Advanced Hybrid Closed Loop in Paediatric Population (HyCLIP)

CLINICAL TRIAL PROTOCOL

1 Trial Details			
Protocol/Clinical Trial Title:	Assessment of closed loop technology in young children with type 1 diabetes		
Protocol Number (Version and Date):	V9 07Nov2022		
Short Title:	**Hy**brid **C**losed **L**oop **I**n **P**aediatric Population (**HyCLIP**)		
Trial Start Date:	August 2021	**Trial Finish Date:**	May 2023
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Sponsor Name (if applicable):	Telethon Kids Institute		

Trial Summary

There are an increasing number of young children diagnosed with Type 1 diabetes (T1D) and their management is challenging due to a combination of physiological factors and behavioural temperaments. This cohort is also adapting newer technological devices with parental supervision. However, the time in target range remains lower than in older children and adults. This increases the risk of immediate and long-term complications. There is strong evidence that glycaemic control in the first 10 years of life is a critical determinant of complication development in adulthood and therefore there is significant benefit from optimising glucose outcomes at this young age.

Automated insulin devices like hybrid closed loop (HCL) systems have been shown to reduce hyperglycaemia and improve glucose control in numerous trials and also in real world outcome data. They have provided a platform to improve time in range and glycaemic outcomes in older children and adults (Medtronic 670G approved for children above 7 years of age). Along with this, safety has been established. These systems remain to be tested in the young children with an algorithm which is more suitable for their needs. This study will explore the hypothesis that the advanced HCL (AHCL) system will reduce the glycaemic variability and thereby improve the glycaemic outcomes of children and improve the wellbeing of parents/caregivers.

This proposed study includes a 6-week feasibility phase followed by a 3-month multicentre randomised controlled study in children aged 2 to 7 years of age with T1D on insulin pump therapy. The participants will be randomly assigned to two groups: control group on standard therapy and the intervention group on AHCL system in the Medtronic 780G pumps.

The primary objective is to compare the proportion of *time in target range* (sensor glucose 3.9-10mmol/l) in young children with T1D while using AHCL or standard insulin pump therapy. The secondary aims are to determine the effect of AHCL on hypoglycaemia and hyperglycaemia and to determine the *psychological and social well-being* of caregivers compared to standard care.

The age of the participants means that this is placed in a category more than low risk although the level of parental supervision at this age and the use of a system that allows 24/7 glucose monitoring in reality more than mitigates this theoretical consideration. There are no potential ethical issues in the proposed study.

2 Rationale / Background

Background summary

The incidence of type 1 diabetes (T1D) is increasing by around 3% each year with a prevalence of 1 in 300(1) with most children diagnosed before adolescence. The management of T1D in young children places a combination of challenges to parents/caregivers and to health care professionals. Achieving glycaemic goals without increasing risk of hypoglycaemia remains the management strategy. However, the young age, unpredictable eating and activity patterns, small insulin doses and behaviour, and the organisation required place a significant burden on parents (2) which interfere with the ability to fine tune insulin delivery. The fear of nocturnal hypoglycaemia is common in parents of young children with T1D (3). This induces significant anxiety, poor sleep affecting the quality of life (4). This also leads to maladaptive behaviours permitting hyperglycaemia in an attempt to avoid hypoglycaemia with resultant impact on glycaemic management (5) which increases the risk of long-term microvascular and macrovascular complications. Time in range in this young cohort, not surprisingly, is less than in older children and adults with increasing evidence of reduced time in range associated with more microvascular complications (6). There is strong evidence that glycaemic control in the first 10 years of life is a critical determinant of development of complications in adulthood and therefore there is significant benefit from optimising glucose outcomes at this young age. This highlights the need for optimal management strategies to improve glycaemic outcomes and reduce the psychosocial stressors impacting the quality of life of both children and caregivers.

Technological advancements have provided a platform which could potentially enhance and improve the management of T1D without the risk of hypoglycaemia and glycaemic fluctuations. *Closed-Loop technology* integrates continuous measurement of interstitial glucose levels from a glucose sensor, a pump for delivering insulin and an algorithm that determines insulin delivery without patient intervention. It offers the potential to circumvent the significant glycaemic excursions associated with conventional therapy. AHCL has an automated insulin delivery based on sensor glucose feedback system (AutoMode) although it still requires the user to administer mealtime bolus insulin.

This device was first tested for use in patients >14 years old. AHCL therapy was safe during in-home use by adolescents and adults with increased time in target, and reductions in HbA1c, hyperglycaemia and hypoglycaemia, compared to baseline (7). This system is currently approved for children above 7 years of age after a safety evaluation for 3 months in children between 7-13 years of age (8). The recognition of improved safety of these devices have led clinicians to use these closed loop systems in young children as an off-label use. There have been safety and efficacy reports of children using the 670G AutoMode in a retrospective analysis in 16 children < 7 years of age (mean 4.3±1.2 years, range 2-6) *after off-label use* of the system in a tertiary paediatric diabetes centre (Seattle Children's Hospital) with a follow-up period of three to 12 months (mean 6.3 months) (9). These children were required to have a minimum of 8 units of insulin a day to qualify for Auto Mode use as per the design of the system. The case series showed the glycaemic control improved with no serious adverse events. This shows an unmet need to test these algorithms in clinical trials which will help in optimising diabetes management in this age group. This also highlights the confidence in clinicians to trial these devices in younger age group than standard insulin pump therapy (open loop systems) which have no control over insulin delivery in real-time.

The algorithm in the commercially available Medtronic 670G pump has been modified to increase time in range with automated correction boluses and additional target set point in order to reduce AutoMode exits and improve user experience and the time spent in AutoMode. Results of the in-home USA pivotal trial in 118 adults and 39 adolescents aged 14-75 years old with this AHCL algorithm showed that the trial successfully met both safety and glycaemic endpoints and demonstrated no occurrences of severe adverse events (10). Likewise, the device was also studied in a cross-over study in 60 individuals with T1D aged 7-70 years and reported significant improvement in glycaemic control with improvement in time in target by 12.5% with no increase in hypoglycaemia (11). These short-term studies with 4 to 6 week of AHCL use have provided the preliminary safety data in children and adults.

This algorithm is also being currently tested in the ongoing multicentre randomised controlled trial (RCT) in adolescents and young adults with suboptimal glycaemic control (RGS0000000886). Algorithms have also been studied in the younger population (1-7 years) and these studies have established preliminary feasibility and safety with use of the systems in short term(12, 13).

The study device used in this project (MiniMed 780G Pump) has a CE mark (Europe) however; it does not at this point in time have TGA or FDA approval and hence is an investigational device. The MiniMed 780G Pump is similar to the existing Medtronic 670G insulin pump, with the exception that it has an advanced algorithm as above (10,11) and has an added feature of Bluetooth connectivity which permits remote monitoring. The study proposes to conduct a two-phase study. The first step is to conduct a feasibility phase to establish the clinical parameters and settings of the device to inform the second phase of a longer RCT to test for the effectiveness of the device in this age group.

This proposal explores the hypothesis that this AHCL system will result in improved glycaemic control in young children compared to standard therapy. The study will examine the glycaemic outcomes, but have a strong emphasis on anxiety and quality of life in the caregivers.

Intervention

The **advanced hybrid closed loop system** compromises the Medtronic MiniMed™ 780G insulin pump containing the AHCL algorithm, and communicates via bluetooth wireless communication with the compatible devices in the MiniMed 780G System. The MiniMed 780G Pump works with the following major components: 1) Continuous Glucose Monitoring (CGM) that includes the Guardian Link (3) Transmitter that is connected to the Guardian Sensor (3) to receive sensor glucose values at 5 minute intervals; 2) blood glucose meter (Roche Accu-Chek®) that will be used to calibrate the sensor and has the ability to send blood glucose values wirelessly as a convenience to the user; 3) MiniMed Mobile App to allow upload of data wirelessly to the CareLink therapy management software; and 4) Pump Accessory devices to deliver insulin (infusion sets and reservoirs)..

The algorithm is contained in the pump and receives sensor glucose data every 5 minutes, computing and adjusting “basal rate” insulin delivery based on the glucose levels. Therefore, standard “basal” insulin that is pre-programmed in standard insulin pump therapy is replaced by the algorithm-derived insulin delivery (given as a micro-bolus every 5 minutes). Automated correction doses will be delivered by the system as per the set target glucose levels. Meals will still be announced, and an insulin bolus delivered according to the individualised patient’s carbohydrate ratio.

Unlike the HCL available in the commercially available Medtronic MiniMed™ 670G,

1) This system is designed to automate the delivery of correction boluses when the user experiences, or is predicted to experience, prolonged high glucose levels based on their sensor glucose readings.
2) The system has additional target points (5.5 mmol/L, 6.1 mmol/L, and 6.7 mmol/L),
3) The system will also have an additional Bluetooth capability which will make it possible to monitor the glucose level via a phone app and is therefore more suitable for this young cohort.

Glucose monitoring: All participants will be issued with a study meter (Roche Accu-Chek®) and test strips will be provided. For participants randomised to AHCL, this allows for data to be directly sent to the insulin pump.

CareLink Software: The Carelink Therapy Management System (CareLink) is a Medtronic web-based platform which is used for storing insulin pump data. Insulin pump data is then accessible for download by the investigators.

3 Trial Aims / Objectives / Hypotheses

Aims:

Feasibility phase

The primary aim of the 6-week feasibility phase is to increase the clinical experience with the device and to identify logistical barriers that may affect the optimal conduct of the subsequent randomised controlled trial (RCT).

Secondary aims of the feasibility phase are:
1. To assess the likelihood of uptake and engagement with the device (MiniMed 780G Pump)
2. To gather further estimates of glycaemic control metrics in children with T1D

Randomised Controlled Trial (RCT) phase

The primary aim of this phase is to determine the effectiveness of 3 months AHCL versus standard therapy (CSII with or without CGM) on time in target glucose range (3.9-10.0 mmol/L) in young children with type 1 diabetes.

The secondary aims are
1. To determine the effect of AHCL on *psychological and social well-being* of caregivers compared to standard care.
2. To determine the effect of AHCL on *glycaemic parameters (on hypoglycaemia and hyperglycaemia)* compared to standard care.
3. To explore the relationship between dietary intake and the use of AHCL compared to standard therapy.
4. To determine the cost effectiveness of AHCL compared to standard therapy with regard to parental quality of life.
5. To determine the user interactions with the device (human factors) to understand strategies to improve outcomes.

Hypotheses
1. AHCL will improve time in range as compared to standard insulin pump therapy
2. AHCL will have a positive impact on quality of life and fear of hypoglycaemia (as determined by parent questionnaires) compared to standard insulin pump therapy.
3. AHCL will be a cost-effective intervention for the management of type 1 diabetes compared to standard insulin pump therapy.

