Institutional logo

Participant Information Sheet

Closed-loop in adults with type 2 diabetes (COYOTE)

Chief Investigator

Prof Roman Hovorka
rh347@cam.ac.uk

Principal Investigators

Dr Charlotte Boughton (Cambridge University Hospitals NHS Foundation Trust)
cb2000@medschl.cam.ac.uk

Dr Lalantha Leelarathna (Imperial College Healthcare NHS Trust)
Lalantha.Leelarathna@mft.nhs.uk

Dr Hood Thabit (Central Manchester University Hospitals NHS Foundation Trust)
Hood.Thabit@mft.nhs.uk

Dr Sankalpa Neupane (Norfolk & Norwich University Hospitals NHS Trust)
Sankalpa.neupane@nnuh.nhs.uk

Dr Yee Cheah (King's College Hospital NHS Foundation Trust)
y.cheah@nhs.net

Dr Sufyan Hussain (Guy's and St Thomas' NHS Foundation Trust)
sufyan.hussain@kcl.ac.uk

Prof Pratik Choudhary (University Hospitals of Leicester NHS Trust)
pratik.choudhary@leicester.ac.uk

Dr Emma Wilmot (Derby and Burton NHS Foundation Trust)
emma.wilmot2@nhs.net

Closed-loop in adults with type 2 diabetes

We would like to invite you to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish.

- **Part 1 tells you the purpose of this study and what will happen if you take part.**
- **Part 2 gives you more detailed information about the conduct of the study.**

Ask us if there is anything that is not clear or if you would like more information. Take your time to decide whether or not you wish to take part.

Part 1

Introduction

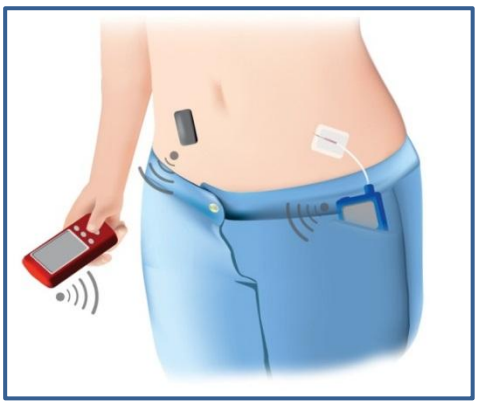
A healthy pancreas releases insulin according to the body's needs to keep blood glucose levels within a narrow range. In type 2 diabetes the pancreas is unable to produce enough insulin and often people need to take tablets and/or inject insulin to control their blood glucose levels.

Research studies have shown that having high glucose levels in diabetes can lead to long-term health problems affecting the eyes, kidneys, feet and heart. To lower the risk of these complications, tight control of blood glucose levels is recommended. However, intensive insulin treatment is associated with increased risk of low glucose levels ('hypos'), so achieving the recommended glucose levels can be difficult.

Currently the doses of insulin used to manage diabetes depend on the results of finger stick glucose checks, often several times a day. The more often the glucose levels are measured, the easier it is for you or your diabetes team to adjust the insulin dose. Recent advances in technology have led to the availability of glucose sensors (continuous glucose monitors; CGM) which continuously measure glucose levels through a very thin fibre that is inserted just beneath the skin and changed every 2 weeks.

Instead of insulin injections several times a day, insulin pumps continuously infuse insulin through a very thin tube inserted under the skin which is changed every 2-3 days. The glucose sensor and the insulin pump are two of the three components of a closed-loop system. The remaining component is a computer algorithm that calculates the correct insulin dose based

on the sensor readings. These three interlinked components form the closed-loop (see picture below).



The closed-loop system used in this study is CamAPS HX. This system has been approved for use in people with type 2 diabetes. It comprises: (1) Freestyle Libre 3 glucose sensor (Abbott Diabetes Care, CA, USA), (2) CamAPS HX App (CamDiab, UK) on a smartphone that works out how much insulin is needed based on the sensor glucose information to keep your glucose in the target range, and (3) YpsoPump insulin pump (Ypsomed, Switzerland) that delivers the insulin. The smartphone communicates wirelessly with the insulin pump and the CGM.

What is the purpose of the study?

The purpose of this study is to test how effectively and safely the closed-loop system can manage glucose levels in adults with type 2 diabetes compared to standard insulin therapy with a glucose sensor in the home setting over 6 months. Results from participants using the closed-loop system (**CL group**) will be compared with results from participants using standard insulin therapy with a glucose sensor (**control group**).

