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Personalised advice for breaking up prolonged sitting in people with type 2 diabetes

Submission date
21/08/2020

Recruitment status
No longer recruiting

Registration date
14/01/2021

Overall study status
Completed

Last Edited
18/01/2023

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Background and study aims
Spending a large amount of time sitting during the day, and particularly in prolonged unbroken bouts is known to have a negative impact on blood sugar levels. The good news is that regularly breaking up sitting time by doing simple activities, such as standing, stretching, etc. for a few min can be very effective at improving blood sugar levels as well as many other aspects of health such as the ability to perform daily tasks, heart health, and risk of developing foot ulcers. For example, in people with type 2 diabetes, research has shown that doing simple activities for 3 min every 30 min over a 6-8 h period significantly improves blood sugar control. The research team want to expand on this research by asking people with type 2 diabetes to take part in a 4-week programme designed to regularly break up sitting time throughout the day with a variety of simple activities. This study will test how well this programme works for improving blood sugar levels and various other measures of overall health.

Who can participate?
People with type 2 diabetes, aged 40-75, who meet all the inclusion criteria can participate

What does the study involve?
On giving signed consent, participants will be invited to attend a total of 4 visits to the research centre to have measures of their health taken. Participants will be asked to take part in a programme designed to regularly break up sitting time over a 4-week period during daily life (not at the research centre). There will also be two 8-day periods of wearing activity monitors and a glucose monitor (which measures the amount of sugar in the blood), once at the start and once at the end of the study.

Visit 1: 4-5 h
The first time participants come to the research centre will be for consent and baseline measurements. Participants will be asked to refrain from eating food and drinking anything other than water from the night before their appointment. They will also need to avoid alcohol, caffeine, and exercise 48 h prior to the visit, and avoid vigorous exercise 72 h before the visit. Participants are encouraged to take a finger prick test before travelling, and, if there is a risk of this, to call the trial team to reschedule their appointment. First, the inclusion and exclusion criteria will be reviewed to check that there are no issues. This may require a small fingerprick

blood sample to be taken. After this has been confirmed, the baseline measurements are as follows:

Anthropometric Measures
The study team will measure the participant's body composition (body weight and relative amounts of muscle, fat, etc.) using bioimpedance assessment. This device is very similar to a set of weighing scales. A small electric charge will pass through the body but should not be noticeable. Height and waist circumference will also be measured.

Resting Metabolic Rate
This will indicate how much energy is used by participants when at rest. From this, how many calories their body needs can be calculated. This will involve lying as still as possible (whilst remaining awake) under a clear hood. The test takes around 30 min.

Blood Sample
A sample of blood from a vein in the participant's arm will be taken to measure the levels of sugar and fat in the blood. Some blood will also be frozen to allow measurement of other markers of health-related to type 2 diabetes.

Health Questionnaires
Participants will be asked to complete a short questionnaire booklet which should take around 30 min to complete. This contains nine questionnaires which will ask about the participant's ability to perform various daily tasks, quality of life, breathlessness, anxiety and depression, chronotype (whether they are more of a morning or evening person), chronic pain, fatigue, and dietary intake.

Mixed Meal Challenge
The research team will provide a standard breakfast (options will be provided). They will then take small blood samples at 15-30-min intervals up to 3 h (15, 30, 45, 60, 90, 120, 150, 180 min). This will allow the study team to test the body’s response to food.

Physical Function
The research team will measure standing balance, usual walking speed, ability to stand from a chair, hand grip strength, and ask participants to perform a routing selection of activities which include: walking 50ft, putting on and removing a coat, picking up a penny, standing up from a chair, lifting a book, climbing one flight of stairs, and safely turning in a circle. Participants will also be asked to do a simple fitness test that involves walking between two points, 10 m apart. The speed of walking will be set to a recorded “beep”. The beep will get progressively faster until participants are no longer able to maintain the pace. These tests should take a total of around 20 min.

Physical Activity and Glucose Monitors
Participants will be given two small activity monitors to wear, one on the wrist and one taped to the leg. These will measure how much time is spent sleeping, sitting, and moving. Participants will also be given a continuous glucose monitor to monitor the changes in blood sugar throughout the day – attached to the arm. Participants will not be required to do anything to these monitors and they will be recording measurements without any input. They can be worn all day and night and whilst showering/bathing. Participants will be asked to fill out a wake and sleep log. All these devices will be worn for 8 days, starting on the day participants come to the research centre.

