rates in the recent past, a plateau has developed in the last 10 years, showing that 18% of lupus patients in developed Western countries still do not survive 15 years.[3]

The symptoms of SLE are very heterogeneous. Patients' clinical symptoms range from non-specific general ailments such as

fatigue, fever and weight loss to skin conditions, osteoporosis, severe renal and central nervous system disorders and increased cardiovascular risk.[4–6] From a physical perspective, patients with SLE show impaired aerobic capacities of 18.8–25.78 mL/kg/min VO2max and only met 11%–29.8% of the WHO's activity recommendations.[7–13]

Additionally, regarding medical treatment, increasing physical performance is a possible approach to treat fatigue and prevent cardiovascular diseases. The current update of the European Alliance of Associations for Rheumatology (EULAR) recommendations for the non-pharmacological management of SLE and systemic sclerosis lists physical exercise as a complement to adequate medical treatment, which should be considered for patients with SLE.[14] In addition, weight control, blood pressure, and lipid and glucose regulation should be emphasised.[15]

The beneficial effects of physical activity and exercise in rheumatic diseases are well described and were implemented in several rheumatic disease-specific recommendations.[16–19] Furthermore, a positive effect on potential disease-associated symptoms such as fatigue is also shown and recommended.[7 19–28]

Additionally, a rheumatic disease inflammation regulation model was established for exercise, and there is a consensus that physical activity interventions generally do not increase the health risk for patients.[23 29–31]

For SLE, an increasing yet small number of studies and reviews with meta-analysis exist to explore the effect of strength and endurance training.[7 11 13 23 24 26 27 32–41] Usually, moderate training intensities with a maximum of three training sessions per week in an ambulant or group setting are described.[7 23]

Exercise has a dose-dependent effect on health. Therefore, high-intensity interval training (HIIT) seems to be more time-efficient and additionally shows a higher cardiorespiratory outcome than low-intensity interventions.[42–44] Boström *et al* describe their 1-year physical activity programme consisting of high-intensity aerobic exercise and strength training twice a week, which positively affects VO2, physical activity level and mental health.[45]

Nevertheless, there is still a lack of studies comparing different intensities, types and training settings, especially those focusing on training with a high cardiorespiratory load.

Focusing on quality of life (QoL), it appears that fatigue, a rather subjective symptom with partly unknown pathophysiology, may have a greater impact on QoL than disease activity or the damage index of SLE.[46 47] Often described as a constant feeling of exhaustion, fatigue affects physical activity and psychological aspects of life and is associated with abnormal illness behaviour and frequent work disability.[48]

This highlights the importance of chronic fatigue as an SLE-associated complaint, occurring in 67%–90% of patients regardless of ethnicity.[48 49] Many of these patients report fatigue as the most limiting disease symptom.[47] Therefore, the disease itself, in combination with the associated fatigue, leads to increased social isolation, inactivity, muscle atrophy and depression.[7 50 51] The aetiology of fatigue is not yet fully understood. A multifactorial pathogenesis is discussed.[52]

However, the success of medical treatment, for example with belimumab, supports the assumption that fatigue is at least partly caused by antibodies or can be improved by reducing antibodies.[53] In addition, it was found that therapy with belimumab significantly improves health-related QoL, which can improve additional factors crucial for the patient, such as the ability to work and well-being.[54]

Recently, the presence of anti-N-methyl-D-aspartate receptor antibodies (NMDA) in rheumatic diseases was shown. Additionally, a correlation between the concentration of the subunit NR2 antibodies against the NMDA-receptor (anti-NR2 antibodies) and the severity of fatigue, disease activity and anti-dsDNA antibodies was described.[53 55] Furthermore, a correlation between anti-NR2 antibodies in the brain and neuropsychiatric symptoms, cognitive dysfunction, decreased short-term memory and learning and depression was already addressed.[56–58]

This trial aimed to investigate how and whether a 4-week inpatient HIIT training is feasible in patients suffering from SLE and how high the VO2peak (1) increase is compared with the literature. Additionally, a 12-week home-based training was performed after a 4-week inpatient rehabilitation. In advance of the intervention, daily physical activity was tracked to offer the opportunity to classify and compare the physical activity level of patients with SLE for 12 weeks.