Why have I been invited?

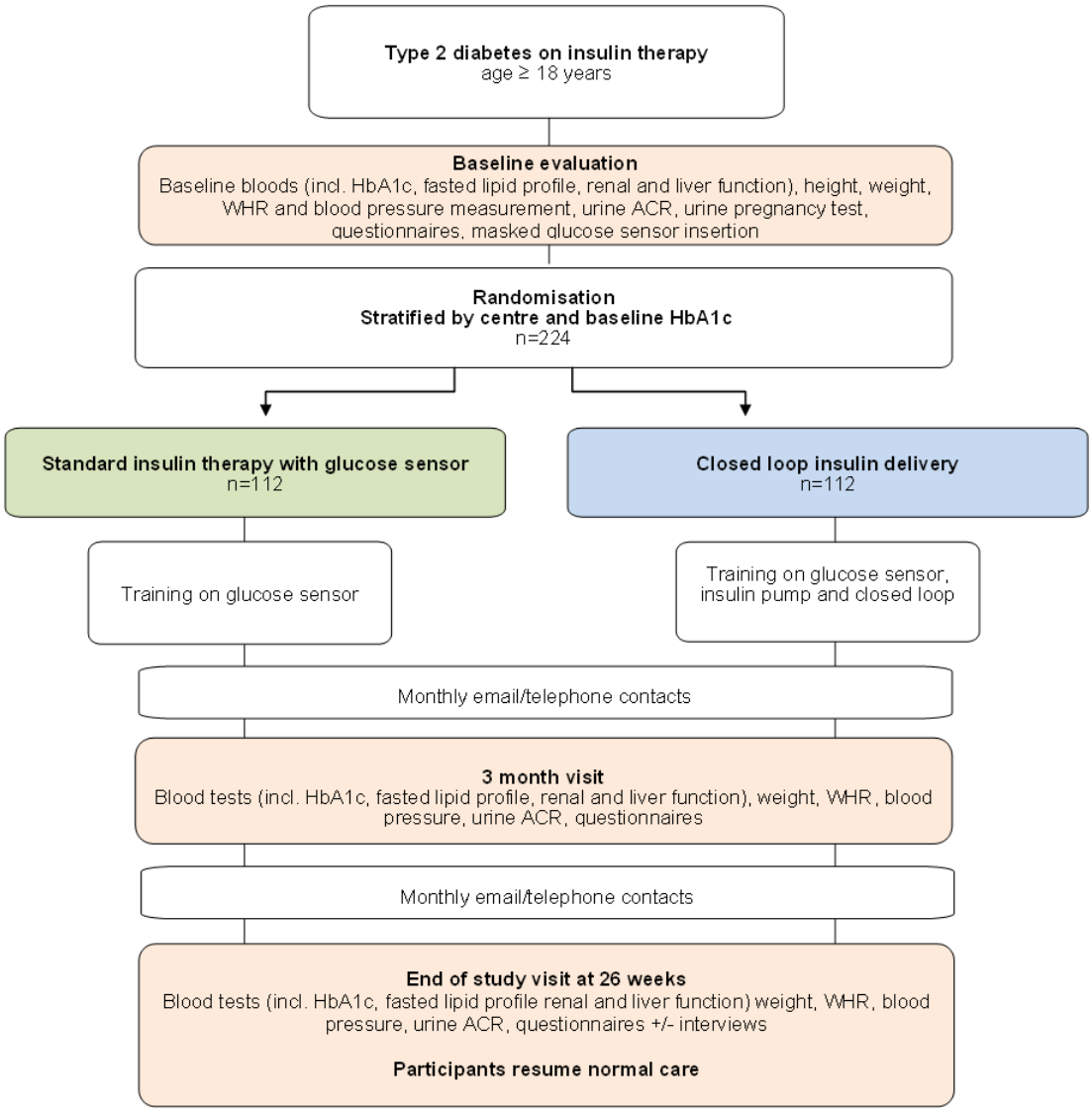
You have been invited because you have type 2 diabetes, an HbA1c level ≤15% (140mmol/mol) and have been using insulin to manage your diabetes for at least 6 months. We aim to include 224 adults with type 2 diabetes in the study from across the UK and Europe.

Do I have to take part in this research?

No. It is up to you to decide whether or not to take part. If you do, you will be given more detailed information and will be asked to sign a consent form. You are still free to withdraw at any time and without giving any reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

The study consists of up to 5 visits which will take place at the Clinical Research Facility or the diabetes clinic. The total study duration is around 7 months.