4 Trial Design

4.1 Study Endpoints

Feasibility phase

a. A collated list of difficulties/solutions encountered in this phase
b. Recruitment rate
c. Retention rate
d. Device setting adjustments
    i. Insulin carbohydrate ratio
    ii. Active insulin time
e. Glycaemic control
    i. HbA1c (%)
    ii. Percent time in range (3.9-10 mmol/L)
    iii. Coefficient of variation of sensor glucose values

RCT Phase

The glycaemic endpoints chosen for the study are as provided by the consensus report for artificial pancreas trials (10). The psychological well-being of parents will be assessed using validated questionnaires.
Primary endpoint: Time in range (3.9-10 mmol/l) collected at baseline and at study end (3 months)

Secondary endpoints:

1. Psychosocial well-being (parents)
    a) Functional health status QOL: WHO 5, EQ5D
    b) Fear of hypoglycaemia: HFS Parent
    c) Diabetes-related distress: PAID-Parent
    d) Anxiety: GAD-7
    e) Sleep quality: Pittsburgh Sleep Quality Index
    f) Technology acceptance and satisfaction: DTQ
    g) Semi structure interview
2. Glycaemic outcomes:
    a) HbA1c
    b) % CGM Time <2.8 mmol/L
    c) % CGM Time <3.0 mmol/L
    d) % CGM Time <3.3 mmol/L
    e) % CGM Time <3.9 mmol/L
    f) % CGM Time 3.9-7.8 mmol/L
    g) % CGM Time >10.0 mmol/L
    h) % CGM Time >13.9 mmol/L
    i) % CGM Time >16.7 mmol/L
    j) Glycaemic variability: Standard Deviation and Coefficient of Variation of CGM values
3. Nutritional adequacy of child's diet
    24- hour food recall to identify the proportion of children meeting current macronutrient ratios (for fat, protein and carbohydrate expressed as % of total energy intake) as per International Society for Pediatric and Adolescent Diabetes (ISPAD) Nutrition Guidelines on any given day, and food group serves as per the NHMRC's Australian Guide to Healthy Eating for Children and Adolescents recommendations.
4. Health-economic outcomes:
    a) QALYs calculated from the EQ-5D
    b) Hypoglycaemic events and HbA1c
    c) Admission to hospital due to diabetes-related events
    d) Parental work interruption and leave due to child's diabetes
    e) Child's school absenteeism due to diabetes
    f) Investigator reporting time spent on training, education and support, by the type of health professional resource used
    g) Diabetes management consumables (glucose strips, ketone strips, batteries, sensors, site dressings, lancets, needles, insulin)
5. Human factors:
    Determine the participant technology interaction and adherence patterns with the use of AHCL.

Study Device Overview

The MiniMed 780G is an ambulatory, battery operated, rate-programmable micro infusion pump. It is intended for continuous delivery of insulin for the management of diabetes in persons requiring insulin.

In addition to insulin delivery, the pump is designed to receive, display, and store real-time sensor glucose values from a compatible glucose sensor transmitting device that is part of a continuous glucose monitoring system. The sensor signals are converted by the transmitter to sensor glucose values (based on calibration values from a blood glucose meter) which are then transmitted wirelessly to the pump for display to the user.

When used with CGM, sensor signals are converted by a compatible transmitter to sensor glucose values (based on calibration values from a blood glucose meter) which are transmitted to the pump for display to the user. Sensor glucose and insulin delivery data is stored by the pump and may be further uploaded to a personal computer using a Medtronic therapy management software application via a compatible communication device. Uploaded data can be used to track patterns and improve diabetes management. The MiniMed 780G Pump leverages existing pump therapy and allows the user to optionally use an off-the-shelf suitable consumer electronic device to more conveniently assist with the management of their therapy. The MiniMed 780G Pump is similar to an existing Medtronic insulin pump, the MiniMed 670G Pump (CE Marked), with the exception that it is Bluetooth enabled and contains modifications to the closed loop Algorithm. The modifications to the closed loop algorithm include the addition of adjustable target setpoints (5.5mmol/L, 6.1 mmol/L, and 6.7 mmol/L), an auto correction bolus without user input or acknowledgement and fine tuning of safeguards in order to reduce auto mode exits and improve user experience.

The MiniMed 780G System has the capability to operate in Manual Mode (also referred to as open loop) or SmartGuard (also referred to as Advanced Hybrid Closed Loop (AHCL), Auto mode or closed loop).

- Manual Mode is when insulin delivery is the responsibility of the user and will be based on the user defined basal rates. Meal boluses are the responsibility of the user. Manual Mode also has the capability of suspending insulin if the sensor glucose is predicted to fall below predefined threshold values (also referred to as Suspend on Low/Suspend Before Low)
- SmartGuard is when the insulin delivery is being commanded by the AHCL algorithm to a set threshold of 5.5 mmol/L, 6.1 mmol/L, and 6.7 mmol/L as determined by the user. The AHCL algorithm will calculate the insulin dose at five-minute intervals, based on CGM data, in order to achieve glycaemic control throughout the day. Meal boluses are the responsibility of the user.

Advanced Hybrid Closed Loop Algorithm (SmartGuard)
SmartGuard (also referred to as AHCL) is part of the Smart Guard technology that is an optional feature. When SmartGuard is on, the AHCL algorithm will calculate the insulin dose at 5-minute intervals, based on CGM data, to the set threshold of either 5.5 mmol/L, 6.1 mmol/L, or 6.7 mmol/L as determined by the user. Users have the option to enable automatic delivery of correction boluses.

The MiniMed 780G Pump works with the following major components: 1) Continuous Glucose Monitoring (CGM) that includes the Guardian Link (3) Transmitter that is connected to the Guardian Sensor (3) to receive sensor glucose values at 5 minute intervals; 2) blood glucose meter that will be used to calibrate the sensor and has the ability to send blood glucose values wirelessly as a convenience to the user; 3) MiniMed Mobile App to allow upload of data wirelessly to the CareLink therapy management software; and 4) Pump Accessory devices to deliver insulin (infusion sets and reservoirs).

The pump interfaces with devices within the MiniMed 780G System to provide therapy to patients.

MiniMed 780G Pump (MMT-1885)
The MiniMed 780G Insulin Pump houses electronics, a pumping mechanism, a user interface, and a medication reservoir within the same physical device. The insulin pump communicates via BLE wireless communication protocol with the compatible devices in the MiniMed 780G System: Transmitter, Roche's Accu-Chek Guide™ Link Blood Glucose Meter, consumer electronic devices with the MiniMed Mobile App, and Blue Adapter with CareLink.

MiniMed 780G pump is an insulin delivery system designed to help people living with diabetes and on intensive insulin pump therapy. MiniMed 780G is the next iteration in Medtronic's hybrid closed loop technology for closed loop insulin delivery. In addition to delivery of insulin, the MiniMed 780G pump is designed to receive and display real-time glucose values received via a compatible transmitting device (as applicable). Glucose values and pump history can be stored for later upload so that it can be analyzed to track patterns and improve diabetes management via the Carelink Therapy Management System.

Glucose Sensor Transmitter – Guardian Link (3) Transmitter (MMT-7911)
The glucose sensor transmitter is a component of Medtronic Diabetes CGM. The Guardian Link (3) Transmitter is a portable, electrical current meter intended to process, store, and transmit glucose sensor values to the compatible insulin pump. The Guardian Link (3) Transmitter sends sensor glucose (SG) values and sensor integrity (SI) data from the Guardian Sensor (3) to the compatible insulin pumps via BLE wireless communication protocol.

Glucose Sensor – Guardian Sensor (3) [MMT-7020]
The Guardian Sensor 3 is used with Medtronic Diabetes glucose sensing systems to continuously monitor glucose levels in persons with diabetes. The existing sensor is compatible with the MiniMed 780G System with no design changes necessary.

BG Meter
The Roche Accu-Chek® Guide Link Blood Glucose Monitoring System (BGMS) is the BG meter that is compatible with the MiniMed 780G pump and indicated to send BG readings wirelessly to the pump via BLE communication. The BG meter can also be used without being linked to the pump with BG values being entered manually via the pump user interface.

Accessories

Carelink Therapy Management System (Personal-MMT-7333, System-MMT-7350,)
The Carelink Therapy Management System is an optional accessory device that tracks patterns and is used to improve diabetes management. The Carelink software supports data uploads from the MiniMed 780G pump to the cloud through the Mobile App or PC/Mac application using a Blue Adapter. Additionally, Carelink Connect is a set of features that allows for display of CGM and pump data on compatible consumer electronic devices for a CarePartner. For uploading to Carelink, the patient uses either the MiniMed Mobile App or the Blue Adapter.

MiniMed Mobile App/CareLink Connect App
The MiniMed Mobile App is an optional accessory that is not a medical device which receives pump data via BLE communication. The MiniMed Mobile App provides users with the convenience to transfer pump data to CareLink and also provides a mirroring display of the pump screen. The MiniMed Mobile App is not designed to control or monitor the performance of the insulin pump nor for direct monitoring of pump data. As a mirroring display, the app can provide alerts to the patient via the user interface. All alerts must be addressed on the insulin pump.

The MiniMed Mobile App will then interface with the **CareLink Connect** App that is an optional accessory that is not a medical device which receives pump data wirelessly from the CareLink server. The **CareLink Connect** App provides a mirroring display of the MiniMed Mobile App screen, for remote monitoring by a care partner (i.e. care giver or health care provider). The **CareLink Connect** App is not designed to monitor the performance of the insulin pump nor for direct monitoring of pump data. As a mirroring display, the app can provide notifications to the care partner via the user interface.

Blue Adapter
The Blue Adapter (also known as the BLE Dongle) is a USB accessory that allows for data uploads from MiniMed 780G pump to Carelink via USB interface of PC or Mac devices. The Blue Adapter is a commercial-off-shelf-component provided by Career Technologies. The Medtronic accessory number is ACC-1003911. The Blue Adapter is not a medical device thus no labeling is needed

Reservoir and a Tubed infusion set
Besides BLE communication with system components, the pump system employs a reservoir and a tubed infusion set to create an insulin delivery pathway. The pump is durable devices while the reservoir and infusion set(s) are single-use consumables that are replaced at regular intervals. The pump and reservoir can connect to a range of infusion sets to accommodate different users and different use conditions.

4.2 Study Design

This is a two-phase study and comprises a shorter feasibility phase followed by a larger RCT.

Feasibility Phase

This is a prospective, single-arm study, in free-living conditions in young children with T1D on insulin pump therapy. Participants will have a 2-week run-in phase (±1 week) during which participants will use the system in Manual Mode followed by a 6-week study phase (±1 week) during which SmartGuard is enabled. The study duration is for 8 weeks (±2 weeks).

The study design is as shown in the Figure 1 as below.