Visit 2: 6 h
The second visit to the research centre will be to undergo a 5.5 h period of sitting down with a simple 2 min physical activity breaks occurring every 20 mins to break up the sitting. This will give the study team a good understanding of how the body responds to different types of breaks in sitting. Once again, participants should attend this visit having not consumed food or drinks other than water since the previous evening, and breakfast will be provided. Participants will also be provided with a snack during the visit, but lunch will not be provided. If necessary /desired, lunch can be brought to consume at the end of the experiment. Participants will be invited to return the two activity devices (wrist and thigh) and be given two new ones to wear during the visit. The same continuous glucose monitor will be used until the end of the visit.

At various points throughout the day at the visit, we will be taking measurements for the following:

Muscle Activation
Participants will be given a pair of “smart shorts” to wear for the duration of the session. These shorts have electrodes embedded into the fabric which allow the assessment of which muscles are being activated and how much during each of the physical activity breaks. These are similar to cycling shorts and can be worn under normal clothes. If participants are not comfortable with this, then they can opt-out of this element of the study.

Breath Analysis
Around 5 min before the start of each of the 16 physical activity breaks, participants will be fitted with a mask which covers the mouth and nose and advised to keep their normal breathing pattern. This will allow for the measurement how difficult the activity is for the body. The mask will be removed at the end of the activity break.

Exertion, Pain, and Feelings
Towards the end of each physical activity break, participants will be asked to rate how difficult they think the activity was, how much pain the activity caused, and how pleasant/unpleasant they feel the activity was. The activities are simple, familiar movements, including stretches, squeezing a stress ball, and balancing on one leg.

Intervention
The following phase of the study is the 4-week intervention. Participants will be randomly assigned to one of two groups: to either receive generic advice on how to reduce sitting time; or to receive personalised advice based on the data collected in the previous two visits. Participants will also be given a choice from a variety of commercially available tools to help monitor sitting time. These will range from wristwatches (like the Fitbit) to mobile apps or computer programmes which keep track of sitting time. This may require participants to periodically upload data to a system which the research team can monitor. The research team will review the measurements that were taken at previous visits to design a personalised programme for participants to reduce their sitting time. This will include looking at sleep patterns, responses to food, and the reactions to different types of activities used to break up sitting. All participants will receive regular weekly contact from the study team to keep track of their progress.

Visit 3: 10 min
During the final 8-days of the intervention period, participants will return to the research centre for a short visit to be fitted with new activity devices and a continuous glucose monitor. These

should be worn until the end of the intervention. If preferred, it can also be arranged for the devices to be posted to participants and the research team will schedule a video call with to guide them through how they should be worn.

Visit 4: 4-5 h
Finally, participants will attend the research centre for one further session which will replicate Visit 1. Once again, they will need to come to this visit in a fasted state and breakfast will be provided. Participants will be asked to avoid alcohol, caffeine, and exercise 48 h prior to the visit, and avoid vigorous exercise 72 h before the visit.

What are the possible risks and benefits of taking part?
While there is no direct monetary benefit to taking part in the study, participants will receive data on their health which has been gathered from the study and will have access to any information which has been collected from them, including blood analysis, assessments of physical function, and glucose responses to consuming a meal.

Those who choose to participate in the study will be required to dedicate some of their time to be at the research centre. Participants may experience some bruising from the blood tests and may experience slight irritation from the activity and glucose monitors, although this is not common.

Where is the study run from?
Leicester Diabetes Centre, Leicester General Hospital (UK)

When is the study starting and how long is it expected to run for?
From October 2020 to April 2022

Who is funding the study?
The University of Leicester and the NIHR Senior Investigator Award (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
281671

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 281671

Study information

Scientific Title
bREaking up prolonged Sitting in People with type 2 diabetes: Optimising the respoNSE (RESPONSE) - a randomized controlled trial

Acronym
RESPONSE

Study objectives
A personalised approach to breaking up prolonged sitting time is more effective than a generic approach for improving glucose control in people with type 2 diabetes

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/11/2020, London – Surrey Research Ethics Committee (Nottingham Centre, The Old Chapel, Royal Standard Place, Nottingham, UK, NG1 6FS; +44 (0)207 104 8129; surrey.rec@hra.nhs.uk), ref: 20/LO/1102

Study design
Randomized controlled trial

Primary study design
Interventional

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Improving glucose control in people with type 2 diabetes

Interventions
This study consists of two distinct parts. Part 1 is a lab-based study and Part 2 is a 4-week intervention. This study has 2 randomisation elements. To determine the order of assessment activities during the 5.5 h sitting condition in Part 1 – Lab-based, and to determine allocation into different arms of Part 2 – Intervention.

Part 1 – Lab-based: Activity Order (visit 2)
Activity break types and activities will be randomised and performed in a cycle until all 16 activities have been completed. Randomisation will be conducted by a statistician.