The following sections describe what happens at each of the study visits in detail.

Visit 1 - Recruitment visit

Once you have had enough time to read this information sheet, if you would like to hear more about the study or would like to participate, you will be invited to attend the recruitment visit. You will be provided with detailed information about the study and any questions you have will be answered. If you decide to participate, you will be asked to sign a consent form. At the visit, your height, weight, waist hip ratio, blood pressure, demographics, medical and diabetes history, medications and insulin therapy will be recorded. During this visit you will have a blood test to measure HbA1c, liver and kidney function and lipids, and a urine test to measure urine protein levels. A urine pregnancy test will be done for all females of childbearing age. If you are pregnant at the visit you will not be able to take any further part in the study. You will be asked to wear a masked glucose sensor where you cannot see your glucose levels for the next 2-3 weeks while you continue with your current insulin therapy. If you are already using a glucose sensor, you can continue using this too. You will also be asked to complete some questionnaires.

Visit 2 – End of Run-in and randomisation visit: 2-3 weeks after Visit 1

Two to three weeks after the recruitment visit you will be invited to Visit 2. The aim of this visit is to review the data from the masked glucose sensor, to make sure that enough data has been recorded. A minimum of 10 days of data are needed for you to be able to start the study. Randomisation to determine which of the two groups you will be in will be done at this visit. You could either be randomised to use the fully-closed loop (**CL group**) for the next 6 months or to continue with your current insulin therapy and use a glucose sensor for the next 6 months (**control group**). The group you are allocated to is a chance selection (like the toss of a coin) by a computer programme. The research team have no control over this decision. This visit can be done remotely if preferred or can be combined with Visit 3.

Visit 3 - Training and initiation of the study devices

You will be invited to attend the clinical research facility or diabetes clinic. This visit includes training on the study devices to ensure safe and effective use. This visit can be combined with Visit 2 if you and the study team feel this is appropriate.

Closed-loop group: You will be shown how to use the study insulin pump, the glucose sensor and the closed-loop system, including how to manage high and low glucose levels (hyper- and hypoglycaemia). You will be provided with all the study devices including a smartphone with

the closed-loop App if required. The session will be conducted by a diabetes educator or member of the study team and you will also be provided with easy-to-follow user guides for the closed-loop system. Your ability to use the closed-loop system will be assessed by the study team. For safety reasons, you need to be able to show competent use of the system to continue with the home study phase. If you are not able to show that you are competent to use the insulin pump, glucose sensor or app you will not be able to continue in the study. Closed-loop glucose control will start once the training is completed.
You will be asked to use the closed-loop system at home alongside your other non-insulin diabetes medications over the next 6 months. You will be able to drive while following the standard precautions and regulations. A telephone helpline will be available to support you with any problems using the closed-loop system.

Control group - standard insulin therapy and glucose sensor: You will be shown how to use the glucose sensor and how to review your glucose patterns. The session will be conducted by a diabetes educator or member of the study team and you will be provided with easy-to-follow user guides for the glucose sensor. Your ability to use the glucose sensor will be assessed by the study team. For safety reasons, you need to be able to show competent use of the glucose sensor to continue with the home study phase. If you are not able to show that you are competent to use the glucose sensor you will not be able to continue in the study. You will be asked to continue with your usual insulin therapy and other diabetes medications and wear the glucose sensor over the next 6 months. A telephone helpline will be available to support you with any problems using the glucose sensor.

Study contacts

You will be contacted by email/telephone within 48 hours and one week after the training visit. After the first week you will be contacted (email/telephone) each month to record any medical issues, device issues, changes in insulin and/or other medication, other medical conditions.

Visit 4 – 3 month visit

Three months after visit 3 you will be invited to attend the clinical research facility or diabetes clinic. Your weight, waist hip ratio and blood pressure will be recorded. During this visit you will have a blood test to measure HbA1c, liver and kidney function and lipids and provide a urine sample to measure urine protein levels. You will also be asked to complete some questionnaires.

Visit 5 – End of study visit

Six months after visit 3 you will be invited to attend the clinical research facility or diabetes clinic. Your weight, waist hip ratio and blood pressure will be recorded. During this visit you

will have a blood test to measure HbA1c, liver and kidney function and lipids and provide a urine sample to measure urine protein levels. You will also be asked to complete some questionnaires. The study devices will be returned, and you will continue with your usual insulin therapy and glucose monitoring that you were doing before the study.

