Government of **Western Australia**
Child and Adolescent Health Service

Perth Children's Hospital

PARTICIPANT INFORMATION SHEET

Perth Children's Hospital

Redefining Glucose Level for Hypo Treatment in Children and Young Adults on Closed loop Therapy

Why are we asking you?
We are asking you to take part in this study because you have had type 1 diabetes for more than 12 months, are between 18 and 25 years of age and you are on closed loop insulin pump therapy.

Why are we doing the study?
Glucose levels between 3.0 and 3.9 mmol/L can be considered as normal in healthy individuals with no diabetes. However, hypo treatment (treatment for low glucose level) is advised at glucose level below 3.9 mmol/L in people living with type 1 diabetes. This level is chosen to prevent glucose level from dropping below 3.0 mmol/L. We do not want your glucose level to be below 3.0 mmol/L as this can affect the way your brain functions.

Hypo treatment below 3.9 mmol/L is recommended by international guidelines although there is limited information on why this level was chosen. This is a reasonable glucose level to start hypo treatment for people using insulin injections and non-automated insulin pump therapy. However, with current automated insulin pump therapy (closed loop) with the pump suspending basal insulin when it predicts your glucose level is dropping, the need for hypo treatment below 3.9 mmol/L is less understood. Furthermore, there are more chances to go high with glucose levels > 10 mmol/L following treatment of a hypo.

The first step was to reach out to all families to explore how they manage hypos, at what glucose level hypo is initiated and how they treat hypo. The second step is this study which we are doing to see if we can safely lower the glucose level for hypo treatment with no increase in time and number of hypo episodes below 3.0 mmol/L.

In this study we will be trialling two hypo treatment plans: treating at the standard glucose level below 3.9 mmol/L and treating at a lower glucose level equal to or below 3.6 mmol/L. We will ask you to trial each hypo treatment plan for 4 weeks.

Who is carrying out the study?
The study is being carried out by Dr Mary Abraham, together with the Diabetes Research Team at Perth Children's Hospital (PCH). The study is funded by a Perth Children's Hospital Foundation Stan Perron Grant.

What will the study tell us?
This study will tell us if treating hypos at a lower level than the current recommended level of less than 3.9 mmol/L is acceptable and medically safe for managing type 1 diabetes in children and young adults using closed loop therapy.

Do you have to take part?
No, you do not have to take part in this study.

If you decide to take part and then later change your mind, that is ok. It will not change the way you are treated by your clinic team. You can pull out of the study at any time.

What will you be asked to do if you decide to take part in this study?

If you are interested in the study, we will first have to screen you for eligibility to participate in the study. If you are not able to recognise when you are having a hypo, or you are worried about having hypos or you spend a fair bit of time in hypo or had an episode of severe hypo in the last 12 months, you are not eligible to participate in the study.

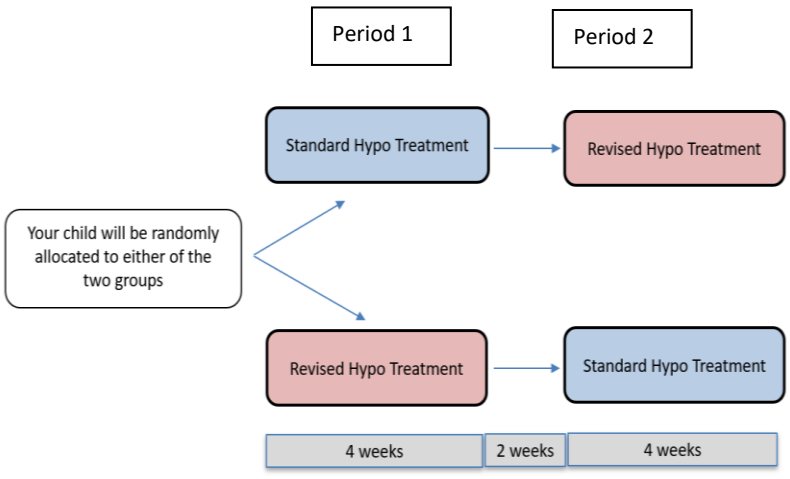
If you are eligible to participate, we will recruit you into the study.

Study outline:
This study will take 10 weeks and there are 4 visits. You will need to come to the research facility at PCH at least for the first visit, with the option of either face-to-face (F2F) or telehealth for the other visits.

