UNIVERSITY OF BIRMINGHAM

PARTICIPANT INFORMATION SHEET

Title of the project:
Acute effect of breaking up sitting on vascular function in adults with type 1 diabetes using closed-loop systems

NHS Research Ethics Committee Approval Reference:
IRAS Number: 338230

Chief Investigator: Dr Katie Hesketh (University of Birmingham)

UK Investigators: Mr Joseph Jenkins (University of Birmingham), Dr Sam Lucas (University of Birmingham), Dr Catarina Rendeiro (University of Birmingham), Dr Parth Narendran (University of Birmingham), Dr Matthew Cocks (Liverpool John Moores University), Dr Joseph Maxwell (Liverpool John Moores University), Dr Tiago Pecanha (Manchester Metropolitan University),

School/Faculty: School of Sport, Exercise & Rehabilitation Sciences, University of Birmingham (UoB)
School of Sport and Exercise Sciences at Liverpool John Moores University (LJMU)
Department of Sport and Exercise Sciences at Manchester Metropolitan University (MMU)

You are being invited to participate in a research project. However, before you give consent, it is important that you understand why this research is being completed and what will be required of you. Please take time to read through this information document. If there is anything that is not clear, or that you would like more information on, feel free to contact the researchers who will be happy to provide this information for you.

What is the purpose of this study?

Sedentary behaviour (sitting or lying down for prolonged periods) has been identified as a public health problem but if people take regular active breaks (short periods of physical activity) they can improve their health. However, little is known of how active breaks can potentially improve health for those who have type 1 diabetes – in particular, risk of heart disease and glucose control. The aim of this study is therefore to assess how taking regular active breaks can influence vascular function and glucose control in people with type 1 diabetes.

Am I eligible for this study?

You are likely to be eligible for this study if you:

- have been diagnosed with type 1 diabetes for at least three years;
- Aged 18-66 years;
- Not currently meeting physical activity guidelines of > 150 min/week of moderate-intensity exercise or >75 min/week of high-intensity exercise;
- are sedentary (normally spend more than 5h per day sitting or lying down);
- use a closed loop insulin delivery system
- are aged 18-66.

Meeting any of the criteria below will prevent you from participating in the study:

- Under the age of 18
- regularly complete planned exercise (e.g. running, cycling, gym or sports);
- are pregnant or planning to become pregnant;

- are less than 6 months post childbirth or stopped breastfeeding less than 1 month ago;
- have existing cerebrovascular or cardiovascular disease;
- have a history of hyperglycaemia (HbA1c >85 mmol/mol);
- have a history of severe hypoglycaemia requiring third party assistance within the last 3 months;
- Have had an illness within the past 2 weeks

If you are unsure on any of these, then please contact the research team and we will help.

Females only: Female participants will be asked to provide details of their menstrual cycle in medical screening questionnaire. It is crucial that we test female participants in a similar phase of their menstrual cycle or similar pill phase of the combined pill oral contraceptive to minimise the effects of fluctuating sex hormones on blood vessel function. Female participants are provided with the option to opt-out of this question during the questionnaire. Female participants are welcome to talk to a female member of the research team on request. If they do not wish to disclose this information, then they will be excluded from the study and will not complete any further procedures detailed in this document.

Do I have to take part?

There is no obligation to take part in the study. Even after giving consent to participate, you can **withdraw at any time.**

There is no obligation to take part in the study. If you would like to participate, you will be asked to sign a consent form, but you are still free to withdraw at any time and without giving a reason, for up to two weeks after your last laboratory visit. You should feel under no pressure to participate and if at any time you are asked questions that you are not comfortable with answering you are free to not disclose this information. However, please note that not answering some questions may mean you cannot participate. Please also bear in mind that all information collected will be kept strictly confidential. If you do decide to withdraw, any data collected relating to you will only be retained following your consent at the time of withdrawal.

What are the benefits of taking part?

You will receive reimbursement for your time upon completion of the study (see *Expenses and payments)*. You will also get an opportunity to see how breaking up sitting affects your glucose and insulin requirements, and also how your vascular function (blood flow) changes.