The secondary aim of this trial was the effect of HIIT on fatigue, measured by patient-related outcomes and the number of anti-NR2 antibodies (2) in patients with SLE.

Further considered aims were to determine the effect on further parameters such as cardiorespiratory fitness (3), general physical activity level (4), disease activity (5), QoL (6) and the number of severe adverse effects (7). Additionally, patients treated with belimumab were compared with patients treated with other immunosuppressants/corticosteroids (8).

The concept behind the trial is quite straightforward. Patients with a severe disease like SLE, commonly suffering from fatigue, extend their physical fitness (VO2peak) as much as possible in a short time with high training loads in a medically controlled and supervised setting. The first small steps for a regular exercise and training regimen were set during inpatient rehabilitation before patients exercised for a longer period with independently monitored and tracked uploaded data.

Based on the results of this proof-of-concept study, further planned studies will compare the effectiveness and feasibility of different intensities, settings and types of training to provide the optimal objective and

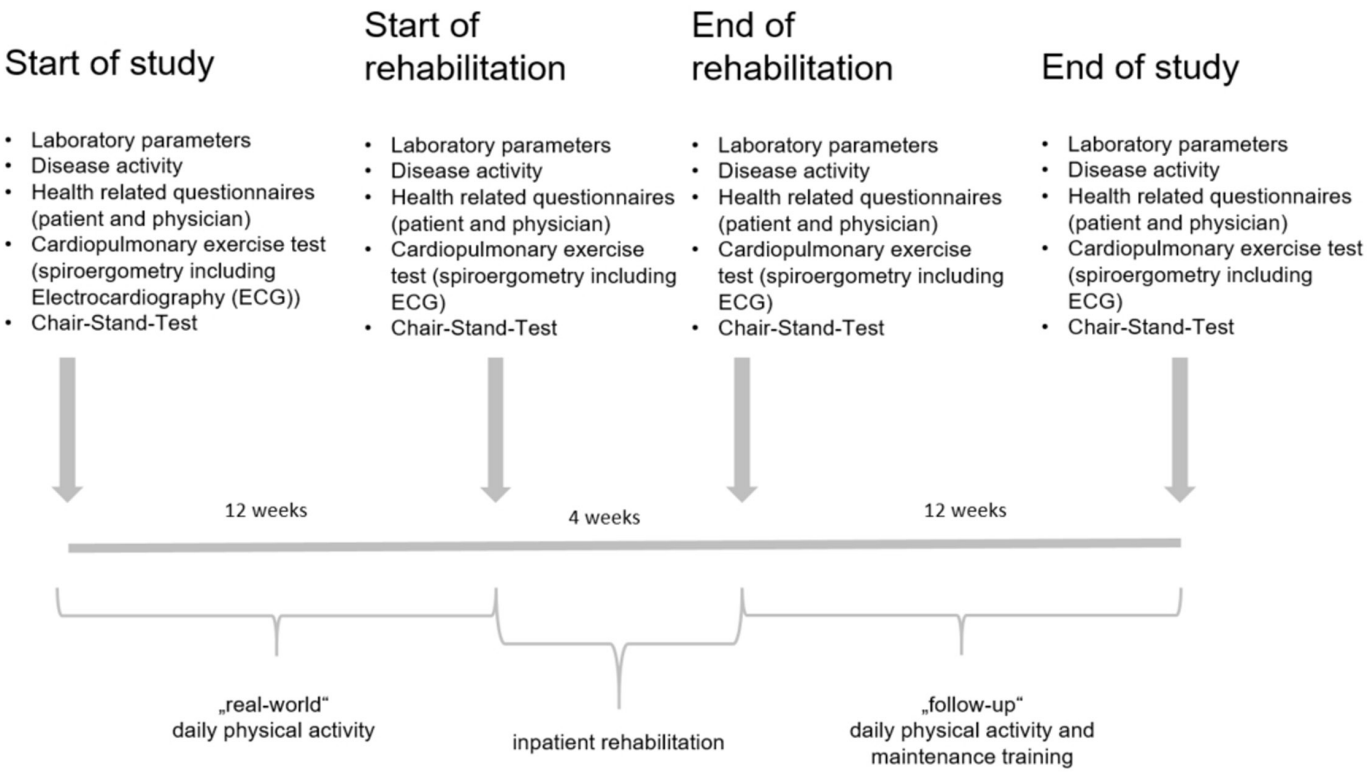

Figure 1 Timeline of the ActiLup study.

subjective outcomes if defining training and exercise as the important adjuvant treatment in SLE management in accordance to the current EULAR recommendations.[14]

METHODS

Study design

The study consisted of three sections with a total duration of 28 weeks, with a routine examination of each participant having four measurement time points (see figure 1).

In the first phase, patients' training and daily activities were recorded over 12 weeks under daily life conditions. For this purpose, all study participants received a fitness watch (Polar Ignite, Polar Kempele Finland). Independent of the study phase, the participants were asked to upload the data once a week to an online database (Polar Flow database—coaching module), which a sports therapist monitored.

In phase 2, all participants participated in a structured inpatient rehabilitation programme for 4 weeks at the Rheumatism Centre Rhineland-Palatinate in Bad Kreuznach. In addition to the rehabilitation programme, participants of the ActiLup trial performed five additional supervised training sessions per week.