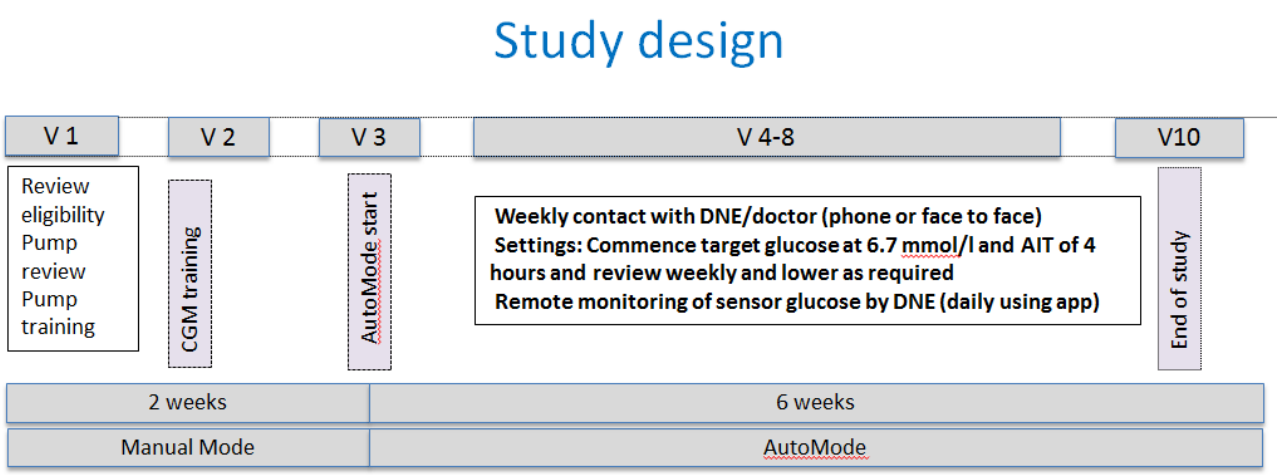


Figure 1: Feasibility phase design

Study Device

Participants will use the investigational study device. The target glucose set point will be initially set at 6.7mmol/l. This will be reviewed weekly by the research doctor. If there is no significant hypoglycaemia (< 4% below 3.9 mmol/l and < 1% below 3.0 mmol/l) and there is scope to improve time in range, the target will be revised to 5.5mmol/l. The active insulin time will be set at 4 hours at commencement and adjusted as required.

VISIT 1 (2 to 3 hours)
(Eligibility Confirmation, Baseline data collection, Pump training).

Participants will be checked if they meet the inclusion criteria listed below in Section 5.2. The following data will be recorded:

Visit 1

1. Consent signed by parent and investigator
2. Auxology
    a. Height
    b. Weight
    c. BMI
3. Demographic
    a. Date of Birth
    b. Gender
4. Diabetes clinical

a. Date of diagnosis
b. Current pump/CGM therapy
c. HbA1c
d. History of severe hypoglycaemia – coma or convulsion or episodes requiring third party assistance (events in last 12 months).
e. History of diabetic ketoacidosis (DKA) in the last 12 months
f. Hospital admissions in the last 12 months (DKA, Hyperglycaemia, Hypoglycaemia, Non diabetes related)
g. Total daily dose of insulin (mean of previous 7 days)
h. Co-morbidities and medications

5. Record/review pump settings and review download capability.
6. Review hypoglycaemia/hyperglycaemia management
7. Pump training

Parents will be trained on how to use the Medtronic 780G insulin pump. They will be provided with a compatible meter (which communicates with the pump) along with the glucose strips for the study. Parents will also be instructed on how to upload the pump. At this visit, all participants will be provided with a participant record book. All participants will also be provided with a record book to log hypoglycaemia, hyperglycaemia and technical issues related to the device.

Visit 2: CGM training (1 to 2 hours)

Parents will be instructed on how to link their child's CGM to the Medtronic 780G pump and issued with compatible next generation sensor and transmitter, as well as CGM user guide. Initial low and high alarms will be set at 4.0 mmol/L and 15 mmol/L respectively, although these can be changed according to individual preference. Sensor naïve individuals will have familiarisation phase of 7 to 10 days to get used to wearing a sensor.

Visit 1 and 2 could be combined for participants already on Medtronic pumps/sensors.

Visit 3: Commencement of AHCL (1-2 hours)
Once CGM data has been established for a minimum of 3 to 7 days, participant returns for face-to-face instruction on AHCL use and initiation of 'SmartGuard'. Target glucose will be set at 6.7 mmol/l and active insulin time will be set at 4 hours.

During this visit, the sensor will be replaced to demonstrate sensor warm up and AHCL initiation, and provide an opportunity for those unfamiliar with CGM use to practice a sensor change with supervision. The ability of the family to upload the pump at home will be confirmed.

Visits 4-8: Weekly follow-up

Participants will upload their pump weekly and will also have weekly communication with the research nurse and doctor (face to face or video call) to provide support for the following 6 weeks. The need to adjust target glucose or active insulin time will be reviewed with every visit.

Glucose levels will be remotely monitored continuously 24/7 by both caregivers/parents and study staff via CareConnect app. A default urgent low setting alert will be set at 3 mmol/L and caregivers/parents will be contacted by the study staff if this alert persists for more than 20 minutes (an expected recovery time following hypoglycaemia treatment). Communication can be more often – as per clinical need. Adverse events, if any, will be logged at each visit.

Visit 9: End of feasibility phase

This marks the end of the 6-week study period. Clinical data (HbA1c) along with total daily insulin requirement and pump settings at the end of the study will be collected. Short questionnaire asking for feedback using the 780G pump with SmartGuard, will be given to parents (optional).

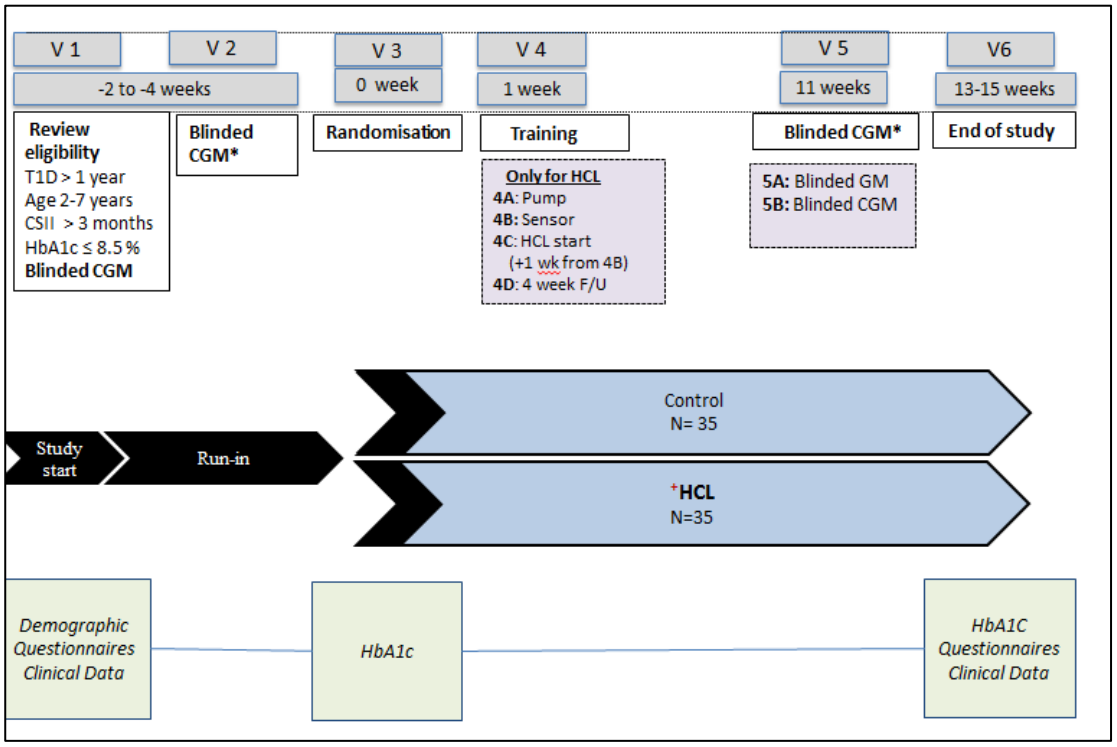
Wash-out period: There should be a minimum wash-out period of 3 months for participants willing to enrol for the larger RCT. The 3-month period is chosen to minimise the impact of any carry over of glycaemic impact with AHCL into the larger RCT.

Randomized Controlled Trial (RCT) Phase

This is a **prospective multicentre randomised controlled, two-arm unblinded, parallel study** in free-living conditions, in young children with type 1 diabetes on insulin pump therapy. Participants will be randomised in two groups; either the control group (standard therapy) or the intervention group (AHCL). The control group will be participants on continuous subcutaneous insulin infusion (CSII) with or without CGM (continuous glucose monitoring). The study duration is for 3 months. This phase will be conducted at four tertiary paediatric diabetes centres (Perth Children's Hospital, WA, Westmead Children's Hospital, NSW, Women's and Children's Hospital, SA, and Royal Children's Hospital, VIC).

AHCL group: Investigational pump for 3 months OR Control group: Standard CSII for 3 months.

The study design is as shown in the Figure 2 as below.



*Visits 2B,2C, 5C, 5D optional if data requirement from blinded CGM not met, Visit 5 Blinded CGM only for control group.

Figure 2: Study design RCT

VISIT 1

(Eligibility Confirmation, Baseline data collection and commencement of run-in period).

Information sheets will be provided in advance to participants who potentially fit inclusion criteria. HbA1c should be available from last clinic visit within 3 months of Visit 1.

Participants will be checked if they meet the inclusion criteria listed below in Section 5.2. The following data will be recorded:

1. Consent signed by parent and investigator

2. Auxology
    a. Height
    b. Weight
    c. BMI
3. Demographic
    a. Date of Birth
    b. Gender
4. Diabetes clinical
    a. Date of diagnosis
    b. Current pump/CGM therapy
    c. HbA1c
    d. History of severe hypoglycaemia – coma or convulsion or episodes requiring third party assistance (events in last 12 months).
    e. History of diabetic ketoacidosis (DKA) in the last 12 months
    f. Hospital admissions in the last 12 months (DKA, Hyperglycaemia, Hypoglycaemia, Non diabetes related)
    g. Total daily dose of insulin (mean of previous 7 days)
    h. Co-morbidities and medications
5. Psychology measures: Psychological scales will be administered to the parents on an electronic platform . (Questionnaires are included in the appendix)
    a. Functional health status: Quality of life (QOL) WHO 5(11), EQ5D(12)
    b. Fear of hypoglycaemia: Hypoglycaemia fear survey Parent(13)
    c. Diabetes-related distress: Problem Areas in Diabetes PAID-Parent version(14)
    d. Anxiety: GAD-7(15)
    e. Sleep quality: Pittsburgh Sleep Quality Index(16)
    f. Technology acceptance and satisfaction: DTQ(17)
6. Review pump settings and download capability.
7. Insertion of the first blinded sensor (next generation sensor and transmitter) to collect baseline glycaemic data. This constitutes first of the two sensors, each sensor provides data for 7 days. Parents will be instructed to test their children for a minimum 3 to 4x/day using the study meter provided.