Interviews

When you sign the consent form, you will be given the opportunity to indicate whether you would be willing to take part in an interview study which has received separate funding from Diabetes UK. This interview study will involve some people who are randomised to the closed-loop group and its purpose is to understand what people like and dislike about using a closed-loop and how it affects their quality of life. If you are selected for an interview, this interview would take place near the end of your participation in the trial and would be conducted by telephone or using an online video platform depending on your preference. It would be carried out by an experienced researcher and would last around an hour, although this would depend on what you have to say. Interviews will be audio recorded using an encrypted digital recorder. The interview files are encrypted as they are recorded, password protected and uploaded to a secure file store only accessible to the research team. Recordings are not kept long-term on the recording device. Recording files are transferred securely to a third party trusted professional service for transcription. Direct quotes from the interview may be published but would be anonymised.

Will I be reimbursed?

As an appreciation of your time and effort you will receive £80 for completing the study. In addition, all reasonable travelling expenses will be reimbursed. Reimbursement will be paid either by bank transfer (if you are willing to provide your bank details) or vouchers from the research team's organisation. If you take part in the interview study, you would be offered a further £50 voucher to thank you for your time.

Return of study devices

Study devices remain the property of the study team and will need to be returned at the end of the study to protect the integrity of the study. There are currently no NHS funded routes for ongoing access to insulin pumps after the study.

What are the possible risks of taking part?

During this study, you may experience a hypo (low glucose level) similar to the ones that may happen in everyday life with diabetes. We will ask you to treat it in the same way you normally treat a hypo. There is a risk of possible hyperglycaemia (high glucose) which is similar to the risk that a person with type 2 diabetes experiences on a daily basis. We aim to minimise these risks by providing you with training about managing hypo- and hyperglycaemia. We will spend

time helping you to set the alarms on the devices so that you are warned in advance about any hypos or if your blood glucose rises too high.

You will have to attach the small glucose sensor to your upper arm every 14 days. Inserting the sensor has a low risk of developing a local skin infection. Some bruising, itchiness, redness or bleeding at the site of sensor insertion may occur. Potential risks associated with insulin pump therapy include slight discomfort or bruising at the time of insertion of the insulin delivery cannula. In addition, when blood samples are taken for the study, some bruising or minor discomfort may also occur at the site where the blood was taken.

In some people who already have eye problems related to diabetes (retinopathy), improving glucose levels very quickly can initially make this worse. This only happens rarely, and in the longer-term good glucose control reduces the risk of eye problems progressing. We will ask you to make sure you attend your usual eye screening appointments, to ensure any changes are picked up early. The questionnaires and interview will include personal questions about your diabetes and its management. It is possible that you may find these questions to be uncomfortable or upsetting, but these reactions are uncommon.

What are the possible benefits of taking part?

We cannot guarantee that taking part in this study will benefit you. The information provided by the closed-loop system and/or glucose sensor can be used to optimise your usual diabetes treatment and this may have benefits beyond the study period. Taking part in this study could help in further development of closed-loop systems that can manage blood glucose in people with type 2 diabetes.

Who should I talk to if I have any questions or concerns?

If you have any questions regarding this study, please contact the following person:

Contact details of the local clinical study team

On behalf of the Study Team, we would like to thank you for taking the time to consider participating in this important research study.

This completes part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

What if relevant new information becomes available?

You will be informed as soon as possible if any new information becomes available during the course of the study that may affect your willingness to participate in the study. If you decide not to continue, the study doctor will arrange for your usual care to continue.

What will happen if I don't want to carry on with the study?

If you decide not to participate in this study, it will not affect your future treatment in any way. If you agree to take part, you are free to withdraw at any time without explanation. If you withdraw from the study we will use the data collected up to your withdrawal.

What if there is a problem?

If you have a concern about any aspect of this study, please ask to speak to the researchers who will do their best to answer your questions (see contact details above). If you are unhappy about the conduct of the study and wish to complain, you can do this through (name and contact details of the local patient advice and liaison service – institution specific)

In the unlikely event that something does go wrong, and you are harmed during the research study, appropriate healthcare arrangements will be made. Healthcare arrangements may include advice from clinical members of the study team or your local diabetes clinic team, or use of emergency health services. There are no special compensation arrangements unless this was due to the negligence of one of the doctors or nurses or due to harm resulting from the study design. In this case you may have grounds for legal action for compensation but you may have to pay your legal costs. The normal hospital complaints mechanism will still be available to you. In addition, any harm arising due to study design (both negligent and non-negligent) will be covered under the Sponsor's insurance policy.