In phase 3, physical activity and 3 weekly training sessions were conducted again for 12 weeks.

For the evaluation of the study results, laboratory parameters, disease activity scores and questionnaires (table 1) were collected during examinations, as well as a check of performance by means of cardiopulmonary exercise testing (spiroergometry and ECG) and chair-stand tests/sit to stand tests.

Recruitment

The study was open to patients aged 18–75 who meet the 2019 EULAR/American College of Rheumatology

Table 1 ActiLup inclusion and exclusion criteria

ActiLup inclusion and exclusion criteria	
Inclusion criteria	**Exclusion criteria**
Age ≥18 years	Therapy changes within the last 6 weeks
Diagnosis of SLE according to classification criteria	Major organ dysfunction (not related to active SLE)
Stable medication for 6 weeks	Chronic infections
Moderate to severe fatigue, according to the FSMC score	Other fatigue-related diseases, such as fibromyalgia, malignant diseases, pericarditis, myocarditis, anaemia, hypothyroidism or multiple sclerosis
German or English speaking	Conflict to maximum performance testing[63]
Written consent	Inpatient rehabilitation during the last 4 years
	Lack of ability to consent or doubts about the ability to consent

FSMC, Fatigue Scale for Motor and Cognitive Functions score; SLE, systemic lupus erythematosus.

classification criteria for SLE (>10 points).[59] In addition, the patient must be diagnosed with moderate to severe fatigue using the Fatigue Scale for Motor and Cognitive Functions score (FSMC). The patient must be treated with a biological or another immunosuppressant/corticosteroid and be adjusted to it. Written informed consent from the patient was a prerequisite for the study.

Exclusion criteria are refusal of the examination by the patient, lack of capacity to consent or doubts about the capacity to consent, insufficient knowledge of German, life-threatening situations, severe organ dysfunction (independent of SLE), existing pregnancy, chronic infections, a change in therapy within the last 6 weeks, diseases that can lead to fatigue (eg fibromyalgia, malignant diseases, presence of manifest heart involvement (pericarditis, myocarditis), anaemia, hypothyroidism or multiple sclerosis).