At this visit, all participants will be provided with the study meter and a participant record book.

VISIT 2

<u>VISIT 2A</u> (7 days after Visit 1)

Insertion of 2nd blinded sensor: Participants will return 7 days after sensor insertion to remove and download the first week of CGM data. The glucometer will be uploaded. A new sensor will be inserted and a fresh transmitter attached.

A total of 2 weeks of blinded sensor is required with at least 10 days of data (18). In participants who do not meet this requirement or if the sensor falls off/removed accidentally, repeat sensors will be offered till a maximum of 4 attempts of data collection (2B, 2C).

Hence, the run-in period duration will be over 2 to 4 weeks.

<u>Visit 2B</u>

1. The blinded sensor is removed
2. Insertion of 3rd blinded sensor (if applicable) and to be removed a week later
3. 24-hour food recall interview (to capture baseline dietary pattern)

Visit 2C Insertion of 4th blinded sensor (if applicable) and to be removed a week later

Participants who do not meet the run-in requirements i.e demonstrate ability to use CGM (in sensor naïve individuals) and/or have insufficient data on blinded CGM will not proceed to randomisation and will be withdrawn from the study.

VISIT 3 (Randomisation)

This visit is the treatment allocation visit (see section 4.4 for details).
The following data will be collected prior to randomization:

1. Diabetes clinical
    a. HbA1c
    b. Total daily dose of insulin (mean of previous 7 days)
    c. Severe hypoglycaemia in the run-in period
    d. Diabetic ketoacidosis in the run-in period
    e. Hospital admissions in the run-in period

2. Review carbohydrate (CHO) counting and offer dietetic support if needed
3. Pump upload and review of settings
4. Review of hypoglycaemia/hyperglycaemia management.

The control group will continue on their insulin pump therapy with or without CGM. They will attend the 3-monthly regular clinic appointments.

The intervention group will use the study device with the compatible CGM. They will attend additional visits required for device training and to review the pump settings. They will continue to attend their 3-monthly clinic appointments.

If needed, Visit 3 and 4A can be combined for intervention group.

VISIT 4 (Only for participants randomised to AHCL arm)

The additional visits for the HCL group are for device training to support the use of HCL.

Visit 4A: Pump training (2 hours)

Parents will be trained on how to use the Medtronic 780G insulin pump. They will be provided with a compatible meter (which communicates with the pump) along with the glucose strips for the study.

Visit 4B: CGM training (2 hours)

They will be instructed on how to link CGM on the Medtronic 780G pump and issued with compatible next generation sensor and transmitter, as well as CGM user guide. Initial low and high alarms will be set at 4.0mmol/L and 15mmol/L respectively, although these can be changed according to individual preference. Sensor naïve individuals will have familiarisation phase of 7 to 10 days to get used to wearing a sensor.

Visit 4A and 4B could be combined for participants familiar with sensors.

Visit 4C: Commencement of AHCL (1-2 hours)

Once CGM data has been established for a minimum of 3 to 7 days, participant returns for face-to-face instruction on AHCL use and initiation of 'SmartGuard'. During this visit, the sensor will be replaced to demonstrate sensor warm up and AHCL initiation, and provide an opportunity for those unfamiliar with CGM use to practice a sensor change with supervision.

Participants will subsequently have weekly communication via phone call or email for support for the following 4 weeks, and upload their pump weekly. Investigators will log all time spent training and in communication with participant. Communication can be more often – as per clinical need, and logged.

Visit 4D: Review of AHCL (after 4 weeks from commencement of AHCL, 1 hour)

Face-to-face meeting to upload insulin pump, review CareLink reports and revise settings (CHO ratio and Insulin action time)

Participants will be issued with enough consumables for the study.

Research staff will review CGM data at 8 weeks' with participants encouraged to contact the team if support/assistance required.

VISIT 5 (11 weeks after randomisation for control arm only)

Visit 5A: Insertion of blinded CGM: This constitutes first of the two sensors, each sensor provides data for 7 days. Parents will be instructed to test their children for a minimum 3 to 4x/day using the study meter.

Visit 5B: Insertion of 2nd blinded CGM: Participants will return 7 days after sensor insertion to remove and download the first week of CGM data. The study meter will be uploaded. A new sensor will be inserted and a fresh transmitter attached.

A total of 2 weeks of blinded sensor is required with at least 10 days of data. In participants who do not meet this requirement, repeat sensors will be offered till a maximum of 4 attempts of data collection

Visit 5C: Insertion of 3rd blinded sensor (if applicable)

Visit 5D Insertion of 4th blinded sensor (if applicable)

VISIT 6 (1 week after last blinded sensor) **End of RCT Phase**

The following data will be collected:

1. Auxological
    a. Height
    b. Weight
    c. BMI
2. Diabetes clinical
    a. HbA1c
    b. Total daily dose of insulin (mean of previous 7 days)
    c. Pump upload (for intervention group)
    d. Severe hypoglycaemia since Visit 5 for Control arm / Visit 4d for Intervention arm
    e. Diabetic ketoacidosis since Visit 5 for Control arm / Visit 4d for Intervention arm
    f. Hospital admissions since Visit 5 for Control arm / Visit 4d for Intervention arm
3. Psychology measures: Psychological scales will be administered to parents on an electronic platform.
    a. Functional health status: Quality of life (QOL) WHO 5, EQ5D
    b. Fear of hypoglycaemia: Hypoglycaemia fear survey Parent
    c. Diabetes-related distress: Problem Areas in Diabetes PAID-Parent version
    d. Anxiety: GAD-7
    e. Sleep quality: Pittsburgh Sleep Quality Index
    f. Technology acceptance and satisfaction: DTQ
4. 24-hour food recall interview (to capture dietary pattern)
5. Parents of participants will be offered a semi-structured interview at the end of the study to share the lived experiences with use of new technology.

4.3 Bias

4.4 Blinding and Randomisation

To minimise bias, participants will be allocated to treatment group based on minimisation. Blinding is not possible in this open label study and hence the maintenance of breaking codes is not required.

Minimisation will be used to allocate participants to study group based on the following balancing factors measured at baseline: age at Visit 1 (<6 years, 6 years and above), time in target range (<55%, greater or equal to 55%) collected from blinded sensor data, and study site. Minimisation is a method of ensuring excellent balance between groups for known prognostic factors(20). The Minimpy program (MinimPy)(19) will be used to allocate participants. Allocation will be undertaken by the delegated persons at Perth Children's Hospital.

4.5 Device Tracking

Device serial numbers will be attributed to each study participant and recorded on an excel worksheet as well as REDCap when they are issued. At the conclusion of the study, devices will be returned and checked off against the excel worksheet.

4.6 Intervention/Product Description

The AHCL system comprises the Medtronic MiniMed™ 780G insulin pump containing the closed loop algorithm, a next generation glucose sensor and a glucose sensor transmitter. The algorithm is contained in the pump and receives sensor glucose data every 5 minutes, computing and adjusting "basal rate" insulin delivery based on the glucose levels. Automated correction doses will be delivered with high sensor glucose levels. Meals will still be announced, and an insulin bolus delivered according to the individualised patient's insulin carbohydrate ratio.

4.7 Product Accountability Procedures

The study investigators will be responsible for patient safety during the study. The participants on the AHCL system will be contacted on a regular basis to monitor progress and help troubleshoot the problems.

4.8 Trial Duration/Schedule

Feasibility Phase: For each participant, the study duration is 8 weeks.

RCT Phase: The trial is expected to take 24 months for recruitment, completion of study visits and data analysis. For each participant, the expected study duration is 3 months.

4.9 Trial Termination

Study participation is voluntary, and participants may withdraw at any time. The DSMB will report to the ethics committees and investigators if stopping the study is required.

In general, once a participant is randomised, he/she will remain in the study unless the investigator believes it is not safe for the participant to continue. However, the criteria below will be used to determine whether use of the AHCL should be discontinued for a participant.

1. Severe hypoglycaemia (seizure or coma or any episodes requiring glucagon).
2. Severe diabetic ketoacidosis (venous ph <7.2)
3. Non-compliance with the protocol or development of a new medical condition or need for chronic use of a medication which in the judgment of the investigator increases risk for the participant

If AHCL use is stopped according to the above criteria, but the participant is willing, they will remain in the study and will continue to make all of the scheduled visits and participate in all monitoring.

The primary analysis will be intention to treat. Since participants in the usual care arm are following their normal diabetes care regimen, there will be no change in their participation in the study if they experience one of the events that would trigger stopping.

Criteria for Suspending/Stopping Overall Study

The DSMB will provide guidance to the Lead Investigator as to whether the overall study should be stopped.

In case of a recurring system malfunction or participant safety issue observed with multiple participants, the overall study will be suspended while the problem is diagnosed. The study may resume if the underlying problem can be corrected by a protocol or system modification that will not invalidate the results obtained prior to suspension.

The primary safety outcome will be

Severe hypoglycaemia (coma, convulsion or any episodes requiring glucagon). A sequential monitoring approach described by Kramar and Bascoul-Mollevi (2009) will be taken to determine study cessation rules due to excess severe hypoglycaemia. As hypoglycaemia events are experienced during the study, the DSMB will be notified in real time. The maximum acceptable rate of severe hypoglycaemia as well as the approach taken with regard to 'alpha spend' to preserve the nominal alpha of 0.05 will be determined in conjunction with the DSMB prior to the commencement of the study.

An instance of severe DKA from Automode use (algorithm-related) in the AHCL group will result in temporarily stopping additional enrolment of participants until DSMB review of the data to determine whether the event was triggered by the system or not and whether it is safe to proceed. An emergency meeting of the DSMB will be convened within 7 days to review the data. In addition, the DSMB Chair may request a meeting at any time.

4.10 Data identification

Every participant will be given a unique study number. All data on CRF will be de-identified.

5 Source and Selection of Participants

5.1 Source of Participants

Eligible participants will be identified through the Western Australian Children's Diabetes Database (WACDD) and state specific databases. A generic invite with the information sheet will be sent electronically. Participants will also be identified during their clinic visits. We may also use advertisements, notices, and/or media to recruit participants. Examples include flyers posted in public settings, newspaper ads, and radio and television advertisement. All advertisements and recruitment materials (e.g., video, audio, and telephone scripts) will be submitted to HREC for prior approval.

The inclusion and exclusion criteria are the same for both phases. Participants in the feasibility phase are permitted to participate in the RCT after a minimum wash-out period of 3 months.

