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Can exercise reduce disease activity in people with type 1 diabetes?

Submission date
19/01/2022

Recruitment status
No longer recruiting

Registration date
20/01/2022

Overall study status
Completed

Last Edited
03/09/2024

Condition category
Nutritional, Metabolic, Endocrine

[X] 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
Type 1 diabetes (T1D) causes the level of glucose (sugar) in your blood to become too high. Some of the body's own white blood cells attack the pancreas and stop insulin production, resulting in high blood sugar. This process is more prominent during the early stages of the disease. Regular participation in exercise is key to supporting health and wellbeing in people with T1D but it is not clear how regular exercise impacts these white blood cells in patients with new-onset T1D. This project will use a popular and effective home-based exercise program that links to the research team via a mobile phone application. We will test whether this program slows the progression of T1D by altering white bloods cells so they do not attach and enter the pancreas.

Who can participate?
Patients aged over 18 years who have been diagnosed with T1D within three years and that are not highly physically active (less than 150 minutes of structured exercise per week).

What does the study involve?
Participants will undertake a 12-week exercise intervention or control arm in a randomised order, with a 12-week study break (washout) in-between. In the exercise arm, participants will be given a wrist worn fitness watch (Polar Unite) and access to a free online training App (Polar Flow). The fitness watch will act as a personal trainer on the wrist, giving guidance and feedback during exercise on how to complete the planned sessions. The exercise sessions will consist of body weight exercises done at a high intensity (based on heart rate), with the volume of training progressively increasing throughout the 12-week period. In the control arm, participants will continue with their normal levels of activity, with heart rate monitored for each structured exercise session. Before and after exercise intervention and control arms, participants will visit a clinical research facility to donate a blood sample and undertaken various general health and diabetes measurements.

What are the possible benefits and risks of participating?
Benefits
1. Work from our group and Diabetes UK suggest that ≈ 70% of T1D patients do not meet the recommended exercise guidelines; however, our intervention has been shown to be effective

and very popular with patients (≈ 95% adherence). This is important given that there are many barriers to exercise in patients with T1D, including fear of low blood sugar and undertaking exercise outside of their home. It is anticipated that our intervention will encourage patients to uptake this form of exercise as part of their daily lives, educate them on the use of the technology, as well as how to manage this mode of exercise around their diet and insulin injections. This study will enable us to understand how acceptable and feasible a national roll out of this exercise programme is for patients.

2. Participants will be provided with four Abbott Freestyle Libre flash glucose monitor sensors, enough to monitor glucose levels for 8 weeks over the study period. Although participants will be blinded to these during the intervention periods the data collected is likely to be useful to the participant by indicating how exercise affects the regulation of their blood sugar levels.

Risks
1. Participants will exercise under our remote guidance at home for 12 weeks. Exercise can elicit low blood sugar episodes in patients with type-1 diabetes. A body of literature favours the mode of exercise used in this project (i.e., high intensity interval exercise) over continuous moderate intensity exercise for maintaining blood glucose control during exercise. Our intervention has been validated in patients with T1D and is safe, feasible and popular with patients. We will give extensive training to patients on how to manage their diet and insulin injections around exercise. Diabetes consultants on our research team have designed an education package for patients with T1D that gives practical advice on how manipulating diet, exercise and insulin can influence blood glucose concentrations. This information will be made available to the patients in this study verbally and in a PDF document.
2. The venepuncture site of blood collection may bruise, and there is a potential for infection. We will minimize these risks by following good clinical practice and having all procedures conducted by trained, experienced phlebotomists.

3. The maximum total amount of blood taken in this study in a single day will be 50mL. It is safe to provide this amount of blood during a study visit. There are no adverse effects to expect from this procedure, and this will not prevent participants from donating blood. A conservative upper limit of no more than 125mL of blood should be drawn from any donor within a 24-hour period, and 250mL within 30-days. Withdrawing this quantity of blood is reasonable for adults of a healthy weight (≈2.5% and 5% of total blood volume (≈5 Litres) over 24-hours and 30-days respectively).