What will happen if I consent to participate?

Online meeting – Screening, online questionnaires, food and activity monitoring
Duration: ~30mins
Time of the day: Any time of the day

After expressing interest, we will arrange an initial meeting via telephone or video call (depending on your preference), so you can ask any questions you may have about the study. We will also assess your eligibility for the study using a screening questionnaire and if you still wish to take part in the study, we will ask you to sign an electronic consent document using the digital signature tool (HELLOSIGN)– which we will arrange and explain to you.

As part of the pre-visit process, we will then ask you to complete 5 brief online questionnaires in your own time. You can decide not to complete a questionnaire or any specific questions. The questionnaires will ask about: 1 and 2) the impact of your health status on your everyday life, 3) your anxiety and depression levels, 4) your physical activity levels, and 5) a study specific questionnaire asking about your demographics and diabetes treatment.

You will be invited to visit either the School of Sport, Exercise and Rehabilitation Sciences (SportExR) at the University of Birmingham (UoB), the School of Sport and Exercise Sciences at Liverpool John Moores University

(LJMU) or the Department of Sport and Exercise Sciences at Manchester Metropolitan University (MMU) on two separate occasions so that you can complete the two experimental trials. These two visits will need to be separated by at least 4 days.

Pre-trial standardisation (two days before each of the experimental trials)
Duration: 48 hours
Time of the day: all day

The purpose of the pre-trial standardisation in the lead up to the two experimental trials is to ensure your blood glucose is as consistent as possible before each subsequent experimental trial. To assist with this, we will provide you with a physical activity monitor to wear for 48 hours before coming into the lab. We will also ask you to record your diet via an online mobile app called MyfitnessPal. We will give you a study-specific account and login instructions for MyFItnessPal and give you detailed instructions on how to download and use the app via your phone or computer.

We will provide you with food to consume on the evening before (dinner) and the morning of (breakfast) each trial. All food provided will be commercially available and pre-packaged. The food content will be matched to your estimated energy intake for each meal. Some examples of the food we will provide you include ready meals such as pasta/rice dishes, yogurt, fruit, bread, peanut butter and snack bars. We will ask you to only consume the food provided from 2pm onwards on the day before each trial (you can drink as much plain water as you like). All food will be pre-packed and delivered to your home address, and we will email detailed instructions for when you should consume each item. Please let one of the investigators (Dr Katie Hesketh or Joseph Jenkins) know if you have any **allergies** or **food preferences.**

We will need you to avoid **planned** and **strenuous** physical activity during this time. This includes avoiding activities such as the going to the gym, running and social sport e.g. football, netball etc.

Visits 1 and 2 – Main Experimental Trials
Duration: ~8h each
Time of the day: 8am to 5pm

The study will consist of 2 experimental trials: a Sedentary trial and an Active Break trial (visits 1 and 2), and these will need to be separated by at least 4 days – please see the diagram below. On the days of each trial, we will need you to attend your chosen university laboratory (UoB, LJMU or MMU) at 7:30am. Upon arrival, we will again run through what will happen during the day and we will ask you to complete a brief questionnaire regarding your sleep, mood, stress and general health. You will then be asked to rest while we take your blood pressure and complete an ultrasound of the femoral artery on your leg and take measures of your brain blood flow. Finally, we will take a blood sample from your arm. In order to do this we will require you to **wear/bring loose fitting clothing**, e.g. a short sleeve shirt and shorts. All of these procedures are explained in further detail on page 4.