5.2 Participant inclusion criteria.

1. Type 1 diabetes (diagnosis consistent with American Diabetes Association Classification of Diabetes Mellitus, diagnosed at least 1 year ago)
2. CSII therapy for at least 3 months
3. Age 2 to ≤7 years
4. HbA1c ≤ 8.5% in the last 3 months
5. Total daily insulin of ≥8 units/day for the last two weeks
6. Participant and parent willing to follow study instructions
7. Living in an area with internet and cellular coverage

5.3 Participant exclusion criteria.

1. Commenced CGM in the 3 months prior to screening visit
2. Using advanced hybrid closed loop system: Control IQ
3. Uncontrolled coeliac disease
4. Uncontrolled thyroid disease
5. Inability or unwillingness to meet protocol requirements
6. Unwilling to perform 3 to 4 finger stick blood glucose measurements daily
7. Use of Hydroxyurea medication
8. Poor vision (of primary caregiver) precluding the use of investigational technology

5.4 Participant withdrawal criteria

(a) when and how to withdraw participants from the investigational product/study treatment;
The participant may withdraw from the study at any time. They can do so by contacting the research staff.

(b) the type and timing of the data to be collected for withdrawn participant(s);
As this is an intention-to-treat, the data for withdrawn participants will be used for analysis

(c) whether and how participants are to be replaced;
Participants will not be replaced.

(d) the follow-up for participants withdrawn from the investigational product/study treatment.
The participants will go back on their standard therapy and will be followed up as their regular clinic visits.

6 Treatment of Participants

6.1 Description and justification for treatments, interventions or methods to be utilised

The Medtronic AHCL system comprises the Medtronic MiniMed^{TM} 780G insulin pump containing the advanced closed loop algorithm, a next generation glucose sensor and transmitter. This system is the intervention provided to the participants for 3 months.

Rapid-acting Insulin is administered subcutaneously via the pump. The pump delivers insulin (microbolus) every 5 minutes and the amount is dependent on the sensor glucose levels. The system needs the entry of CHO amount by the user at meal times. This AHCL system has an advanced closed loop algorithm from the research studies (, RGS0000000886).

6.2 Permitted medications/treatments

For severe hypoglycaemia, intramuscular glucagon can be administered.

For ketosis > 0.6 mmol/l with blood glucose > 15mmol/l, insulin (rapid-acting) is administered with an insulin pen.

This is taught to every family at the time of diagnosis of T1D and review of their knowledge is established in subsequent clinic follow-ups.

6.3 Monitoring of participant compliance

The study is targeted at young children primarily supervised by parents/caregivers and hence a high degree of engagement with the study is expected.

Participants using the AHCL device will receive support from the research staff to help them familiarise themselves with the AHCL system. As this cohort is already on insulin pump therapy with most of the children on sensors, adaptation of this technology is not expected to be challenging.

Parents will also receive assistance to help troubleshoot sensor issues. They will be able to upload the pump at home, review reports and this will provide an opportunity to engage and encourage the use of the system.

7 Assessment of Efficacy

The efficacy of the device will be assessed through the Randomised Controlled Trial. 7.1 Primary outcomes

The primary outcome is the percentage of time spent in target glucose range (3.9-10 mmol/L) measured at 5-minutely intervals by a blinded CGM over 2 weeks starting at 13 - 15 weeks post randomization. Percentage of time spent in target glucose range will calculated by dividing the number of sensor readings falling in the range 3.9-10 mmol/L by the total number of sensor readings and multiplying by 100. Participants will be considered to have missing data if they have fewer than 10 days with 70% valid sensor readings.

7.2 Efficacy assessment

The effectiveness of the intervention on percent time in target glucose range will be assessed using an ANCOVA including treatment and baseline percent time in range. The analysis will be conducted on an intention to treat basis. The result will be presented as the mean difference in the percent time in target range at the end of the study between treatment arms with 95% confidence interval and p value. A statistically significant result ($p < 0.05$) in the direction in favour of the intervention group will be considered to provide evidence of the effectiveness of the intervention.

8 Assessment of Safety

8.1 Risks and benefits

1. There is a small risk of insulin pump site and glucose insertion site bruising, or skin reaction and/or haematoma. However all participants have used insulin pumps and most would have used sensors previously. This risk is expected to be similar to the current insulin pump and sensor issues in the clinic population.

2. Inaccuracy of sensor glucose with paracetamol. Taking medications that contain paracetamol may falsely raise sensor glucose readings. This may result in an over-delivery of insulin. If using paracetamol, all participants are advised to use glucometer to do blood glucose checks to make treatment decisions. This information is provided to all families at the time of commencement of sensor in clinic. Participants on HCL will also be advised to turn off the Auto correction feature, and consider turning off SmartGuard feature.

3. Risk of hypoglycaemia/hyperglycaemia: Any patient receiving insulin at any time has the potential to develop hyper or hypoglycaemia. These devices specifically aim to minimise the potential for that risk. The sensor glucose levels of all study participants are available to parents/caregivers in real time which will enable them to take appropriate clinical action as required.

   As the AHCL system is semi-automated and is dependent on the sensor glucose levels and the algorithm for delivery of background basal insulin, it could potentially have a risk of over-delivery or under-delivery of insulin.

a) An over-delivery of insulin can cause **hypoglycaemia**. Although this is more likely to be mild, the risk, albeit small, is that of glucose level falling < 3mmol/l and if prolonged, can cause severe hypoglycaemia (coma or convulsions or altered consciousness requiring third party assistance for treatment).
b) An under-delivery of insulin can cause **hyperglycaemia**. Glucose levels if persistently high can cause ketosis and if not corrected, can lead to diabetes ketoacidosis. This will require intravenous fluid hydration and repeated insulin doses for correction.

The management of the risks above are outlined in section 8.2 of the protocol as below.

- For severe hypoglycaemia, intramuscular glucagon can be administered.
- For ketosis > 0.6mmol/l with blood glucose > 15mmol/l, insulin (rapid-acting) is administered with an insulin pen.
- Contact with research team – as may require hospitalisation

This is taught to every family at the time of diagnosis of T1D and review of their knowledge is established in subsequent clinic follow-ups.

Furthermore, the system enables remote monitoring. The parent/caregiver will have real-time glucose readings of the young child on the phone allowing continuous glucose monitoring. High and low alerts will be enabled on the phone which will permit immediate correction of hypoglycaemia/hyperglycaemia.

8.2 Safety

This is a cohort of young children with T1D supervised by their parents/caregivers.
Participants will be contacted on a weekly basis (or more frequently as required) during the entire duration of the feasibility phase and for at least 4 weeks of the larger RCT after commencement of AHCL to review progress. During the feasibility phase, the research nurse will also follow the participant in real-time. Real-time glucose levels will also available to the caregiver/parent at all times.

a. Participants with high blood/sensor glucose levels will be advised to test for blood ketones.
b. Participants with hypoglycaemia will be advised take appropriate clinical action.
c. Weekly review of time spent in hypoglycaemia range will be evaluated by the research doctor. Any instance of a week where percentage of time spent <3.9 mmol/l exceeds 8% and/or percentage of time <3 mmol/L exceeds 2 % will be recorded as an adverse event.
d. Participants using the AHCL system will be informed to contact the research diabetes educator if they experience technical issues with the sensor and/or system and to revert to manual mode (standard pump) in the interim.
e. Participants in the control group will be advised to follow the clinical pathway while participants in the intervention group will be advised to contact the research doctor/diabetes educator.
f. In the event of device (pump) failure, the participant will be advised to switch to their standard pump therapy (own pump) and contact the research doctor/diabetes educator.
g. Patients are educated regarding awareness of insulin infusion failure (rising blood glucose levels and ketones) and how to manage this (using standard injected subcutaneous insulin, and change insulin infusion set).
h. Any admissions to hospital for DKA or severe hypoglycaemia will be reported to the principal investigator with 24hrs with notification to the lead site.
i. Establishment of Data and Safety Monitoring Board (DSMB) to review progress

8.3 Data and Safety Monitoring Board

To safeguard the interests of the study participants, monitor the main safety outcome measures, and monitor the overall conduct of the study, DSMB will be established. The board will receive and review information on the progress and accruing data and provide advice on the conduct of the study to the Investigators.

8.4 Adverse event reporting

Adverse Event

Any undesirable clinical occurrence in a participant whether it is considered to be device related or not, that includes a clinical sign, symptom or condition and/or an observation of an unintended technical performance or performance outcome of the device.

Adverse Device Event

A clinical sign, symptom or condition causally related to the device implantation procedure, the presence of the device, or the performance of the device system.

Severe adverse events

1. Severe hypoglycaemia (seizure or coma or any episodes requiring glucagon)
2. Severe Diabetic ketoacidosis (venous ph <7.2)
3. Requiring inpatient hospitalisation
4. A life-threatening event

8.5 Follow-up of Adverse Events

The follow-up of participants after adverse events will follow standard clinical care pathway of the institution.

9 Data Management, Statistical Analysis and Record Keeping

9.1 Statistics and Interim Analysis

Feasibility Phase

No statistical tests will be conducted with the difficulties encountered/solutions identified at the weekly meetings of the study team. Rather, all difficulties encountered will be discussed on a weekly basis and be collated into a single table at the end of the feasibility phase. This information will be used to design the manual of operations for the larger RCT.

Recruitment rate will be presented as a rate of recruitment per week and retention rate will be presented as a proportion of recruited participants that continued to wear the device to the end of the feasibility phase.

The mean, standard deviation, median, and interquartile range will be presented for insulin to carbohydrate ratio, insulin active time, and percent time in in various glycaemic ranges at the end of the phase.

No interim analyses are planned apart from the DSMB safety review reported above.

RCT Phase

Data collected at baseline and Visit 6 will be used to assess the effectiveness of AHCL therapy as compared to standard therapy.

To test for an effect of treatment group on the primary outcome, an ANCOVA including treatment, baseline percent time in range adjusting for minimisation factors will be conducted on an intention to treat basis. Multiple imputations will be used to handle missing data: a multivariate normal imputation approach will be taken. Results will be presented as the mean difference in the percent time in target range at the end of the study between treatment arms with 95% confidence interval and p value.

Model residuals will be used to assess model fit. If the residuals indicate poor model fit, the outcome variable will be transformed and the model refitted and evaluated. If poor model fit cannot be addressed, nonparametric analysis will be performed.

In the event that residuals are not normally distributed: the Mann–Whitney–Wilcoxon (Wilcoxon Rank-Sum) Test will be employed if raw data are symmetric; if raw data are non-symmetric, bootstrap methods will be used to test the difference between groups.

Continuous secondary outcomes (glycaemic, auxological, clinical, psychosocial) will be analysed using the ANCOVA approach described above. The same assessment of model residuals will be conducted, and the appropriate analysis approach utilised. Where parametric methods are employed using the untransformed outcome measure, mean difference with 95% CI will be presented; where data are transformed, the retransformed effect with 95% confidence intervals will be presented as an indication of the relative effect of the intervention; where non-parametric methods are employed, Hodges-Lehmann median difference with robust 95% CI will be presented.