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

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

Who is funding the study?
Rosetrees Trust (UK)

Who is the main contact?
Trials Email Address: extod-immune@contacts.bham.ac.uk
Miss Megan Quickfall (lead researcher): vmq142@student.bham.ac.uk
Dr Alex Wadley (chief investigator): A.J.Wadley@bham.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
303066

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 51032, IRAS 303066

Study information

Scientific Title
Can a remotely monitored, home-based exercise intervention for individuals with type 1 diabetes reduce immune-driven disease activity?

Acronym
EXTOD-Immune

Study objectives
White blood cells with an affinity to degrade the pancreas will decrease following the exercise intervention, but not the control period

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, Newcastle North Tyneside Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 2071048255; newcastlenorthtyneside1.rec@hra.nhs.uk), ref: 21/NE/0211

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Type 1 diabetes

Interventions
Patients with new-onset type 1 diabetes will be randomised into a control group or validated home-based exercise program, each for a period of 12 weeks, separated by a 12-week washout period.

Exercise Intervention Arm
Participants will undertake our validated 12-week home-based exercise programme following full instructions (coaching session 1). The programme consists of 3 sessions of high intensity interval exercise per week. Participants will wear a fitness watch that acts as a personal trainer on the 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 research team to help them provide personalised feedback throughout the programme:

1. For weeks 1-2 of the intervention, we will ask participants to:
• Perform a low intensity warm up for 3-minutes
• Perform 6 x 1-minute high intensity intervals, interspersed with 1-minute rest intervals (12 minutes). The exercise will be performed at an intensity that elicits 80% of maximum heart rate.
• Total exercise time will be 15 minutes.

2. For weeks 3-4 of the intervention, this will increase to 8 intervals (total exercise time will be 19 minutes).

3. For weeks 5-12 of the intervention, this will increase to 10 intervals (total exercise time will be 23 minutes).

Each interval will use bodyweight exercises, with each interval divided into two different bodyweight exercises performed for 30 seconds with no rest between exercises. Participants can choose from a selection of 18 exercise pairs (e.g., star jumps, burpees). The research team will provide weekly feedback on compliance with the planned exercise targets. During the first month of the programme participants will be asked to provide feedback on your exercise sessions via the training App. The research team will then also provide 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 (Coaching session 2). If necessary, the exercise programme will be modified based on these conversations

Control Arm
The control arm of the study is essential for us to evaluate natural changes in our primary outcome variable over time that aren't influence by the exercise intervention, During the control period, participants will not be given any structured advice on exercise, but normal physical activity is encouraged (e.g. walking to work or shops, or any sport you usually do). A Polar Verity Sense Heart Rate Sensor will give to patients to wear during any structured exercise sessions. Participants will receive no feedback from these sessions from the research team. During both of the study arms, we will ask participants to fill out questionnaire relating to levels of physical activity.

After the Study
Following completion of each study arm, participants will return the necessary equipment (heart rate monitor, wrist worn activity monitor and flash glucose monitor sensor and reader). A telephone and/or video call will be arranged to discuss participants progress with the training programme and how they could continue exercising (Coaching session 3). Acceptability of the intervention, levels of physical activity (GPPAQ), health-related quality of life (EQ-5D) and barriers to physical activity (BAPAD) will assessed via a questionnaire (week 36).

Intervention Type
Behavioural

Primary outcome(s)
White blood cells with an affinity to degrade the pancreas will be measured using flow cytometry before and after the 12-week exercise and control periods