Once your baseline measures have been taken, we will provide you with a desk to sit at for **7 hours.** During this time, you will have access to the internet to use personal electronic devices (e.g. laptop, headphones). While seated at the desk, we will request for. you to keep movement to a minimum. If you are completing the *Active Breaks* condition on the day, we will ask you to interrupt your sitting every **30 minutes** with **3 minutes** of self-paced light-intensity walking, these walking breaks will be supervised by a member of the experimental team. If you are completing the *Sedentary* condition on the day we will ask you to remain seated continuously. After 3.5 hours during each trial, we will provide you with a standardised lunch meal to eat at your desk. This meal will be commercially available, pre-packaged and matched to your estimated energy intake. Water will be freely available for you to drink during both trials, and you will be able to use the bathroom whenever you need (even if not during a designated toilet break), however, to minimise unnecessary movement we will use

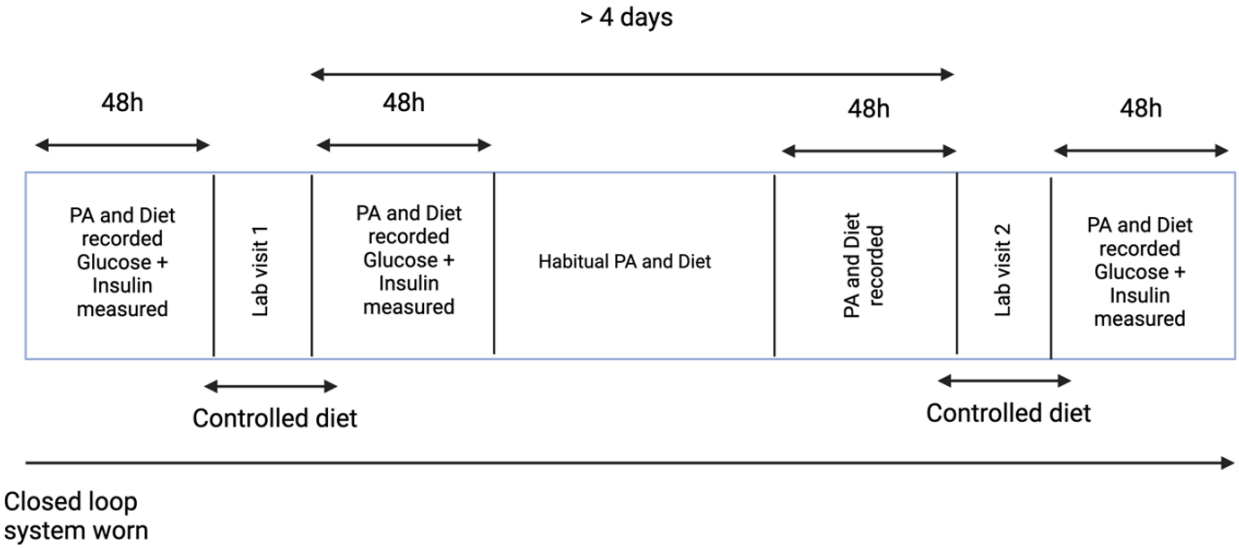
a wheelchair to transport you to the nearest bathroom. In addition, we will try and replicate the number of timing of bathroom breaks between your two trials.

Should you experience a hypo during the lab visit day we will ask you to treat the hypo in a controlled way. If your blood sugar goes below 4mmol/l we will give you 15g of carbohydrate (Skittles). We will then reassess your blood sugar after 10 minutes. Should your blood sugar still be below 4mmol/l after 10 minutes we will give you another 15g of carbohydrates. This process will be continued until your blood sugar goes above 4mmol/l.

Prior hypoglycaemia has the potential to affect the function of your blood vessels. As such should you experience a hypo (blood glucose reading <4.0mmol/l) the day before the laboratory visit the visit will be rescheduled. In addition, hyperglycaemia on the day of the trial can affect blood vessel function. As such, should your blood glucose be above 10mmol/l before baseline blood vessel function measures the testing day will be rescheduled.

Post-trial follow-up (two days following each of the experimental trials)
Duration: 48 hours
Time of the day: all day

The purpose of the post-trial follow-up is to assess any possible carry-over effects of the intervention on your blood glucose for 48 hours. To assist with this, we will provide you with another physical activity monitor to wear for 48 hours after coming into the lab. We will also ask you to continue to record your diet via the MyfitnessPal app. In addition, we will need you to continue to avoid **planned** and **strenuous** physical activity during this time e.g. going to the gym, running, social sport.