Secondary count outcomes will be analysed using Poisson regression or, where overdispersion is apparent, negative binomial model with a maximum likelihood-estimated dispersion parameter. 'Exposure' will be the number of hours wearing the sensor for CGM-derived outcomes and total number of days enrolled in the study for non-CGM-derived outcomes.

To assess the cost effectiveness of the intervention, the 'cost per quality of life year (QALY)' will be calculated using an incremental cost effectiveness ratio.

All hypothesis testing will be two-sided with an α of 0.05. No corrections for multiplicity are planned to control Type I error; rather, the effectiveness of the intervention will be assessed based on the clearly specified primary outcome; secondary outcomes are exploratory in nature and will be labelled as such in publications arising from the study.

No interim analyses are planned apart from the DSMB safety review reported above.

9.2 Sample Size

The feasibility phase aims to recruit 12 participants. This number has been selected as it will allow sufficient participants to be enrolled to familiarise the study team with the device and identify any major difficulties that may be encountered within the protocol in the larger RCT.

The power calculation for the RCT is for a parallel study design with two groups of equal size. Based on CGM data in this age group (8, 9)we would expect control group to spend on average 55% of TIR with SD 11.5. With alpha set at 0.05, 31 participants would be required per group to have 80% power to detect an increase of 8% points. It is assumed the total dropout rate will be up to 10% based on previous studies, so we plan to recruit 70 participants in total.

9.3 Study Power and Significance
All hypothesis testing will be two-sided with an α of 0.05.

9.4 Statistical plan deviations:
Any deviations to the original statistical plan will be reported to relevant ethics committees, governance committees and the DSMB.

9.5 Selection of participants for analyses:
The selection of participants to be included in the analyses (e.g. all randomised participants, all dosed participants, all eligible participants, or all evaluable participants).

9.6 Data management
Data collected from each site will be stored in the respective study sites' secured servers, in accordance to data storage policies in each site. These data will all be entered, in a de-identified manner into a robust

data capture platform, REDCap, in which the forms were built and validated by a data manager based in Telethon Kids Institute.

All anonymised data will not be able to be linked back to any individual participant. Data will be stored on secure servers and electronic device capture systems with secure access for study staff only. All data will be stored at least for 25 years in line with GCP requirements on secure servers. Hard copies of participant notes will be stored in secure filing cabinets at each site and archived in secure facilities' at the end of the study.
All anonymised data will be risk rated at the completion of the study and stored in data repositories according to the Institution's data sharing policies and plan, and may be used for unspecified future research. Only published and permanently de-identified data will be deposited into publicly accessible repositories which will be safeguarded by Australian Data Archives (ADA) through a data sharing agreement with Telethon Kids Institute. The ADA main server is based in ANU and is a Core Trust Seal Certified repository.

Medtronic CareLink® System:
This system allows the study device to send information over the internet using a telecommunication network (such as a cellular network, wireless network, etc.). The information available from the Medtronic CareLink system is the same information the study team would collect from your device during an in-person office visit. Medtronic will receive participant's coded (deidentified) device data from CareLink®.

Medtronic takes steps to protect the privacy of the health information sent to the Medtronic CareLink Network over the internet. However, Medtronic cannot guarantee the health information is protected against unauthorised interception.

9.7 Procedures for missing, unused and spurious data:
Multiple imputations using multivariate normal regression imputation will be employed to account for missing/spurious data. Analysis using complete case and multiple imputation methods will be presented.

10 Monitoring / Audit

10.1 Monitoring, Audit and Regulatory Inspections Statement
The study investigators/institutions will permit study-related monitoring, audits, and regulatory inspections, providing direct access to source data/documents

10.2 Procedures for monitoring and auditing
The study is monitored by the coordinating principal investigator monthly. The DSMB will have access to the data.

11 Quality Control and Quality Assurance

11.1 Compliance statement
The trial will be conducted in compliance with the protocol, Good Clinical Practice and the application regulatory requirements.

11.2 Quality control
All staff will be trained to ensure appropriate data collection in accordance with ICH-GCP guidelines. They will be trained on how to fill out the CRFs to ensure quality of data. Study staffs are experienced diabetes educators and have been involved with research. The investigator will be monitoring the AHCL system, and will have the back-up of the Medtronic R&D team.

12 Ethics

Participants are informed that their consent is voluntary and their participation in the study or not will not affect their treatment in the clinic.

Separate consents will be taken for the feasibility phase and the RCT.

Participants will also be informed that they are unable to keep the investigational devices. Separate consent will be required for participant to consent to having their anonymised data to be put into a data repository at study completion for future research.

Budget, Financing, Indemnity and Insurance

Budget, financing, indemnity and insurance addressed in a separate section.

This is a Telethon Kids Institute sponsored study with grant from JDRF Australia. Detailed budget will be addressed in a separate Budget Form which will be submitted as part of RGS and site governance.

14 Publication

The study will be registered at Australia New Zealand Clinical Trial Register (ANZCTR). Final results will disseminated in a publication and presented at local and international conferences. All participants will be invited to a publicly open research evening hosted annually by the diabetes and endocrinology department where results will be presented. The results will also be disseminated through clinic newsletter and will be available on Children Diabetes Centre (CDC) website for families.

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16 Appendices

Appendix A – Psychosocial Questionnaires

i. Functional health status QOL: EQ5D
ii. Functional health status QOL: WHO 5
iii. Fear of hypoglycaemia: HFS Parent
iv. Diabetes-related distress: PAID-Parent
v. Anxiety: GAD-7
vi. Sleep quality: Pittsburgh Sleep Quality Index
vii. Technology acceptance and satisfaction: DTQ

Appendix B – 24 hour dietary intake recall

Appendix C – Interview questions

Appendix D– Feedback Questionnaire – Feasibility study

Appendix A – Psychosocial Questionnaires

i. Functional health status QOL: EQ5D

By placing a tick in one box in each group below, please indicate which statements describe your own health state today.

Mobility

I have no problems in walking about ❑

I have some problems in walking about ❑

I am confined to bed ❑

Self-Care

I have no problems with self-care ❑

I have some problems washing or dressing myself ❑

I am unable to wash or dress myself ❑

Usual Activities *(e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑

I have some problems with performing my usual activities ❑

I am unable to perform my usual activities ❑

Pain / Discomfort

I have no pain or discomfort ❑

I have moderate pain or discomfort ❑

I have extreme pain or discomfort ❑

Anxiety / Depression

I am not anxious or depressed ❑

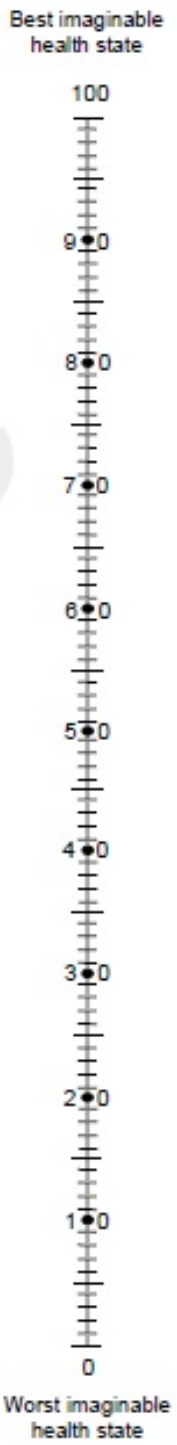
I am moderately anxious or depressed ❑

I am extremely anxious or depressed ❑

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



WHO (Five) Well-Being Index (1998 version)

Please indicate for each of the five statements which is closest to how you have been feeling over the last two weeks. Notice that higher numbers mean better well-being.

Example: If you have felt cheerful and in good spirits more than half of the time during the last two weeks, put a tick in the box with the number 3 in the upper right corner.

	Over the last two weeks	All of the time	Most of the time	More than half of the time	Less than half of the time	Some of the time	At no time
1	**I have felt cheerful and in good spirits**	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0
2	**I have felt calm and relaxed**	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0
3	**I have felt active and vigorous**	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0
4	**I woke up feeling fresh and rested**	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0
5	**My daily life has been filled with things that interest me**	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0

Scoring:

The raw score is calculated by totalling the figures of the five answers. The raw score ranges from 0 to 25, 0 representing worst possible and 25 representing best possible quality of life.

To obtain a percentage score ranging from 0 to 100, the raw score is multiplied by 4. A percentage score of 0 represents worst possible, whereas a score of 100 represents best possible quality of life.

iii. Fear of Hypoglycaemia: Hypoglycemia Fear Survey – Parents of Young Children (HFS-PYC)

HFS-PYC items
Behavior scale
1. Feed my child large snacks at bedtime
2. Avoid allowing my child to be away from me when his/her sugar is likely to be low
3. Try to run a little high to be on the safe side
4. Keep my child's sugar higher when he/she will be away from me
5. Feed my child as soon as I feel or see the first signs of low blood sugar
6. Reduce my child's insulin when I think his/her blood sugar is low
7. Keep my child's blood sugar higher when I know he/she is planning to be at a long event (e.g., school, party)
8. Always carry fast-acting sugar
9. Don't allow my child to play excessively when I think his/her blood sugar is low
10. Check my child's blood sugar often when he/she is planning to be at a long event (e.g., school, party)
Worry scale
11. Not recognizing that my child is having a hypoglycemic event
12. Not having food or fruit juice with me for my child
13. Having my child dizzy or pass out in public
14. Feeling that my child will have a low blood sugar while he/she is asleep
15. My child embarrassing him/herself in front of friends/family in a social situation
16. My child having a low blood sugar when he/she is away from me
17. My child being disoriented
18. My child losing control
19. No one being around to help my child during a hypoglycemic event
20. My child making a mistake or having an accident at day care/school
21. My child getting a bad evaluation at day care/school because of something that happens when his/her sugar is low
22. My child having seizures
23. My child developing long-term complications from frequent low blood sugars
24. My child feeling light headed or faint
25. My child having an insulin reaction
26. My child having a hypoglycemic event while I'm driving

HFS-PYC, Hypoglycemia Fear Survey – Parents of Young Children.

Likert scale 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Very Often

Patton, SR, Dolan, LM, Henry, R and Powers, SW, Parental fear of hypoglycemia: young children treated with continuous subcutaneous insulin infusion. Pediatric Diabetes; 2007; 8: 362-368. doi:10.1111/j.1399-5448.2007.00242.x

Patton SR, Dolan LM, Henry R, Powers SW: Fear of hypoglycemia in parents of young children with type 1 diabetes mellitus. J Clin Psychol Med Settings 2008;15:252–259

Patton SR, Noser AE, Clements MA, Dolan LM, Powers SW. Reexamining the Hypoglycemia Fear Survey for Parents of Young Children in a Sample of Children Using Insulin Pumps. *Diabetes Technol Ther*. 2017;19(2):103-108. doi:10.1089/dia.2016.0389

PROBLEM AREAS IN DIABETES—PARENT (PAID-PR) SURVEY REVISED

The following statements describe diabetes-related issues that may or may not be a concern for you. For each item, choose the ONE answer that best describes how much you agree or disagree with that statement.