Patients were recruited by the Division of Rheumatology and Clinical Immunology at the University Medical Center in Mainz, Germany and the Rheumatology Center Rhineland-Palatinate, Bad Kreuznach, Germany.

Intervention

Fundamentally, this concept consists of three pillars. The total duration of physical activity and the exercise data collected was 28 weeks.

During the first 12 weeks, no intervention was performed, and daily physical activity data were tracked (eg step count and activity time) to provide a general overview of the physical activity level in patients with SLE.

In the second part of the study, all test participants received a structured endurance and strengthening programme adapted to the performance testing data, regardless of the medication used. The therapists and medical doctors closely monitored the patients during these 4 weeks. Due to the personalised performance recording and training control, the aim was to achieve optimal performance development of the patient. The patient was protected from overexertion or underexertion by means of conscientious risk assessment.

Endurance training took place in the aerobic or anaerobic range on the bicycle ergometer on the premises of the rehabilitation facility. The strength training units were carried out using the patient's body weight.

Both training methods were guided or supervised to avoid incorrect stress, overstraining and understraining.

In phase 3 of the study, patients received training information materials and illustrated exercise instructions for 3 weekly training sessions in paper or PDF format after the rehabilitation. This was to maintain activity on their own based on the exercise performed during the inpatient rehabilitation period while still being monitored.

Technical setup

The cardiopulmonary exercise tests (spiroergometry) were performed on a Geratherm Ergometer IQ-5, using a breath-by-breath method and with the Geratherm respiratory software V.1.3.06 and the AmedTEC ECGpro.

Data collection, exercise testing

All patients performed this test setup at each of the four visits.

Patients received a questionnaire to fill out and bring to the testing appointment 3 days before a testing day. After welcoming, the patient's weight and blood pressure were measured, and blood and urine samples were taken. Then, the 1 min chair-stand test was conducted.[60] There was a 60 min gap, at minimum, between the chair-stand test and the cardiopulmonary exercise testing.

Before exercise testing, a blood gas analysis and pulmonary function test were performed in accordance with current guidelines.[61] Three attempts at maximal expiratory flow volume loops were performed to measure forced expiratory volume 1 sec (FEV1, L), forced vital capacity (L) and peak expiratory flow (L/min).

For determining individual cardiopulmonary performance capacity at the four visits, a standardised stepwise bicycle ergometer test until exhaustion was performed. The performance protocol began with 3 min of resting on the ergometer and 1 min smooth pedalling without load. The initial load was 20 watts increasing by 10 watts every minute until participants exhaustion. The pedal rounds per minute should be 52–60 during the test. After completion, the load was reduced to 20 watts for 3 min. After every step, patients were asked to rate perceived exertion on the Borg scale. Every 3 min, blood pressure was measured. Completion criteria during the exercise testing were defined according to guidelines.[62] The analysed testing parameters were transmitted to the Polar Ignite watch.

Exercise and training programme

During the inpatient rehabilitation phase, the patients received an individualised exercise programme consisting of five training sessions per week in addition to the standardised rehabilitation programme according to the American College of Sports Medicine guidelines.[63]

One training session consisted of 30 min of ergometer training with a constant load at 70% heart rate peak (HR peak) based on the results of the exercise testing.

The two HIIT sessions had a duration of 38 min, divided into a 10 min warm-up (70% HR peak) and four high-intensity sections with a duration of 4 min per section (85–95 HR peak) intermitted by a 3 min active regeneration pause with a load of 70% HR peak. The last regeneration interval is the cool-down phase.

The two functional HIIT sessions (endurance and strength) use a slightly modified tabata protocol.[64] The 20 sec performance time with high subjective intensity and the 10 sec break within the 4 min training section are maintained while two exercises are always performed four times alternately. A warm-up (70% HR peak) and an individual cool-down, each lasting 4 min, were conducted at the beginning and the end.