Schematic of the study overview

What will be measured

Questionnaires: Short questionnaires evaluating your recent sleep, mood, stress and general health

Resting blood pressure: Your resting blood pressure will be measured using an automated stress-testing blood pressure monitor using a cuff placed around your upper arm in addition to using a small cuff placed around

the index finger and inflated to a low pressure. These cuffs will pulsate at regular intervals but should not be uncomfortable. We will measure your blood pressure before (baseline) and after (post) each of the two trials.

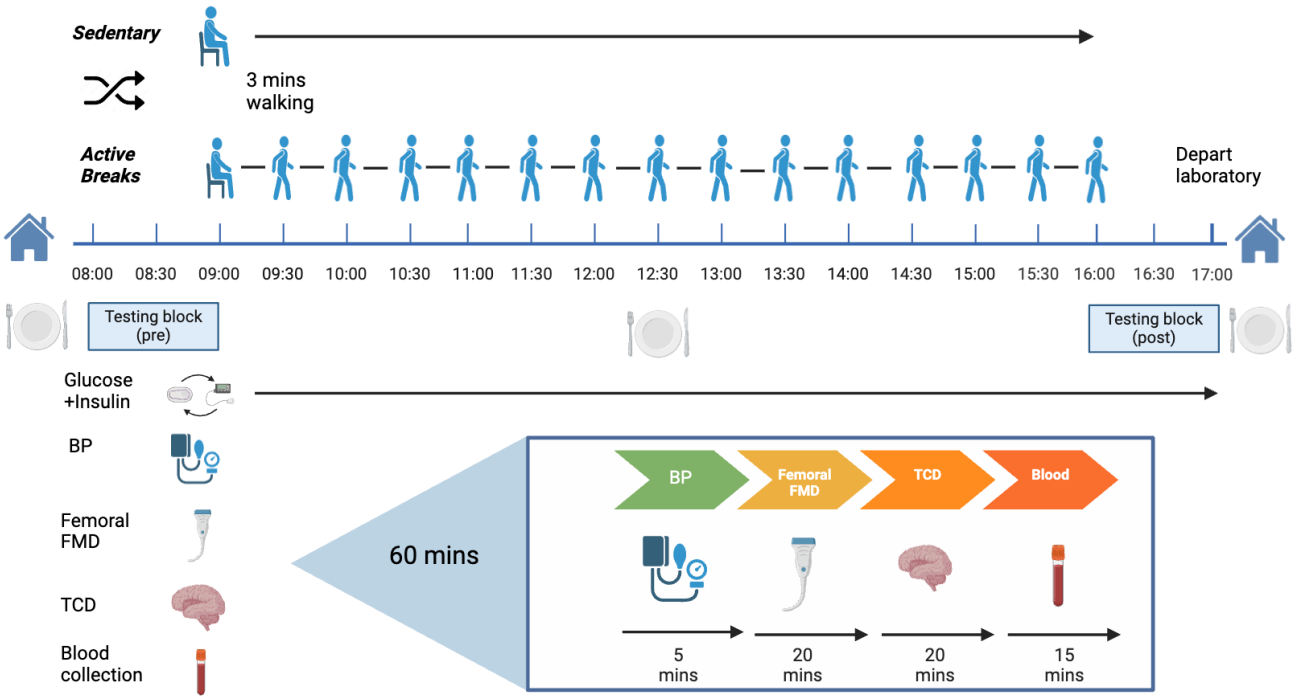
Leg blood flow functional assessment: We will use ultrasound to capture an image of your blood vessels in your leg. This non-invasive procedure will involve inflating a cuff around your calf, you will feel a tingling sensation ('pins and needles') or brief numbness from the pressure of the inflated cuff on your calf. This will stop once the cuff is deflated. It is very important that you remain as still as possible, so the ultrasound probe does not move during the procedure. We will measure your blood flow before (baseline) and after (post) each of the two trials.

Brain blood flow (Transcranial Doppler Ultrasound): We will also use ultrasound to assess blood flow in your brain and this will require you to wear a cushioned headband and remain still while two small non-invasive probes are placed to each side of your head (slightly in front of your ears) and fixed to the headband. As such, we will require you to not be wearing any clothing or material on your head at the time of assessment. However, If you wear clothing or material that covers your head/neck area that cannot be removed, you will be allowed to forego this measure without any impact on your overall participation of the study.