	Agree				Disagree
1. I feel discouraged with my child's diabetes treatment plan.	⓪	①	②	③	④
2. I feel scared when thinking about my child having/living with diabetes.	⓪	①	②	③	④
3. I have difficulty dealing with school staff (e.g., nurses, teachers, principals).	⓪	①	②	③	④
4. I feel that my child is deprived regarding food and meals.	⓪	①	②	③	④
5. I feel that my child is excluded from activities/events because of his/her diabetes.	⓪	①	②	③	④
6. I feel upset when my child's blood sugars are out of range.	⓪	①	②	③	④
7. I worry about my child having a low blood sugar.	⓪	①	②	③	④
8. I feel angry when I think about my child having/living with diabetes.	⓪	①	②	③	④
9. I feel constantly concerned about what my child eats.	⓪	①	②	③	④
10. I worry about the future and the possibility of serious complications for my child.	⓪	①	②	③	④
11. I feel upset when my child's diabetes management is "off track".	⓪	①	②	③	④
12. I worry that my child will not be taken care of when away from home.	⓪	①	②	③	④
13. I feel like the "diabetes police".	⓪	①	②	③	④
14. I feel that diabetes takes up too much mental and physical energy.	⓪	①	②	③	④
15. I feel alone in managing my child's diabetes.	⓪	①	②	③	④
16. I feel that other family members are not supportive in managing my child's diabetes.	⓪	①	②	③	④
17. I worry whether or not my child will remember to eat his/her snack.	⓪	①	②	③	④
18. I feel "burned out" by the constant effort to manage diabetes.	⓪	①	②	③	④

v. Anxiety: GAD-7

GAD-7

Over the last two weeks, how often have you been bothered by the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Having trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

(For office coding: Total Score T_____ = ___ + ___ + ___)

vi. Sleep Quality: Pittsburgh Sleep Quality Index

	Very good (0)	Fairly good (1)	Fairly bad (2)	Very bad (3)
9. During the past month, how would you rate your sleep quality overall?				

Component 1	#9 Score	C1_____
Component 2	#2 Score (≤15min=0; 16-30 min=1; 31-60 min=2, >60 min=3) + #5a Score (if sum is equal 0=0; 1-2=1; 3-4=2; 5-6=3)	C2_____
Component 3	#4 Score (>7=0; 6-7=1; 5-6=2; <5=3)	C3_____
Component 4	(total # of hours asleep)/(total # of hours in bed) x 100 >85%=0, 75%-84%=1, 65%-74%=2, <65%=3	C4_____
Component 5	Sum of Scores #5b to #5j (0=0; 1-9=1; 10-18=2; 19-27=3)	C5_____
Component 6	#6 Score	C6_____
Component 7	#7 Score + #8 Score (0=0; 1-2=1; 3-4=2; 5-6=3)	C7_____

Add the seven component scores together _____ **Global PSQI Score** _____

Buysse, D.J., Reynolds III, C.F., Monk, T.H., Berman, S.R., & Kupfer, D.J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Journal of Psychiatric Research, 28*(2), 193-213.

Reprinted with permission from copyright holder for educational purposes per the University of Pittsburgh, Sleep Medicine Institute, Pittsburgh Sleep Quality Index (PSQI) website at http://www.sleep.pitt.edu/content.asp?id=1484&subid=2316.

h. Have bad dreams				
i. Have pain				
j. Other reason(s), please describe, including how often you have had trouble sleeping because of this reason(s):				
6. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
8. During the past month, how much of a problem has it been for you to keep up enthusiasm to get things done?				

Diabetes Technology Questionnaire
Part 1: Impact and Satisfaction
Baseline Version

Thank you for giving us your time and effort in taking part in this study. Your opinions about using diabetes technology are very valuable to us and we hope that you can now help us learn how this has affected your daily life with diabetes. Below you will see some statements about different kinds of diabetes treatments that include using different diabetes devices such as a blood glucose meter, insulin pump, continuous glucose monitor or closed loop insulin delivery system.

Please tick the box below that lists the diabetes devices you are using now as part of treatment. If you aren't sure, ask the diabetes nurse to help you.

- ❑ Glucose Meter(s) and daily use of an insulin pump
- ❑ Glucose Meter(s) and a Continuous Glucose Monitor (Medtronic, Dexcom or Libre) and daily use of an insulin pump

For those just entering the study: Now we'd like to ask you some questions about the treatment approach that you selected above. We've listed below some parts of living with diabetes that might be made better or worse by your use of diabetes devices. For each of these, please circle the number that best tells how much of a problem it is now.

	Is this a problem now?				
	Very Much		Just A Little		Not At All
1. Worry or fear about high blood sugar	1	2	3	4	5
2. Effort to keep low blood sugar from happening	1	2	3	4	5
3. Worry or fear about low blood sugar during sleep	1	2	3	4	5
4. Feeling different from others	1	2	3	4	5
5. Amount of time spent thinking about diabetes	1	2	3	4	5
6. Not knowing how eating affects blood sugar	1	2	3	4	5
7. Amount of time and effort needed for diabetes from my family or me	1	2	3	4	5
8. Worry or fear about long term health	1	2	3	4	5

	Is this a problem now?				
	Very Much		Just A Little		Not At All
9. Worry or fear about daytime low blood sugar	1	2	3	4	5
10. Effort to keep high blood sugar from happening	1	2	3	4	5
11. Pain or discomfort from finger sticks or monitors	1	2	3	4	5
12. Pain or discomfort from insulin injections or pump sets	1	2	3	4	5
13. Family arguments or worries about diabetes	1	2	3	4	5
14. Trouble sleeping well	1	2	3	4	5
15. Strictness of the meal plan	1	2	3	4	5
16. Coping with work or school along with diabetes	1	2	3	4	5
17. Taking part in sports, exercise or playing despite diabetes	1	2	3	4	5
18. Knowing how much insulin to take	1	2	3	4	5
19. Keeping up with friends or peers who don't have diabetes	1	2	3	4	5
20. Reacting to all of the blood sugar results that I get	1	2	3	4	5
21. Dealing with others who ask about diabetes	1	2	3	4	5
22. My amount of responsibility for taking care of diabetes	1	2	3	4	5
23. Being sure that pre-meal insulin covers the amount of carbohydrates eaten	1	2	3	4	5
24. Getting the right amount of insulin when meals are skipped or delayed	1	2	3	4	5
25. Reacting to all of the alarms from diabetes devices	1	2	3	4	5

	Is this a problem now?				
	Very Much		Just A Little		Not At All
26. Getting the right amount of insulin on sick days.	1	2	3	4	5
27. Feeling that diabetes devices run my life	1	2	3	4	5
28. Getting the right amount of insulin after exercising more than usual	1	2	3	4	5
29. Coping with carrying and using several devices	1	2	3	4	5
30. Looking different because of diabetes and using devices	1	2	3	4	5

Diabetes Technology Questionnaire
Part 1: Impact and Satisfaction
Follow-Up Version

Thank you for giving us your time and effort in taking part in this study. Your opinions about using diabetes technology are very valuable to us and we hope that you can now help us learn how this has affected your daily life with diabetes. Below you will see some statements about different kinds of diabetes treatments that include using different diabetes devices such as a blood glucose meter, insulin pump, continuous glucose monitor or closed loop insulin delivery system.

Please tick the box below that lists the diabetes devices you are using now as part of treatment. If you aren't sure, ask the diabetes nurse to help you.

❑ Glucose Meter(s) and daily use of an insulin pump

❑ Glucose Meter(s) and a Continuous Glucose Monitor (Medtronic, Dexcom or Libre) and daily use of an insulin pump

For those completing a follow-up study visit: Now we'd like to ask you some questions about the treatment approach that you selected above. We've listed below some parts of living with diabetes that might be made better or worse by your use of diabetes devices. For each of these, please circle the number that best tells how much of a problem it is now and then circle the number that best tells how it has changed for you **compared to the treatment received before you entered this study.**

	Is this a problem now?					How has it changed compared to your treatment before the study?				
	Very Much		Just A Little		Not At All	Much Worse	A Little Worse	Same	A Little Better	Much Better
1. Worry or fear about high blood sugar	1	2	3	4	5	1	2	3	4	5
2. Effort to keep low blood sugar from happening	1	2	3	4	5	1	2	3	4	5
3. Worry or fear about low blood sugar during sleep	1	2	3	4	5	1	2	3	4	5
4. Feeling different from others	1	2	3	4	5	1	2	3	4	5
5. Amount of time spent thinking about diabetes	1	2	3	4	5	1	2	3	4	5
6. Not knowing how eating affects blood sugar	1	2	3	4	5	1	2	3	4	5
7. Amount of time and effort needed for diabetes from my family or me	1	2	3	4	5	1	2	3	4	5

	Is this a problem now?					How has it changed compared to your treatment before the study?				
	Very Much		Just A Little		Not At All	Much Worse	A Little Worse	Same	A Little Better	Much Better
8. Worry or fear about long term health	1	2	3	4	5	1	2	3	4	5
9. Worry or fear about daytime low blood sugar	1	2	3	4	5	1	2	3	4	5
10. Effort to keep high blood sugar from happening	1	2	3	4	5	1	2	3	4	5
11. Pain or discomfort from finger sticks or monitors	1	2	3	4	5	1	2	3	4	5
12. Pain or discomfort from insulin injections or pump sets	1	2	3	4	5	1	2	3	4	5
13. Family arguments or worries about diabetes	1	2	3	4	5	1	2	3	4	5
14. Trouble sleeping well	1	2	3	4	5	1	2	3	4	5
15. Strictness of the meal plan	1	2	3	4	5	1	2	3	4	5
16. Coping with work or school along with diabetes	1	2	3	4	5	1	2	3	4	5
17. Taking part in sports, exercise or playing despite diabetes	1	2	3	4	5	1	2	3	4	5
18. Knowing how much insulin to take	1	2	3	4	5	1	2	3	4	5
19. Keeping up with friends or peers who don't have diabetes	1	2	3	4	5	1	2	3	4	5
20. Reacting to all of the blood sugar results that I get	1	2	3	4	5	1	2	3	4	5
21. Dealing with others who ask about diabetes	1	2	3	4	5	1	2	3	4	5
22. My amount of responsibility for taking care of diabetes	1	2	3	4	5	1	2	3	4	5
23. Being sure that pre-meal insulin covers the amount of carbohydrates eaten	1	2	3	4	5	1	2	3	4	5
24. Getting the right amount of insulin when meals are skipped or delayed	1	2	3	4	5	1	2	3	4	5

	Is this a problem now?					How has it changed compared to your treatment before the study?				
	Very Much		Just A Little		Not At All	Much Worse	A Little Worse	Same	A Little Better	Much Better
25. Reacting to all of the alarms from diabetes devices	1	2	3	4	5	1	2	3	4	5
26. Getting the right amount of insulin on sick days.	1	2	3	4	5	1	2	3	4	5
27. Feeling that diabetes devices run my life	1	2	3	4	5	1	2	3	4	5
28. Getting the right amount of insulin after exercising more than usual	1	2	3	4	5	1	2	3	4	5
29. Coping with carrying and using several devices	1	2	3	4	5	1	2	3	4	5
30. Looking different because of diabetes and using devices	1	2	3	4	5	1	2	3	4	5

24 Hour Food Recalls – Instructions

The triple-pass method

Participant's parents are asked whether or not the day to be recalled was typical of their child's usual food intake, or if it was unusual or restricted in any way and if so for what reason. Record food intake on the template provided

1. **A quick list of foods eaten or drunk**
   Participant and the parents are asked to report everything the participant had to eat or drink (e.g. on the previous day between midnight and midnight) in an uninterrupted free flowing list.