During the main training session, five sections for different body areas were performed (squats and good mornings with raised arms, push-ups and superman's,

sit-ups and hip-raises, dips and steps, butterfly reverses and leg levers).

The training during the follow-up phase consisted of 1 week out of two constant HR training sessions (30 min) and one functional training session. In contrast, in the other week, two functional training sessions and one constant HR training session (30 min) were performed with a minimum regeneration time of 48 hours between the training sessions.

Adherence and tolerability

During the inpatient training, a sports therapist introduced the patients to the additional training sessions in the rehabilitation training facility and supervised the training sessions. The Polar Ignite watch recorded the physical activity in general and the training sessions.

The tolerance of the training, particularly the HIIT, was explored by disease activity with flares.

Outcomes

The study's main purpose was to evaluate the interaction of physical activity and performance parameters with the fatigue level, considering various variables such as medication.

Primary outcome

The primary outcome measure is the increase of oxygen capacity mL/min/kg (VO2peak) during the three study phases with a focus on the inpatient rehabilitation phase and second on the effect of fatigue measured by the FSMC.[65 66] The Functional Assessment of Chronic Illness Therapy-Fatigue questionnaire and the laboratory parameter anti-NR2 antibodies were added to collect different aspects of fatigue.

Secondary outcome

Additional cardiopulmonary exercise parameters such as the FEV1, watt performance and the results of the chair-stand test were considered.

Furthermore, the disease activity, medication differences, patient-reported outcomes and domains related to physical activity were analysed.

An overview of the target variables, their type and the time of survey are listed in table 2.

Statistical analysis

Normal distributed continuous variables were presented as mean±SD and tested with a t-test for independent samples. Non-normally distributed variables were presented as a median with IQRs (first to third quartile) and compared by the Mann-Whitney U test. Categorical variables were represented as relative frequencies, and χ^2 test determined differences.

Spearman's correlation coefficient was determined to investigate the association between oxygen uptake or other parameters and continuous variables. Statistical analyses were performed with SPSS (IBM) and the statistical software R (V.4.3.1).

The primary analysis was done on all patients, and a two-sided significance level α=0.05.

Sample size/power calculation

The primary research question was to prove an increase in oxygen uptake from the beginning of the inpatient rehabilitation to the end. The target variable was the difference in the measured oxygen uptake values, recorded using cardiopulmonary exercise testing.

The calculation of the number of cases aimed to show a significant change in oxygen uptake from the start of rehabilitation to the end of rehabilitation.

Based on the literature, a mean difference of 1.85 mL/kg/min (95% CI 1.12 to 2.58) with an SD of 3.84 was determined to be.[23] The number of cases calculated was like a paired t-test. Assuming a power of 0.80, a two-sided significance level of 0.05, a mean difference of 1.85 and an SD of 3.84 resulted in a case number of 36 people. To account for potential drop-outs, the sample size was increased to 40 participants, resulting in a power of 0.84. The calculation used the power.t.test function in the statistical software R (V.4.3.1).

RESULTS

The initialisation of the study was in October 2020, and the first patient exercise testing was in January 2021. The unpredictable progression of the SARS-CoV-2 pandemic impacted the healthcare system's inpatient rehabilitation formula and influenced the ActiLup trial during recruiting. The study is planned to end in March 2025 (the last exercise testing).

Currently, 27 patients have already completed the study. At this time, six patients dropped out of the study: three due to SARS-CoV-2 infection, two due to non-approval of the inpatient rehabilitation and one due to personal reasons. No serious adverse events have been observed, and data collection is ongoing. Laboratory parameters such as anti-NR2 antibodies will be analysed after collecting all samples.

