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

Perth Children's Hospital

PARENT 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 and your child to take part in this study because your child has type 1 diabetes for more than 12 months, is between 6 and 18 years of age and is 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 levels from dropping below 3.0 mmol/L (significant hypo) as glucose levels below 3.0 mmol/L are thought to impact brain functioning.

Hypo treatment below 3.9 mmol/L is recommended by international guidelines although there is limited information on why this level was chosen. This may seem appropriate on therapies like insulin injections and non-automated insulin pump therapy. However, with current automated insulin pump therapy (closed loop) with pump suspending basal insulin with downward trend of glucose levels, 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.

This study has the potential to provide evidence to inform future guidelines and recommendations. This study is funded by a Perth Children's Hospital Foundation Stan Perron Grant. We have also sought the interest and feedback from people and their families living with type 1 diabetes to ensure your needs are met.

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).

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 your child is treated by your clinic team. You can pull out at any time. Your data will be stored using your project identification number and will be kept unless you instruct us not to do so.

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

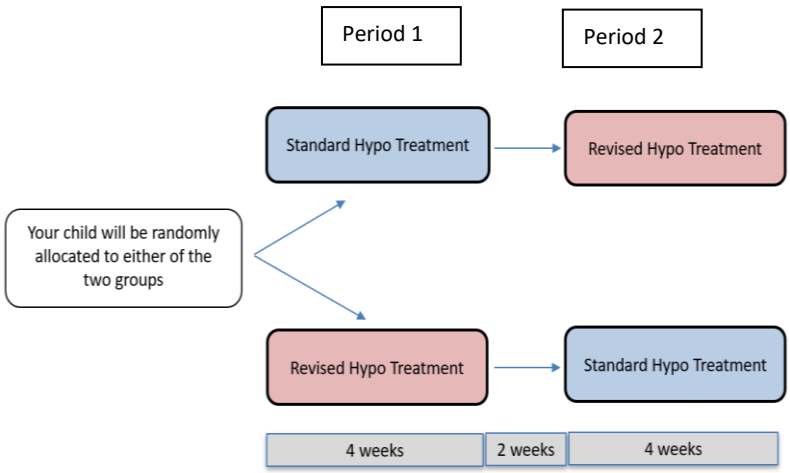
If you are interested in the study, we will first have to screen your child for eligibility to participate in the study. If your child is not able to recognise hypo, or there is a fear around hypo in you/your child, or if your child spends a fair bit of time in hypo or had an episode of severe hypo (loss of consciousness, seizure or the need of glucagon injection to treat hypo event) in the last 12 months, your child is not eligible to participate in the study.
If your child is eligible to participate, we will recruit you into the study.

Study outline:
This study will take 10 weeks and there are 4 visits. You and your child 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, your child 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 your child was in the standard hypo treatment, they will move on to the revised hypo treatment and if your child was in the revised hypo treatment, they 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:
Your child should continue to wear sensors during the entire duration of the study and be on closed loop therapy. If your child is 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, for your child.
   - Low alerts will be turned **ON**, in keeping with the glucose threshold 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 mmol/L and glucose levels are stable on sensor and your child is 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 child's eligibility for the study again by asking a few questions about hypo awareness and review your child's sensor glucose reports. If your child is 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 child's clinical care. This will include:
- 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 your child 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 your child is in the revised hypo treatment plan, we will ask you not to treat any hypos until your child's glucose level is less than 3.6mmol/L. However, treatment should be initiated earlier if your child is lower than 3.9 mmol/L and is likely to go *below* 3 mmol/L due to insulin bolus, insulin on board, exercise and/or activity.

We will give you an up-dated school management plan for the next four weeks, to give to your child's teachers explaining the new hypo management plan to be followed. We will also give you a diary to record hypo events and treatment.

We will contact you weekly throughout the study, to ensure your child is 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 your child has been using for the last 4 weeks. At this visit, we will:

- Ask you and your child to complete a questionnaire about hypo's
- Collect diabetes clinical data

Then for the next 2 weeks, we will ask you and your child 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 child's hypos at the lower glucose level.
  We will give you an up-dated school management plan for the next four weeks to give to your child's teachers explaining the new hypo management plan to be followed.
- If you used the lower glucose level hypo treatment plan first, you will now treat your child's hypos at the standard level less than 3.9 mmol/L.

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 and your child 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 and your child for your time participating in the study, 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 evidence in the scientific field to help optimise hypo managements 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 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 equates to less than 1% of time below 3.0 mmol/L on your child's CGM report.

We will be monitoring your child weekly to ensure that this threshold is not reached. However, you can contact us anytime if you believe that your child is having more hypos below 3.0 mmol/L. If your child spends more than the recommended time below 3.0 mmol/L, we will first review the circumstances around the cause of hypo and discuss with you if they are true hypos.

However, if your child spends higher than expected time in hypo due to the revised threshold itself, we will discuss with you whether your child will continue in the study.

The study is designed in such a way that if there is a known cause which will potentially lead to a hypo, treatment should be initiated earlier. *You should treat for a hypo if your child is lower than 3.9 mmol/L and is likely to go below 3.0 mmol/L due to insulin bolus, insulin on board, exercise and/or activity.*

What are the possible discomforts and/or inconveniences?
You/your child 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 with the research team prior to participating in the study.

While your child is using the revised hypo treatment level of 3.6 mmol/L, we will give you a letter of participation in the study and a revised school diabetes management plan for hypo treatment.
You will need to inform your child's teachers that they are participating in the research study and the treatment of any hypos at school should be managed as per the revised management plan.

Where is my child's information kept?
Any information obtained for the purpose of this research project that can identify your child 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) as well as 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 your child collected in the study will be shared with your child's clinical team and stored in the diabetes database.

What about my child's privacy?
Your child's 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 your child by name.

Information about your child's participation in this research project will be recorded in your child's health records. Information about your child may be obtained from your child's health 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 or your child would like any more information about this study, please do not hesitate to 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 and your child 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

FORM OF CONSENT
(For Parent/Guardian of Participant)
Perth Children's Hospital

PLEASE NOTE THAT PARTICIPATION IN RESEARCH STUDIES IS VOLUNTARY AND YOUR CHILD 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 or my child asked have been answered to my satisfaction.

I agree to allow

……
(full name of participant and relationship of participant to signatory)

to participate in the study.

I understand that I may withdraw my child from the study at any stage and withdrawal will not impact on routine care.

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

I agree that my child's 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 Telethon Kids Institute 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.

Parent or Guardian's Signature..... Date: ……

Child'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: ……