This is a cross-over study with a 2-week gap between the two 4-week hypo treatment plans. In the study, you will be randomly allocated to one of the two groups a) Standard Hypo Treatment or b) Revised Hypo Treatment for the first 4 weeks. This will be followed by a 2-week period during which we ask you to treat hypo as per your usual practice.
After this 2-week period, if you were in the standard hypo treatment, you will move on to the revised hypo treatment and if you were in the revised hypo treatment first, you will move on to the standard hypo treatment for 4 weeks.

During Standard Hypo Rx, we will ask you to treat a low glucose level < 3.9 mmol/L as per the current recommendation.
During Revised Hypo treatment, we will ask you to treat for a hypo at a lower glucose level (3.6 mmol/L).

Figure: Study Design



During the study:
You should continue to wear sensors during the entire duration of the study and be on closed loop therapy. If you are not on sensor or not in closed loop, standard hypo treatment should be taken.

During the study, you are also advised to follow the current standard recommendations to commence exercise and driving.

1. Alerts
   - Default (device in-built) urgent low alert at 3.0 mmol/L or 3.1 mmol/L will be **ON,** at all times, on your pump.
   - Low alerts will be turned **ON**, in keeping with the glucose level of the study arm (3.9 mmol/L or 3.6 mmol/L)
   - Predictive low alerts are **optional**, this will be your choice.

2. Revised Hypo Treatment
   - Always treat when the revised glucose threshold of 3.6 mmol/L is reached.
   - Always treat when sensor glucose < 3.9 mmol/L with downward trend arrows on sensor, there is active insulin on board (post meal-bolus) or during and post exercise/activity.
   - Hypo treatment to be avoided when sensor glucose is above 3.6 and glucose levels are stable on sensor and you are in closed loop therapy.

Below is a summary of all the study visits:

Visit 1*: Screening, Consent, Data collection, Hypo education and Randomisation* **(2 hrs)**

This is a face-to-face visit at PCH research rooms.
We will check your eligibility for the study again by asking a few questions about hypo awareness and review your sensor glucose reports. If you are eligible, we will make sure you understand everything you need to do in the study before you sign a consent form.

After the consent form has been completed, we will collect the following information about your clinical care. This includes:
- Height, weight ,HbA1c and CGM data
- Upload pump information
- Questions about diabetes management, any other medical history or any other treatments.
- Current hypo management

We will then randomise you into one of the two hypo treatment plans:
– using the standard hypo treatment with glucose level less than 3.9 mmol/L for 4 weeks, or
– using the revised hypo treatment with glucose level equal to or less than 3.6 mmol/L for 4 weeks

If you are in the revised hypo treatment plan, we will ask you not to treat any hypos until your glucose level is equal to or less than 3.6mmol/L. However, treatment should be given if your level is less than 3.9 mmol/L and likely to go *below* 3 mmol/L due to insulin bolus, insulin on board, exercise and/or activity.

If you are in the revised hypo treatment plan, we will contact you weekly to ensure you are not spending more time in hypo < 3.0 mmol/L than what we anticipate.

Visit 2*: End of Period 1 | 4 weeks after visit 1 (F2F or telehealth)* **(30 mins)**
This is the end of the first hypo treatment plan that you have been using for the last 4 weeks. At this visit, we will:

- Ask you to complete a questionnaire about hypos
- Collect diabetes clinical data

Then for the next 2 weeks, we will ask you to treat any hypos in your usual way.

Visit 3*: Start of Period 2 | 2 weeks after Visit 2 (F2F or telehealth)* **(1 hr)**
This is the start of the next 4-week study period. We will ask you to start using the other hypo treatment plan.

- If you used the standard hypo treatment plan first, you will now treat your hypos at the lower glucose level.
- If you used the revised hypo treatment plan first, you will now treat your hypos at the standard level less than 3.9 mmol/L.

If you are in the revised hypo treatment plan, we will contact you weekly.

Visit 4*: End of Period 2 and study end | 4 weeks after Visit 3* **(30 mins)**
This is the final study visit.
We will:

- Ask you to complete questionnaires about hypos and about your experience with using both the standard and the revised hypo treatment plan.
- Collect diabetes clinical data

Is there likely to be a benefit to me?
You may not directly benefit from the study. However, it has the potential to help you understand what happens if hypo treatment is started at a lower glucose level than what we currently recommend.
To thank you for your time and participation, you will receive a $50 gift voucher at the completion of the study.

Is there likely to be a benefit to other people in the future?
The information that we gather will be useful for doctors and scientists to help improve hypo management plans in people with type 1 diabetes, using closed loop therapy.