DISCUSSION

The potential benefits of physical activity and exercise in increased aerobic capacities, strength and QoL, and decreased depressive symptoms and fatigue were analysed in patients with SLE in a few previous studies.[7 23 67]

The relevance of additive non-pharmacological treatments such as physical activity and exercise are recommended in current SLE treatment guidelines.[14 15 19] The positive effects of HIIT have already been shown for chronic diseases such as cardiovascular, pulmonary and diabetes conditions.[68]

Currently, in rheumatology, the EXEheart trial uses HIIT in patients with inflammatory joint diseases, focusing on cardiovascular disease risk, showing positive results after intervention and after a 6-month follow-up.[69 70] In the case of SLE, a current abstract describes positive interim results of the combination of aerobic HIIT and resistance training when focusing on VO2max, watt load,

Table 2 Data collection overview

Outcome	Description	Time point
Patient-specific data		
Gender		Baseline
Age		Baseline
Ethnicity		Baseline
Family status		Baseline
Educational level		Baseline
Laboratory parameters		
ESR	Erythrocyte sedimentation rate	Baseline, week 12,16, 28
CRP	C reactive protein	Baseline, week 12,16, 28
Complement level	C3 and C4 levels C3: 0.9–1.8 g/L; C4: 0.1–0.4 g/L	Baseline, week 12,16, 28
Autoantibody titre	dsDNA titre (≤20 IU)	Baseline, week 12,16, 28
Anti-NR-2-antibodies	Anti-N-methyl-D-aspartic-acid receptor 2	Baseline, week 12,16, 28
Urine		Baseline, week 12,16, 28
Cardiopulmonary exercise and strength test		
Peak oxygen uptake*	VO2peak, mL/kg/min and L/min	Baseline, week 12,16, 28
FEV1	Forced expiratory value in 1 s	Baseline, week 12,16, 28
Peak heart rate	HR peak, beat/min	Baseline, week 12,16, 28
VCO2	Ventilation of CO2	Baseline, week 12,16, 28
VT1	Ventilatory threshold 1	Baseline, week 12,16, 28
VT2	Ventilatory threshold 2	Baseline, week 12,16, 28
Watt		Baseline, week 12,16, 28
CST	Chair-Stand test (number of repetitions)	Baseline, week 12,16, 28
CVD risk factors		
BMI	Body mass index	Baseline, week 12,16, 28
Smoking status		Baseline, week 12,16, 28
Total cholesterol	(mmol/L)	Baseline, week 12,16, 28
HDL	High-density lipoprotein cholesterol (mmol/L)	Baseline, week 12,16, 28
LDL	Low-density lipoprotein cholesterol (mmol/L)	Baseline, week 12,16, 28
Triglycerides	Triglycerides (mmol/L)	Baseline, week 12,16, 28
Resting heart rate	(beat/min)	Baseline, week 12,16, 28
Disease specific parameters		
Duration of disease-specific symptoms		Baseline
Age at diagnosis		Baseline
Main symptoms		Baseline, week 12,16, 28
Comorbidities		Baseline, weeks 12, 16, 28
Medication	Belimumab group and non-belimumab group	Baseline, week 12,16, 28
Disease activity	Visual Analogue Scale 0–100 (Medical doctor and patient's perspective)	Baseline, week 12,16, 28
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index. 24 items, including laboratory in clinical parameters, within the last 10 days.	Baseline, week 12,16, 28
ECLAM	European Consensus Lupus Activity Measurement 12 items, including laboratory in clinical parameters.	Baseline, week 12,16, 28
Safety parameters	Number of flares	Week 28