Part 2 – Intervention: Intervention Allocation
Participant numbers will be assigned sequentially as each participant enters the study. The participants will be assigned to a measurement condition order through a randomisation schedule based on the randomisation plan, stratified by sex. Randomisation will be conducted by a statistician. The two experimental conditions A (generic advice for breaking up sitting time) and B (personalised advice for breaking up sitting time) will not be blinded as this is not possible as the conditions require the participant to alter their behaviour. Participants will be contacted by telephone to make them aware of their group allocation.

Baseline Assessment
Participants will first come in for their baseline assessments. This will involve attending Leicester Diabetes Center in a fasted state, where participants will receive a full explanation of the study and be given the opportunity to ask any questions before providing informed consent.

Following this, participants will complete a health questionnaire, and measurements for height, weight, waist circumference, and body composition will be taken. Body composition will be assessed with bio-impedance measurement. Participants will stand on a device similar to a set of weighing scales and a small electrical impulse will be passed through their body. This will be imperceptible.

Resting metabolic rate will be assessed using a ventilated hood system. The participant will lie on their back and relax, remain awake, and be still. The hood will be placed over the participant's head and the gases they breathe out will be analysed.

A small blood sample will be taken for the assessment of various measures associated with glucose control.

Participants will then perform the mixed meal challenge. They will be provided with a standard meal which is similar to a meal of a typical Western diet. Blood samples will be collected at regular intervals (15-30 min) until 3 h have passed.

The participant will be given a series of questionnaires that assess functional capacity, quality of life, breathlessness, anxiety and depression, chronotype, chronic pain, fatigue, and dietary intake.

Hand grip strength will be assessed using a hand grip dynamometer. The participant will hold the device in one hand with the elbow bent at a right angle. They will then squeeze the device as hard as they can. This will be repeated several times on each hand.

The Short Physical Performance Battery consists of 3 parts:
1. Chair stands: The participant will start from a seated position on a hard, upright chair (such as a dining chair), with the feet flat on the floor and the knees bent at 90°. For the test, the time taken for the participant to stand up fully and then return to sitting, without using the hands 5 times is measured.
2. Standing balance: Tests in three progressive positions. If the participant can complete 10 seconds in the specified position, then the position is progressed to the next stage:
2.1. Feet together
2.2. Semi-tandem
2.3. Tandem
3. Gait speed: The time taken for the participant to walk 4m on a level course. It is measured a second time after a short break.

The modified Physical Performance Test includes seven standardised tasks: walking 50 ft, putting on and removing a coat, picking up a penny, standing up from a chair, lifting a book, climbing one flight of stairs, and safely turning 360°.

The incremental Shuttle Walk Test involves participants walking consecutive 10 m shuttles in consistent time with an audible beep. This beep will become progressively faster until the participant is no longer able to maintain the pace.

Participants will then be taken through familiarisation for the second visit.

Finally, the participant will be fitted with two activity monitors (a wrist-worn accelerometer, a thigh-worn activPAL) and a continuous glucose monitoring device. The participant will not need to do anything with the devices once they have been fitted. They should be worn for 8 days and the accompanying sleep diary should be completed during the same period.

Part 1 - Lab-based
Participants will arrive at the research centre and will change over their wrist-worn accelerometer and the activPAL device. They will then be given a standardised breakfast before beginning the test. During the test, they will also be given a standardised snack.

Participants will engage in a 5.5 h period of sitting, with 2 min activity breaks occurring every 20 min. The activities will include:
standing; self-paced walking; two footed tip toe balance; mini squats; self-paced arm cycling while seated; standing calf stretch; resistance band biceps curls while seated; wall press-ups; sideways leg lifts; chest stretch; step-ups; back stretch; single-leg balance; standing hamstring

stretch; resistance ball squeezing (with hands) while seated; and heel taps while seated. In the final 30 s of each break in sitting, participants will be asked to rate the difficulty of the task on the Borg RPE scale, enjoyment on the feeling scale, and pain on the Borg CR10 scale. Where capacity allows, lower body muscle activation will be monitored for the full duration of the assessment using electrode embedded clothing (similar to cycling shorts). Around 5 min before each activity break starts, participants will be given a mask which covers their mouth and nose. This will allow the study team to analyse the air which they breathe out during the activity break. The mask will be removed at the end of the activity break.

Part 2 - Intervention
All participants will be given a 4 week intervention. They will be randomly assigned to either a control group, and will receive generic advice, or a personalised group, and receive information informed by the previous data collected during baseline and Part 1.

The control group will be given advice to reduce their sitting time by 30 min per day and will have regular telephone contact from the study team to track their progress.

The personalised group will receive more in-depth information on the types of physical activity breaks they should use, when they should be breaking up their sitting time, how to target spikes in blood sugar associated with meal times, and how to best break up their sitting time based on their sleep patterns.

All participants will have the same level of contact from the study group, only the content of these sessions will vary.