What are the possible risks and/or side effects?
Closed loop systems automate the background basal insulin depending on the sensor glucose levels with overall better time in range and less hypo. Hence, we are only recruiting children and young adults on closed loop therapy as the pump suspends insulin when the glucose level is trending down. Asking you to treat at a lower glucose level can potentially increase the number of times the glucose level could go below 3 mmol/L. The international guidelines recommend not more than 15 minutes/day in time below 3.0 mmol/L. This is 1% of time below 3.0 mmol/L on your CGM report.

We will be monitoring you weekly to ensure that this upper limit is not reached. However, you can contact us anytime if you believe that you are having more hypos below 3.0 mmol/L. If you spend more than the recommended time below 3.0 mmol/L, we will first review the reasons around the cause of hypo and discuss with you if they are true hypos. However, if you spend higher than expected time in hypo due to the revised threshold itself, we will discuss with you and your parent whether you wish to continue in the study.

Regardless of the group you are in, *you should treat for a hypo if your glucose level is lower than 3.9 mmol/L and is likely to go below 3 mmol/L due to insulin bolus / insulin on board /exercise or activity.*

What are the possible discomforts and/or inconveniences?
You may find treating glucose levels at a level lower than the usual 3.9 mmol/L discomforting. If you feel this is likely to happen, you may want to discuss the study the research team before participating in the study.

While you are using the revised hypo treatment level of 3.6 mmol/L, we will give you a letter of participation in the study.

Where is my information kept?
Any information obtained for the purpose of this research project that can identify you will be treated as confidential and securely stored. Information will be coded and de-identified.
All data will be stored in a password-protected database at Perth Children's Hospital (PCH) and The Kids Research Institute Australia ("The Kids") and retained for 25 years. Data will be kept for until the youngest child in study turns 25 years, and then securely destroyed in line with hospital policy. Clinical data about you collected in the study will be shared with your clinical team and stored in the diabetes database.

What about my privacy?
Your personal data will be coded and stored on secure PCH and The Kids computers.
Any data published and presented from this study, will not identify you by name.

Information about your participation in this research project will be recorded in your health records. Information about you may be obtained from your records held at this, and other, health services for the purposes of this research.

Who has approved the study?
The ethical aspects of this research project have been approved by the Child and Adolescent Health Service Human Research Ethics Committee.
This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2023)* produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

Who to contact for more information about this study:
If you would like any more information about this study, please contact the research team. They are very happy to answer your questions.

Name: Julie Dart
Telephone contact: 08 6456 4608
Email: Julie.Dart@health.wa.gov.au
Email: Diabetes.Research@health.wa.gov.au

Who to contact if you have any concerns about the organisation or running of the study?
If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research:

HREC name: Child & Adolescent Health Service (CAHS)
Position: HREC Chair
Telephone: (08) 6456 8639
Email: CAHS.HREC@health.wa.gov.au

Site contact:
Name: CAHS Research Ethics & Governance Office
Position: Manager
Telephone: (08) 6456 8639
Email: CAHS.RGO@health.wa.gov.au

What to do next if you would like to take part in this research:
If you would like to take part in this research study, please contact Julie Dart to make an appointment.

THANK YOU FOR YOUR TIME

Government of **Western Australia**
Child and Adolescent Health Service

Perth Children's Hospital

PARTICIPANT CONSENT FORM
Perth Children's Hospital

PLEASE NOTE THAT PARTICIPATION IN RESEARCH STUDIES IS VOLUNTARY AND YOU CAN WITHDRAW AT ANY TIME WITH NO IMPACT ON CURRENT OR FUTURE CARE.

I .....have
Given Names *Surname*

read the information explaining the study entitled:

Redefining Glucose Level for Hypo Treatment in Children and Young Adults using Closed Loop Therapy

I have read and understood the information given to me. Any questions I asked have been answered to my satisfaction.

I consent to participating in the study.

I understand that I may from the study at any stage.

I agree that research data gathered from this study may be published.

I agree that my data may be stored in a public data repository at study completion and could be used for unspecified future diabetes studies, provided that names are not used.

I understand that some of the staff working on this study are employed by the Diabetes Research Team which is part of The Kids Research Institute Australia and are not employed by the Government of Western Australia. These staff are working with the approval of the Child and Adolescent Health Service (CAHS) and will follow all the required policies and procedures and will safeguard the confidentiality of the participant information.

Participant's Signature..... Date: ……

I, ... have explained the above
(Investigator's full name)

to the signatory who stated that the child understood the same.

Signature..... Date: ……