Continued

Table 2 Continued

Outcome	Description	Time point
Patient-related outcomes		
FSMC	The Fatigue Scale for Motor and Cognitive Functions scale: 20 items that measure both motor and cognitive fatigue.	Baseline, week 12,16, 28
FACIT-F	Functional Assessment of Chronic Illness Therapy-Fatigue: 13 items to record fatigue within the last 7 days.	Baseline, week 12,16, 28
BDI	Beck Depression Inventory 21 items that survey the severity of depression.	Baseline, week 12,16, 28
SF-36	36-item Short-Form Survey 8 disease unspecific dimensions include vitality, physical functioning, physical pain and psychological parameters.	Baseline, week 12,16, 28
WAI	Work Ability Index 7 dimensions of workability, such as current workability, diagnosed diseases, mental capacities and sick leave.	Baseline, week 12,16, 28
SLEQoL	Systemic Lupus Erythematosus Quality of Life Questionnaire 40 items across 6 domains (physical functioning, activities, symptoms, treatment, mood and self-image).	Baseline, week 12,16, 28
Physical activity parameters		
BQHPA	Baecke Questionnaire Person's Habitual Physical Activity Evaluates physical activity over the previous 12 months. 16 questions to assess work, sport and leisure time physical activity.	Baseline, week 12,16, 28
IPAQ	International Physical Activity Questionnaire Evaluates physical activity over the previous 7 days using 7 questions.	Baseline, week 12,16, 28
Physical activity duration	Minutes per day, measured by Polar Ignite	Baseline, week 12,16, 28
Exercise duration	Minutes per day, measured by Polar Ignite	Baseline, week 12,16, 28
Step count	Steps per day, measured by Polar Ignite	Baseline, week 12,16, 28
Estimated calories	Calories per day, calculated by Polar Ignite	Baseline, week 12,16, 28

*Primary outcome.
CVD, cardiovascular disease.

subjective disease activity, mental health, vitality and physical and social functioning.[71] Furthermore, a trial describes a 12-week internet-based individualised exercise programme in patients with SLE and differentiates between anaerobic and aerobic training.[72]

Currently, 27 patients of the ActiLup trial have already completed the study. No flare or adverse events have occurred to date, which is in accordance with the literature that physical activity is safe and does not increase disease activity in patients with SLE.[7 11 32] Preliminary and presented results of ActiLup are promising.[73]

After the study, the Polar Ignite watches were given to the participants to keep them motivated. It is shown that wearable fitness trackers can motivate and increase physical activity in potentially sedentary individuals.[74] The opportunity to monitor the patients online offers different approaches to quality control and exercise supervision.

Additionally, it is to our knowledge that this is one of the few trials which track the physical activity of patients with SLE during 12 weeks prior to rehabilitation in a daily setting because there is a lack of knowledge of the general activity patterns, which might offer valuable data for activity time, sedentary time and step count.

Based on the results, further planned studies will compare the effectiveness and feasibility of different types of training like strength, endurance, supervised and independent training, to provide the optimal composition of objective and subjective outcomes if training and exercise are taken into account as the important adjuvant part in SLE management as described in the current EULAR recommendations.[14]

Nevertheless, our study shows some limitations. We do not have a randomised controlled design; therefore, the surveyed data can only be compared with the literature. During the standardised inpatient rehabilitation programme, moderate physical activity interventions were performed in accordance with current recommendations.

The focus was to prove the feasibility of HIIT training, the potential increase of performance parameters within 4 weeks and the successful implementation of a

study design in a standardised inpatient rehabilitation programme. Further studies will consider these points.

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Contributors MD was the study's project manager and was responsible for data collection. He was involved in data analysis and wrote the applications and the final manuscript for AS, SP, SE, LG and TW. SP was the responsible medical doctor for the study. SE, LG and TW collected the data. In addition to MD, AS was the guarantor and the principal investigator of this study. He was responsible for the overall content, initiated the idea and the design.

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Competing interests None declared.

Patient and public involvement The design of the ActiLup trial was developed as closely as possible to the current protocol guidelines. SLE-patients of the University Medical Center of the Johannes Gutenberg University Mainz and the Rheumatology Center Rhineland-Palatinate were asked for relevant research questions and methodical practicability. Additionally, the study was presented in the development stage to the regional patient association.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants and was approved by Ethics Committee of the Medical Association of Rhineland-Palatinate (Approval ID number: 2020-15357). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; internally peer reviewed.

Data availability statement Data sharing not applicable as no datasets generated and/or analysed for this study.

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