Will my GP be informed?

We will inform your GP of your participation in this study after you have consented to this.

Will my taking part in the study be kept confidential?

Cambridge University Hospitals NHS Foundation Trust (CUH) and the University of Cambridge are the joint Sponsors for this clinical study in the UK. They will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that they are responsible for looking after your information and using it properly. The Sponsor organisations will keep identifiable information about you for 5 years after the study has finished to ensure your safety and to allow the study to be reviewed by the authorities after it is finished. Electronic data will be stored on password-protected computers. All paper records will be kept in locked filing cabinets, in a secure office

at the investigation centre. Only members of the research team and collaborating institutions will have password access to the anonymised electronic data. Only members of the research teams will have access to the filing cabinet. Paper copies of the data will be stored for at least 15 years in line with the General Data Protection Regulation (GDPR) (EU) 2016/679.

How will we use information about you?

Cambridge University Hospitals NHS Foundation Trust will collect your name, NHS number and contact details to contact you about this study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from the Sponsors and regulatory organisations may look at your medical and research records to check the accuracy of this study. Cambridge University Hospitals will pass these details to the Sponsors along with the information collected from you. The only people in the Sponsor organisations who will have access to information that identifies you will be people who need to contact you in relation to this study and to audit the data collection process. Cambridge University Hospitals will keep identifiable information about you from this study for 5 years after the trial has finished and will be disposed of securely thereafter.

All information collected about you as a result of your participation in the study will be kept strictly confidential. Your personal and medical information will be kept in a secured file and be treated in the strictest confidence.

Once you have agreed to participate in this study, you will be allocated a Study ID Number. This is a unique trial number, which will be used on all of your study documentation.

The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details. Only anonymous trial data, without any personal information will be published at the end of the trial.

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, but we will keep information about you that we already have. We need to manage your records in specific ways for the research to be reliable and accurate. This means that we won't be able to let you see or change the data we hold about you.

Where can you find out more about how your information is used?

To safeguard your rights, we will use the minimum personally identifiable information possible.

You can find out more about how the Sponsors use your information:

- at www.hra.nhs.uk/information-about-patients

- for Cambridge University Hospitals NHS Foundation Trust, please visit: https://www.cuh.nhs.uk/corporate-information/about-us/our-responsibilities/looking-after-your-information, or email the Data Protection Officer at: cuh.gdpr@nhs.net
- for University of Cambridge, please visit: https://www.medschl.cam.ac.uk/research/information-governance/, or email the Information Governance team at: researchgovernance@medschl.cam.ac.uk.

What will happen to any samples I give?

Blood samples for HbA1c collected during this study will be labelled with your study identification number, stored securely and disposed of securely after being transported for analysis at a central laboratory. All other blood samples and urine samples collected during this study will be analysed immediately and disposed of after analysis.

What will happen to the data collected?

Once the study is finished all data will be entered onto a computer and will be used to analyse the results. These study results may be presented at scientific meetings or published in a scientific journal. In addition, fully anonymised data may be shared with researchers and collaborating partners in USA and Europe, or commercial companies for the purpose of advancing the management and treatment of diabetes.

Who is organising and funding the research?

The research study has been funded by Abbott Diabetes Care and Ypsomed. Professor Roman Hovorka who is the Chief Investigator for this study is also Director of CamDiab, the company which makes the closed-loop app. The joint sponsors of the study are the Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge. The University of Cambridge are providing insurance cover for the study.

Who has reviewed the study?

Before any research goes ahead it has to be checked by an Ethics Committee. This project has been reviewed by the East of England - Cambridgeshire and Hertfordshire Research Ethics Committee.

If I agree to join the study

The study will be explained to you in more detail during the screening visit. During this visit you will be able to ask questions and voice any queries. Once you have agreed to take part, we will ask you to sign a consent form.

What will happen at the end of the study?

At the end of the study you will go back to using your usual insulin therapy and glucose monitoring. The study devices will be returned to the research team. Your diabetes care will then be looked after by your usual diabetes team.

When analysis of the data is completed, you will be notified of the results by post or email to the contact details given for that purpose. A summary of the results of the study will also be available on the University of Cambridge departmental website.

This completes part 2 of the Information Sheet.

Thank you for your time and interest in our research.