Whilst we are measuring the blood flow to the brain, the amount of carbon dioxide which you are breathing will be altered slightly, and you will be asked to breathe normally through a mouthpiece so that we can measure how your brain blood flow responds. You will not feel and discomfort from this procedure and there are no risks to you. We will measure your blood flow before (baseline) and after (post) each of the two trials.

Neck artery blood flow (Duplex Ultrasound): Ultrasound will also be used to scan blood vessels in your neck. There will be some gel on the probe which might feel cold against your skin, and you will feel the probe pressing gently on your neck, but it should not cause you discomfort. We will measure your blood flow before (baseline) and after (post) each of the two trials.

Venous Blood Samples: A trained phlebotomist will take a small amount (a total of 3mL or 2 tablespoons) of blood from a vein in your arm on two occasions during each trial. We will take blood samples before (baseline) and after (post) each of the two trials. The UoB policy and procedures for taking blood from research volunteers will be followed at all sites (UoB, LJMU and MMU).



Your baseline testing will begin 8am and will last for 60 minutes. During the testing time we will perform the measures pictured above. Your seated period will then begin 9am with lunch being served 12:30pm. We will then perform the measures mentioned above for a second time once your seated period comes to an end at 4pm, again, this will last for 60 minutes in total.

End of the study

There will be a follow-up by email after each Experimental Trial (Visits 1 and 2) to ensure you have not experienced any adverse reactions (i.e. hypoglycemic events). A final follow-up will be conducted 3 days after the last experimental trial (Visit 2) in order to remind you to send your physical activity monitor back to the research team.

We will need to use information from you for this research project. This will include your name and contact details. People will use this information to do the research (i.e., the study team) or to check your records to make sure that the research is being done properly (i.e., the University of Birmingham Clinical Research Compliance Team). People who do not need to know who you are will not be able to see your name or contact details. Your data will have an ID number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What will the samples collected from me be used for?

We will use the blood (a total of 3mL or 2 tablespoons) to measure markers of inflammation. All samples will be stored in locked freezers with key-code access at either the School of Sport and Exercise Sciences at LJMU, the School of Sport, Exercise and Rehabilitation Sciences at UoB or the Department of Sport and Exercise Sciences at MMU in accordance with each university's respective human tissue storage procedures. All blood samples will be destroyed once analysed.

What are the possible disadvantages and risks of taking part?

The different ultrasound assessments are safe and carry no risks to health – though there may be slight discomfort (pins and needles) when the cuff is inflated for measuring leg blood flow, this will be brief – and disappear when the cuff is deflated after a few minutes.

With the blood sampling, you may experience a slight discomfort during insertion of the needle. There is a very small risk of infection, needle-stick injury, soreness, and bruising around the site of needle insertion but such complications are rare, and the risks will be minimal given that the researchers are well trained in the safe sampling of blood.

During the seated visit of the study, you may experience a degree of restlessness and discomfort staying seated for an extended period of time. While this is to be expected, please be aware that you will be allowed to stand up and move about at any time if required and that this will not affect your participation in the study.

If we require medical advice during your visits, a medically qualified member of the University staff will be on-call. In case of an emergency during your visit we will follow planned emergency procedures; the medically qualified member of the University staff will be informed, an ambulance will be called, and a first aid trained investigator will stay with you until the ambulance arrives. If you feel unwell after any of the study activities, please contact the study team and we will advise you on what action/s should be taken.

What are the possible benefits of taking part?
Throughout the study you will undertake a range of tests that will generate information that you might find interesting – in particular, how light exercise taken every 30 minutes can potentially benefit glucose control and the health of your blood vessels. Financial reimbursements are covered in the *Expenses and payments* section within this leaflet.