Participants will come back to the research centre before the final week of the intervention to be fitted with the wrist-worn accelerometer, the activPAL device, and a continuous glucose monitoring system to track changes during the final week.

Finally, participants will return to the lab for the follow-up assessments after the 4 week intervention. This will be exactly the same procedure as the baseline data collection visit.

Intervention Type
Behavioural

Primary outcome(s)
Part 1 – Lab-based
1. Affective responses to different activities used to break prolonged sitting time measured using the feelings scale during the second lab visit after each activity break in the 5.5 h sitting period at 20, 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, and 320 min

Part 2 – Intervention
1. Postprandial glucose excursions measured using a continuous glucose monitoring system worn in free-living conditions where measurements are taken continuously for an 8 day period at baseline and 4 weeks

Key secondary outcome(s))
Part 1 – Lab-based
1. Relative intensity of each activity used for breaking up sitting time measured using the BORG rate of perceived exertion during the second lab visit after each activity break in the 5.5 h sitting period at 20, 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, and 320 min
2. Energy expenditure of different activities used for breaking up prolonged sitting time

measured through expired gas analysis during the second lab visit after each activity break in the 5.5 h sitting period at 20, 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, and 320 min
3. Degree of muscle activation of different activities used for breaking up prolonged sitting time measured through electromyography during the second lab visit after each activity break in the 5.5 h sitting period at 20, 40, 60, 80, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, and 320 min

Part 2 – Intervention
1. Glucose variability (% and standard deviation), average blood glucose, time in range, time above range, time below range, high blood glucose index, low blood glucose index, number of hyperglycaemic episodes, and number of hypoglycaemic episodes measured using a continuous glucose monitoring system worn in free-living conditions where measurements are taken continuously for an 8 day period at baseline and 4 weeks
2. Area under the curve for postprandial glucose, insulin, triglycerides derived from the mixed meal challenge at baseline and 4 weeks
3. Fasting glucose, insulin, triglycerides, and full lipid profile are measured through a fasted blood sample at baseline and 4 weeks
4. Physical function is measured using the Hand Grip Strength (HGS) test, Short Physical Performance Battery (SPPB), modified Physical Performance Test (mPPT), and incremental shuttle walk test (ISWT) at baseline and 4 weeks
5. Adherence to regular light upright movement breaks, sedentary time (total and time spent in prolonged sitting), sleep duration, and physical activity (total, time spent in light, and moderate and vigorous physical activity) are measured using thigh-worn and wrist-worn accelerometers worn in free-living conditions where measurements are taken continuously for an 8 day period at baseline and 4 weeks

Completion date
01/04/2022

Eligibility

Key inclusion criteria
1. Men and women
2. Age 40 to 75 years, inclusive
3. Diagnosed T2DM with 5 years
4. Diabetes controlled by diet alone, or receiving mono- or dual-therapy
5. HbA1c levels ≤9%
6. Able and willing to give informed consent
7. Able to understand spoken and written English
8. Able to undertake light physical activity
9. Weight stable; ≤ 3kg weight change in the preceding 3 months
10. Willingness and availability to participate in the proposed intervention

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Sex
All

Total final enrolment
37

Key exclusion criteria
1. Type 1, gestational, or monogenic diabetes mellitus
2. On insulin therapy
3. Changes to glucose-lowering medication regime within the preceding 3 months
4. Hospital admission in the preceding 3 months
5. Current or planned pregnancy or breastfeeding
6. Contra-indications to exercise
7. Participation in another research study with investigational medical product in the preceding 3 months
8. Currently participating in a structured exercise programme
9. Serious illness with life expectancy < 1 year
10. Individuals with a history of chronic pancreatitis
11. Previous major amputation
12. Recent cardiovascular event (within 12 months)
13. Steroid use
14. Comorbidity that the research team consider to be a contraindication to involvement in the study
15. Unable to communicate in English
16. Unable to provide written informed consent
17. Diabetic foot ulcers, gangrene
18. Recent diagnosis or treatment for cancer (within 12 months)

Date of first enrolment
11/01/2020

Date of final enrolment
01/03/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR CRN: East Midlands
Knighton Street Outpatients
First Floor
Leicester Royal Infirmary
Leicester

United Kingdom
LE1 5WW

Sponsor information

Organisation
Unniversity of Leicester

Funder(s)

Funder type
University/education

Funder Name
University of Leicester

Alternative Name(s)
UniofLeicester, UoL

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data generated during this study will not be publicly available but may be available upon reasonable request to the study contact.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Other unpublished results	version V1.1	18/01/2023	18/01/2023	No	No

Participant information sheet		04/11/2020	14/01/2021	No	Yes
Participant information sheet	version V1.1	04/11/2020	14/01/2021	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version V1.0	20/08/2020	14/01/2021	No	No