2. **Collection of detailed information**
   For each item of food or drink in the quick list, they are asked to provide additional detail, including:
   - The time at which the food or drink was consumed
   - A full description of the food or drink, including brand name where available
   - Any foods likely to be eaten in combination e.g. milk in coffee
   - Recipes and other combinations of foods e.g. sandwiches
   - The quantity consumed, based on household measures, photographs of different portion sizes of foods, or actual weights from labels or packets
   - Any leftovers or second helpings

3. **A recall review**
   The interviewer reviews all of the food eaten and drunk in chronological order, prompting for any additional eating or drinking occasions and foods or drinks consumed, and clarifying any ambiguities regarding the type of food or drink consumed and portion size. Finally the interviewer asks the participant and the parent to name the place where each food or drink item was consumed.

Prompts and probing

- All of the information is collected with a series of neutral prompts to encourage recall. You should ask neutral questions which do not encourage a specific response.
  Example: So, for individual foods, you should not say specifically "was that boiled or fried?" but "how was that cooked?" for additional foods, you should not presuppose consumption of foods in specific combinations, for example you should say, "what else did you have with that?" rather than "did you have butter on potatoes?"
- However, where initial neutral prompts do not lead to further information it may be necessary to list a series of specific options e.g. "was that boiled, fried, roasted, grilled, etc?" always list the options.
- Where foods come in different varieties e.g. low fat, low kilojoule, caffeine free etc, always refer to the "standard" variety first as well as the low fat/low kilojoule variety i.e. "so was that standard or diet coke?"
- Some foods are commonly consumed in addition to others e.g. sugar in tea/on cereal, butter on potatoes, jam on toast etc.
- Composite dishes: when a food is composed of several different foods e.g. a sandwich or a salad, these should be recorded separately e.g. a sandwich should be split into bread, spread and filling.

Estimation of portion size

A portion size can be described in terms of:

- Household measures (1tsp, 1cup, 1 apple etc)
- Weights (420g tin baked beans, 120g pot yoghurt)

➢ If conducting the interview face to face it can be useful to have an example plate, bowl measuring cups and spoons to assist the respondents in working out their portion sizes.

If a respondent describes the amount they had to eat in spoonfuls, it is important to determine the size of the spoon. Often respondents will say they used a tablespoon when what they actually used was a dessertspoon.

Leftovers & Second helpings

After the respondent described their meal, it is useful to ask whether they ate the whole portion. If not, it's necessary to find out what proportion was 'leftover' (e.g, ½, ¼ etc).

Remember to also ask whether the respondent had second helpings of a main meal as that can easily be forgotten. If so, find out the amount added (e.g 1 extra sausage, ½ cup peas)

Adapted from:

Nelson M, Erens B, Bates B, Church S, Boshier. 24-hour recall instructions. Kings College London. Cited 24 July 2012. Available from: http://dapa-toolkit.mrc.ac.uk/documents/en/24h/24hr_Instructions_LIDNS.pdf

24hr Recall Data Collection Template

Breakfast:

Morning tea:

Lunch:

Afternoon tea:

Dinner:

Supper:

3

Forgotten foods checklist:

Beverages: Coffee, tea, soft drinks, milk or juice, beer, wine, cocktails, or other drinks

Sweets: Cookies, candy, ice cream, or other sweets

Snacks: Chips, crackers, popcorn, pretzels, nuts, or other snack foods

Fruits, Vegetables, Cheese: Fruits, vegetables, or cheese

Breads: Breads, rolls, or tortillas

Condiments: sauces, gravy, dressings, butter/margarine, salt

Other Tips

- Never accept an estimate of the weight from the parent (even if they weighed it ask for a volume– e.g. cups, tablespoon etc.)
- Always get a recipe from them if they had a proportion of a larger meal. Get the whole recipe (including salt and oil etc.) and then what proportion of the whole amount they had eg. 1/6.
- Always ask about cooking method in detail e.g. If they say baked, say "baked in what' – it may be baked in butter or in foil – very different.
- Always ask about drinks with meals
- Always ask about sauces/condiments
- AT the end of a description of a meal, recap with them – and say "so you had grilled flathead, with potato, peas, and beans". So both you and they can picture it and see if they forgotanything
- Ask about mid meal snacks
- Ask about desserts

1. FRUIT

Peeled/unpeeled
Colour – e.g. red/green apple
Tinned – what sort of juice (eg. natural, syrup), how much of the juice did they eat
Juice – 100% or fruit drink, NAS?, added vitamins

2. VEGETABLES

Fresh or frozen or tinned (with or without salt)
Cooking method – boiled with or without salt, baked (with oil / spray?), roasted in oil (what type and how much) microwaved, steamed etc
How much – if using cups is it ¼ cup sliced/whole/mashed/diced, or how much of a whole vegetable (e.g. ½ a medium)
Potato – with or without skin
Colour – e.g. red/green capsicum
Juice – salted/commercial or freshly juiced

3. DAIRY

Milk – brand name and fat content
Yoghurt – brand and with fruit or plain or vanilla
Ice cream – brand and how many cups worth (better than scoops), any additions (e.g. choc chips), fat content
Cheese – brand, if grated how many cups

4. NUTS

Roasted, raw, salted, blanched etc
Whole, chopped, slivered
Mixed – with or without peanuts
How many cups or how many whole nuts

5. BREAD

Toast or sandwich slice (i.e thick or thin)
Toasted or fresh
Rye bread – light or dark
If not standard slice, get participant to weigh it.

6. MARG/BUTTER

Need brand
Salted or unsalted or reduced salt
Reg fat content or reduced fat

7. BAKED BEANS

Need brand
What sauce (ham, tomato, BBQ?)
SR or NAS

8. MEATS

Cooking method (e.g. BBQ, grilled, roasted, fried)
What cut of meat?
Weight cooked or uncooked (and with or without fat / bone)
Ask "how much fat left on?" and "was fat removed b4 or after cooking"
Sausages – thick or thin, number, flavour (e.g. chicken or beef), how cooked
CRACKLE – measure in tb or g
HAM – leg/shoulder, lean or lean & fat
HOT DOG – canned or battered, or crumbed, or weiner (these are the only choices)

9. OTHER

CAKES – cream filled (real cream?), jam filled, iced, flavour, home-made or commercial, cm x cm x cm
CORDIAL – how much base, how much water, what % fruit juice
GARLIC – fresh or jar
MAYO – low fat (<20%) or reduced fat (20-30%)
OLIVES – pickled in brine or oil
GRAVY – from powder? (SR or reg powder), with or without meat juices, get exact amt of powder
SALT / VINEGAR / SAUCE – how much added (tsp)
DIP – g or cups or tsp
SOFT DRINK – diet or reg
PIZZA – thick or thin crust

Appendix C: Interview Questions

RGS3688 Advanced Hybrid Closed Loop in Paediatric Population (HyCLIP)

HyCLIP Interview guide

Primary objective: Time in target range (Sensor glucose 3.9 – 10mmol/l)

Secondary aim: (Aim of the interview)

(1) Determine the effect of AHCL on Hypoglycaemia and hyperglycaemia

(2) Determine the psychological and social wellbeing of care givers

Diabetes management - general

1) How would you describe the management of your child's diabetes before the study?
2) What targets were you aiming for at: bedtime; during the day and night; for activity; When child away from you.
3) Who is responsible for most of your child's diabetes management?

Eating behaviours

- Can you explain what your child's eating patterns were like before the study? e.g. Grazing /snacking; structured pattern; picky eater.
- Do you think your child's eating changed during the study? If so, how?
- How do you think your child's eating behaviours or food intake impacted their glucose levels during the study?
- How do you feel the system managed with the foods your child eats during the study?
- Did you notice any differences in you or your child's feelings about meals and snacks during the study?

Activity

1) What kinds of activities does your child do? What usually happens to your child's glucose level with these activities?
2) How do you think the system managed glucose levels during these activities?

Sleep

1) How would you describe your sleep prior to starting the study?
2) During the study did you feel more rested / less rested/ about the same?
3) How does your child normally sleep? Did their sleep change during the study? If so, how?

Trust and confidence with the system

1) How long did it take you to understand the system and feel confident using it?
2) How did you feel about the system to:

- Give correct insulin
- Maintain glucose levels in range
- Keep your child safe

Information

1) How did you feel with the information the system gave you?
2) How did you use this information?

Thinking about the HCL system

1) How do you feel your child's diabetes has affected your family or work life?
2) How do you think the HCL system could help with this
3) Do you feel comfortable sending your child to day-care / school?
4) Thinking about the support you received from the study diabetes Educator, how did you find the amount of contact? timing of contact? Would you have liked more/less/about the same amount of contact?

Technical issues

Did you encounter any device difficulties during the study? If so, can you explain them to me? -alarms; notifications; correction

Overall user satisfaction

How do you think your child managed with the system?

What was your knowledge / expectations of the system prior to starting the study?

How do you feel after completing the study?

Why did you enrol your child into the study?

Would you recommend this study/ system to others?

Appendix D: Feedback Questionnaire – Feasibility study

Feedback / questions for HyCLIP – final visit:

What were your expectations going into the study / were they met?

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Tell us about your experience using the pump (both positive and negative):

- With sleep / exercise

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- With food and insulin delivery

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Did you get enough information when you started using the 780G insulin pump in Smart Guard?

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Did you feel supported during the study? Did you mind the study staff monitoring your child?

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Did you change your child's management during the day? During the night?

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Are you confident using the system?

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How long did it take you to trust the system?

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How do you feel about going back to your old pump?

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Did you notice any differences in your child's behaviour while he/she was in SmartGuard? And in what way?

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If you could summarise your experience of using the 780G pump in SmartGuard– what would you say?

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Any other comments:

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Many thanks for your feedback! 😊

How did you like using the pump?

(pick the face that matches how your child feels about the pump)