What if something goes wrong?
If you have any concerns about the study, please speak to a member of the research team in the first instance; contact details are available towards the end of this leaflet. If you remain unhappy with their response and wish to complain formally, you can do this by contacting the Sponsor's Research Governance Office at the University of Birmingham (Telephone: 0121 415 8011 or email: researchgovernance@contacts.bham.ac.uk). The University of Birmingham has in place Clinical Trials indemnity coverage for this study which provides cover to the University for harm which comes about through the University's, or its staff's, negligence in relation to the design or management of the trial.

What Information will be collected about me?
You will complete a consent form and a general health questionnaire. These will be the only documents with your identity on and these will be stored with your unique study identification number. All other documents will be identifiable only using your unique participant study ID number to maintain your anonymity. Only the research team will be able to link your unique study ID with your personal identity. No one outside the research team will have access to these codes. All documents will be stored electronically using a password protected computer and only the investigative team will be allowed access to these files. Data will be archived for 10 years as per University of Birmingham codes of practice. If you make contact about the study but choose not to participate your personal data will be removed. If the sponsor (University of Birmingham) or regulatory authorities make queries, then study records will be provided to them whilst maintaining your confidentiality.

What biological samples will be collected from me?
Your blood samples will be identifiable only by your unique study ID participant study identification number.. School of Sport, Exercise and Rehabilitation Sciences These will be stored in freezers at either the School of Sport and Exercise Sciences at LJMU, the School of Sport, Exercise and Rehabilitation Sciences at UoB or the Department of Sport and Exercise Sciences at MMU to which access is restricted to research personnel only. Only the research team will have the links and be able to link your unique study identification number with

your personal identity to the participants. No one outside the research team will have access to these codes. After the study has finished, all remaining samples at each site will be destroyed.

How will we use information about you?
We will need to use information from you for this research project. This will include your name and contact details. People will use this information to do the research (i.e., the study team) or to check your records to make sure that the research is being done properly (i.e., the University of Birmingham Clinical Research Compliance Team). People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?
You can stop being part of the study at any time, without giving a reason. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you. If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?
You can find out more about how we use your information:

- by asking one of the research team, or
- by sending an email to the University's Data Protection Officer (dataprotection@contacts.bham.ac.uk).

Will my taking part in this study be kept confidential?
Yes. All the information about your participation in this study will be kept confidential. You will not be identifiable in any publication or report as the data will be grouped together and all identifying information will be removed. All participants will be allocated a unique ID, and all provided data will be stored with that ID. A separate (electronic) link the participants to the ID that will only be accessed by the research team.

Any personal information will be deleted at the earliest opportunity following data collection (i.e., electronic files permanently deleted). Research data will be stored for 10 years This information will be stored for 10 years and will then be discarded via university approved procedures. No potentially personally identifying information will be included in any dissemination of the study findings.

What are my rights?
It is completely your choice to take part in this study. If you decide to take part, you will be asked to sign a consent form. Furthermore, if you decide to take part in the study, you will be free to withdraw from the study at any time without giving a reason.

Under data protection law, we must provide you with very specific information about what we do with this data and about your rights. We have set out below the key information you need to know about how we will use personal data, this can be found at the end of this information sheet. More information on how the University processes personal data can be found on the University's website on the page called 'Data Protection - How the University Uses Your Data' (https://www.birmingham.ac.uk/privacy/index.aspx).

What will happen to the results of the research study?
Your data may be used in a journal publication of the study findings. We do not know at this time where these data may be published. However, you may contact the study team any time if you wish to learn more about how your data is used in future publications. Should data from this study be published, you will be able to obtain a copy by contacting the study team.

Expenses and Payments
You will receive a £50 Love2Shop voucher upon completion of the study. In addition, any travel costs associated with travel to your chosen University will be reimbursed. If you choose to withdraw after visit 1, you will receive a £25 Love2Shop voucher. If you choose to withdraw from the study after its completion, you will still be eligible for receipt of the £50 Love2Shop voucher. If you decide to withdraw during (i.e. before the end) of either visit 1 or 2, you will only receive reimbursement for your travel expenses for that day.

Who has reviewed the study?
This study was reviewed by London – City & East Research Ethics Committee

Contact for further information
If there is anything that is not clear or if you would like more information, please do not hesitate to contact one of the investigators listed below:

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