Key secondary outcome(s))
1. C-peptide will be measured using ELISA before and after the 12-week exercise and control periods
2. Autoantibodies will be measured using ELISA before and after the 12-week exercise and control periods
3. Insulin dose will be recorded before and after the 12-week exercise and control periods
4. HbA1c will be measured using an automated HbA1c analyser before and after the 12-week exercise and control periods
5. Cholesterol will be measured using an automated analyser before and after the 12-week exercise and control periods
6. Glycaemic control over a 2 week period will be measured by continuous glucose monitoring before and after the 12-week exercise and control periods
7. Blood pressure will be measured using a sphygmomanometer before and after the 12-week exercise and control periods
8. Levels of physical activity will be measured using the General practice physical activity questionnaire (GPPAQ) before and after the 12-week exercise and control periods
9. Barriers to exercise will be measured using the Barriers to physical activity in type-1 diabetes (BAPAD) questionnaire before and after the 12-week exercise and control periods
10. Health related quality of life will be measured using the Health related quality of life (EQ-5D) questionnaire before and after the 12-week exercise and control periods
11. Acceptability/ enjoyment of the intervention will be measured using a validated questionnaire after the exercise intervention

Completion date
31/03/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 14/11/2023:

1. Aged over 18 years
2. Clinical diagnosis of T1D made within the last 3 years
3. Confirmed clinical diagnosis of T1D
4. Confirmed HLA-A2*0201+ genotype
5. Self administering their insulin as part of a multiple dose injection regime or insulin pump therapy.
6. Both participant and physician feel that they are able to exercise safely.
7. Patient is able to estimate carbohydrate content of meals
8. Patient is willing to test glucose and adjust insulin and carbohydrate doses accordingly
9. Patients will be able to recognise hypoglycaemic symptoms before capillary blood glucose falls to 3.5mmol/L
10. Compliance: understands and is willing, able and likely to comply with all study procedures and restrictions.
11. Consent: demonstrates an understanding of the study and willingness to participate, as evidenced by voluntary written informed consent.

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Previous inclusion criteria:

1. Aged over 18 years
2. Clinical diagnosis of T1D made within the last 1 year
3. Confirmed diagnosis of T1D via T1D-GRS2
4. Confirmed HLA-A2*0201+ genotype
5. Self administering their insulin as part of a multiple dose injection regime or insulin pump therapy.
6. Both participant and physician feel that they are able to exercise safely.
7. Patient is able to estimate carbohydrate content of meals
8. Patient is willing to test glucose and adjust insulin and carbohydrate doses accordingly
9. Patients will be able to recognise hypoglycaemic symptoms before capillary blood glucose falls to 3.5mmol/L
10. Compliance: understands and is willing, able and likely to comply with all study procedures and restrictions.
11. Consent: demonstrates an understanding of the study and willingness to participate, as evidenced by voluntary written informed consent.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Mixed

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 14/11/2023:

1. Uncontrolled blood pressure
2. Pregnancy or planning pregnancy
3. Currently engaging in more than 150 minutes of exercise per week
4. Additional health conditions that might put the participant at risk for this study e.g. cardiac disease, active proliferative diabetic retinopathy, autonomic neuropathy and/or a history of severe hypoglycaemia requiring third party assistance within the last 3 months. Any other condition (medical or psychological) that is deemed inappropriate will be at the PI's discretion.
5. Unable to provide full informed consent.

Previous exclusion criteria:

1. Uncontrolled blood pressure
2. Pregnancy or planning pregnancy
3. Adhering to the current recommended physical activity guidelines (> 150 minutes)
4. Additional health conditions that might put the participant at risk for this study e.g. cardiac disease, active proliferative diabetic retinopathy, autonomic neuropathy and/or a history of severe hypoglycaemia requiring third party assistance within the last 3 months. Any other condition (medical or psychological) that is deemed inappropriate will be at the PI's discretion.
5. Unable to provide full informed consent.

Date of first enrolment
01/03/2022

Date of final enrolment
31/03/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way

Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Musgrove Park Hospital
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Study participating centre
Liverpool John Moores University
School of Sport and Exercise Sciences
Tom Reilly Building
Liverpool
United Kingdom
L3 3AF

Study participating centre
Royal Free London NHS Foundation Trust
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Ipswich Hospital
Heath Road
Ipswich
United Kingdom
IP4 5PD

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Rosetrees Trust

Alternative Name(s)
Teresa Rosenbaum Golden Charitable Trust, Rosetrees

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

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

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		30/08/2024	03/09/2024	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes