EVALUATING EARLY INITIATION OF ADVANCED HYBRID CLOSED LOOP THERAPY IN CHILDREN AND ADOLESCENTS WITH A NEW DIAGNOSIS OF TYPE 1 DIABETES

WA HEALTH RESEARCH PROTOCOL

FOR NONCLINICAL TRIALS

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1 Project Details			
Protocol/Research Project Title:	Evaluating Early Initiation of Advanced Hybrid Closed Loop Therapy in Children and Adolescents with a new diagnosis of Type 1 Diabetes.		
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Coordinating Principal Investigator Name:	Professor Elizabeth Davis		
Coordinating Principal Investigator Contact Details:	elizabeth.davis@health.wa.gov.au 08 6456 2222		

1.1 Project Summary

Type 1 diabetes (T1D) is one of the most common chronic diseases of childhood. Improving lives of children and families living with T1D is a critical goal with expected benefits for the individual, caregivers, healthcare system and wider society.

Automated insulin delivery via an advanced hybrid closed loop (AHCL) system is accepted as the most effective management strategy, proven in clinical trials and real-world studies, wherein a continuous glucose monitor (CGM) provides glucose information to an insulin pump which can then adjust insulin delivery via an algorithm (housed in an application or in the pump). Due to the established glycaemic benefits, access to AHCL therapy is recommended for all children with T1D according to the latest international guidelines(1).

However, despite national subsidy for CGM, AHCL access in Australia is limited as insulin pumps are primarily self-funded or accessed via health insurance funds or philanthropic programs. This has led to significant inequity in accessing AHCL.

The Department of Endocrinology and Diabetes at Perth Children's Hospital is implementing a new clinical model of care that will provide early access to AHCL to all children with a new diagnosis of T1D. This study aims to evaluate the impact of the new model of care through a combination of routinely collected clinical information and prospectively collected survey data. Glycaemic control at 6, 12 and 24 months post diagnosis in children with newly diagnosed T1D at Perth Children's Hospital will be compared to a historical cohort (diagnosed prior to this new model of care). The psychosocial wellbeing of participants will be explored and described through prospectively collected data and cost-effectiveness of this model of care will be evaluated. The overall objective is to comprehensively evaluate a model of care providing early access to AHCL following diagnosis of T1D.

There are no potential ethical concerns in the proposed study.

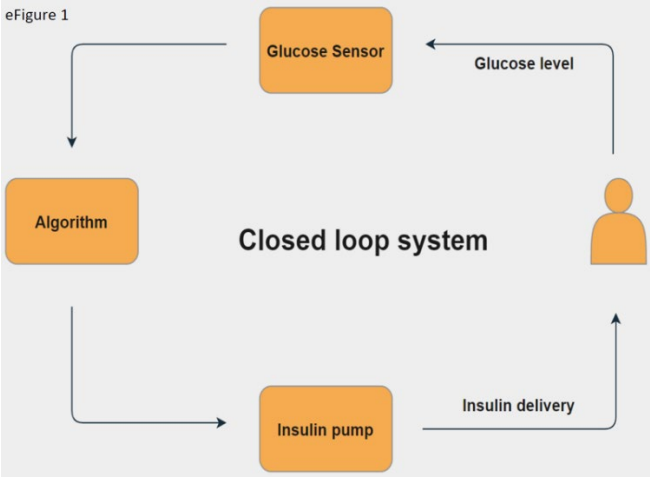
2 Rationale / Background

Type 1 diabetes (T1D) is one of the most common chronic diseases of childhood, with an increasing incidence worldwide (2, 3). Despite significant advances in management strategies for T1D, majority of Australian children and adolescents do not currently achieve the recommended glycaemic goals (4). Glycaemic control directly impacts the 16-year mortality gap for youth diagnosed with T1D at <10 years of age (5), and suboptimal control increases the risk of long-term physical (nephropathy, retinopathy, cardiovascular disease) and mental health morbidity. Data from registry studies demonstrate that the trajectory of glucose control in the first 12 months post diagnosis is strongly associated with long-term glucose control (6). By 12 months post diagnosis, HbA1c, a 3-month measure of glucose exposure to the red blood cell and the primary parameter for monitoring long-

term control in T1D, has risen above target goal in the majority (7). Hence, the importance of providing the best therapies in the newly diagnosed period for establishment and maintenance of early tight glucose control is indisputable.

Technological advancement in diabetes therapy has seen the introduction of advanced hybrid closed loop (AHCL) therapy emerge as the strongly recommended therapy for management in youth with T1D in recently published international guidelines (1, 8). In an AHCL system, insulin delivery is automated, relying on glucose levels from a continuous glucose monitor (CGM) communicating with an insulin pump. The insulin pump then adjusts insulin delivery semi-autonomously via a preset algorithm (please refer to Figure 1 below). AHCL has been demonstrated to be safe and effective in improving glucose control in children in both research and real-world settings (9-11). AHCL therapy reduces diabetes burden for children and their caregivers by reducing the risk of hypoglycaemia and daily work related to diabetes care, thus reducing psychological distress (12). In Australia there are currently three commercially available AHCL systems approved by the Therapeutic Goods Administration (TGA); the CamAPS system with the Ypsomed insulin pump paired with Dexcom G6 CGM (approved for youth >1 year of age), the Tandem t-slim insulin pump paired with Dexcom G6 CGM (approved for youth >6 years of age) and the Medtronic 780G insulin pump paired with Guardian G4 glucose sensor (approved for youth >7 years of age). These systems have become increasingly available in Australia since early-2022 and comprise the primary diabetes management system for approximately half of the children cared for with T1D at Perth Children's Hospital (PCH).

Figure 1



In Australia, current funding models limit access to these AHCL systems for many children. Insulin pumps may be obtained via high tier private health insurance or self-funding, but the significant cost of ongoing private health insurance and the outright cost of insulin pumps (approximately $8000) which require replacement every 4 years due to warranty expiry, represent a major barrier for many in regard to accessing insulin pump therapy, and therefore AHCL therapy. Limited philanthropic programs exist in Australia to support those unable to afford pumps (13). The Perth Children's Hospital Foundation (PCHF) Pump Program funded by a PCHF grant has been instrumental in supporting youth in Western Australia to access pump therapy where this would otherwise have been cost-prohibitive for the family (14). However, within these programs, strict criteria apply and limited pumps are available; thus a significant gap remains in accessing AHCL therapy. In direct contrast, the Australian government has subsidised CGM for children living with T1D since 2017, significantly increasing uptake of this technology (15), such that majority of children now use this as their primary glucose monitoring method.

In research settings where hybrid closed loop has been initiated early following diagnosis of T1D, glycaemic control is significantly improved in comparison to the standard practice of multiple daily injections (MDI) (16). Likewise, there is also real-world data both nationally and internationally which show that children who are commenced on AHCL therapy have improved glycemic outcomes (9-11). These positive outcomes have led to the recommendation of AHCL therapy to be offered to all

children with T1D (8). Hence, as a clinical service, we want to offer a service that meets international guidelines, that is AHCL for all children with introduction of this management strategy as early as possible following diagnosis.

Therefore, the PCH Diabetes Service has implemented a model of care aligning with international guidelines to commence AHCL therapy in children following the diagnosis of T1D, alongside initiating ACHL in those with an established diagnosis of T1D. In youth with newly diagnosed T1D cared for within our service, the time to AHCL commencement has reduced from a mean of 9.37 months in 2022 (inclusive of 45 individuals to date) to 3.55 months in 2023 (inclusive of 30 individuals to date). However, given ACHL access is limited to restrictive pathways based on financial status or limited philanthropy, there is a significant gap in equitable access of essential AHCL therapy. This is reflected by the above numbers of those starting AHCL in the newly diagnosed period, as this represents approximately one third of the newly diagnosed T1D cohort in a 12 month period at PCH. Currently, individuals unable to access AHCL are initiated and maintained on MDI with access to a CGM. Hence, in an attempt to improve access, the department has acquired funded support to provide pumps for children who do not have access to pumps through the existing pathways.

The overarching goal of this study is to evaluate the new model of care within the diabetes department at PCH which aims to offer AHCL therapy to ***all*** children with newly diagnosed T1D, regardless of financial status. AHCL will be offered within 12 weeks following diagnosis of T1D, a time frame in keeping with limited studies in this period, for example the CLOuD trial (16) showing improved outcomes when AHCL was started within 6 weeks from diagnosis, as well as expert input from the Diabetes Clinical Service leads regarding realistic timeframes within current clinical pathways. The combination of a clinical pathway aiming for early initiation of AHCL and equitable technology access for all children is an innovative model of care in T1D. Comprehensive evaluation of the glycaemic outcomes, patient reported outcomes, feasibility and cost-effectiveness of the model are essential and hence are the broad aims of the study.

Real-world evaluation of such models of care represent essential first steps toward collecting the evidence required for improving equitable access to diabetes technology for youth with T1D in both Australia and worldwide.

3 Project Aims / Objectives / Hypotheses

Specific Aims

1. To determine whether a model of care implementing equitable, early access to AHCL in the first 12 weeks post diagnosis of T1D, is associated with improved glycaemic outcomes, compared to recent historical controls, over the first 24 months post diagnosis.

2. To longitudinally assess disease burden, treatment satisfaction and psychosocial well-being in children and caregivers who are initiated on AHCL early post diagnosis of T1D, over the first 24 months post diagnosis.

3. To evaluate the cost-effectiveness of early, equitable AHCL access as a model of care in comparison to a previous model of care.

4. To investigate the feasibility of commencing AHCL within 12 weeks post diagnosis of T1D, specifically uptake and acceptance of early AHCL therapy and if applicable, the rates and reasons for discontinuation of AHCL.

We hypothesise that the new model of care will result in improved HbA1c at 6, 12 and 24 months post diagnosis of T1D as compared to the historical cohort. Furthermore, we hypothesise potential reduction in psychological distress and disease burden within the new model in comparison to recent historical control. We also hypothesise that the AHCL attrition rates will be low and the model will be cost-effective.

4 Project Design

4.1 Project Design

This is a hybrid implementation single centre study evaluating the clinical effectiveness and implementation of a new model of care (as outlined in section 4.2), wherein all youth are equitably offered commencement of AHCL within 12 weeks post diagnosis of T1D.

To achieve the project aims:

-HbA1c and CGM metrics will be collected to determine glycaemic outcomes and will be compared to a historical cohort diagnosed under the previous model of care.

-Psychological/person reported outcomes will be collected to evaluate longitudinally the patient experience and potential benefits of the new model for the individual.

-Economic analysis of the new model will be undertaken utilising health utilisation data and specific health service utilisation questionnaires.

-Uptake and if applicable discontinuation rates of AHCL with the new model of care will also be evaluated to investigate the feasibility of the model.

Majority of the data required for analysis in this study is already collected as part of standard clinical care in the PCH Diabetes service. Additional standardised psychological and validated person-reported survey instruments will be collected in order to explore the well-being and quality of life of patients commencing AHCL treatment under the new model.

4.2 Model of Care

The PCH Clinical Diabetes Service cares for all children in Western Australia with T1D as all individuals newly diagnosed with T1D are transferred to PCH given it is the only tertiary diabetes paediatric centre in the state.

The routine clinical pathway for individuals following T1D diagnosis at PCH includes:

- Brief admission at diagnosis for insulin injection initiation and basic education
- Multidisciplinary team led intensive outpatient education sessions through the Newly Diagnosed Diabetes Clinic
- Transition from this clinic at approximately 12-16 weeks post diagnosis to age group cohorts for those attending at clinics at PCH or outer metropolitan/regional cohorts for those living within these catchments, for ongoing 3 monthly outpatient follow-up as per gold standard recommendation

Individual's with T1D are offered, encouraged and assisted in considering AHCL systems at all points in the above clinical pathway by their diabetes team, unless a clinical decision made by skilled health care practitioners deems that AHCL is not an appropriate management strategy for an individual (for example; families with significant language barriers may not be able to successfully engage with pump system education which is primarily delivered in English and therefore use of AHCL may be deemed unsafe). The primary pathways for ACHL access as previously outlined are high tier private health insurance (approximately 25% of the total clinic cohort), self-funding, or exploration of eligibility for the philanthropic pathways. For individuals meeting these criteria, the clinical team aids them in navigating pump choice and commencement.

Within this model of care, choice is respected for all individuals in regard to insulin management strategy. Individuals self-funding insulin pumps are offered complete choice in their pump, with AHCL initiated where appropriate. For those accessing pumps via philanthropic pathways, pump choice is dependent on eligibility within the program. Finally, some individuals prefer MDI therapy and will not chose to wear a pump; once again, individual choice is always respected.

In the context of independently sourced funds, AHCL will be now offered to all children with T1D within this model of care. As per current model of care, all children accessing insulin pumps irrespective of the pathway to access it, will have extensive support from their diabetes clinical team in regard to management and ongoing access of pump following the 4-year warranty life of their pump, should they wish to continue with this therapy.

4.3 Source and Selection of Participants

Contemporary Cohort: All eligible children and adolescents with newly diagnosed T1D between 1st April 2024 to 31st March 2025 under the care of the diabetes service at PCH will be invited to be recruited in the study. Within this cohort, all eligible patients are to be offered AHCL as per the previously outlined model of care and initiated on AHCL within 12 weeks. Consent for participation in the study will be taken by the research fellow (or in their absence, a member of the research team) who is not involved in routine clinical care of the patient. This will occur during their scheduled Newly Diagnosed Clinic appointments rather than at an additional study visit. It will be made clear to those approached and their families that their routine clinical care will not be impacted by declining study participation.

Historical Cohort: The historical comparison cohort will include those diagnosed with T1D between 1st April 2022 to 31st March 2023, prior to the change in model of care. Individuals will be identified from the WA Children's Diabetes Database (WACDD). WACDD is a clinical resource, where routine clinical data is collected, entered and stored (see section 4.7.2 and 8.6 below) for individuals with T1D undergoing clinical care at PCH. Where data relevant to the historical cohort is missing, a study investigator will retrospectively collect this data where able/applicable.

4.4 Participant inclusion criteria.

1. New Diagnosis of T1D between 1st April 2024 and 31st March 2025.
2. Age 1-17.99 years.
3. Willing to complete study questionnaires.

4.5 Participant exclusion criteria.

1. Age <1 year old (no TGA approved AHCL system for this age group).
2. Unwillingness to complete study questionnaires.
3. Does not have at least one caregiver that can read and write English for instruments that are not available in translated versions

4.6 Participant withdrawal criteria and procedures specifying (if applicable):

(a) when and how to withdraw participants from the project;

Participants may withdraw from the study at any time. This will only impact psychological survey instrument data (as below in section 4.7.2). They will otherwise continue on AHCL and receive standard clinical care as per section 4.2. Participants can withdraw from the study by contacting the research team. Information on how to contact the research team will be provided to the individuals at consent for study inclusion both in verbal and written forms.

(b) the type and timing of the data to be collected for withdrawn participant(s);

All research data for withdrawn participants will be excluded. However, clinical data consented for through WACDD will be used for analysis, unless consent for WACDD is simultaneously withdrawn.

(c) whether and how participants are to be replaced;

Participants will not be replaced.

(d) the follow-up for participants withdrawn from the project.

Participants will continue to receive standard clinical care as per section 4.2. They will continue regular follow up with their diabetes team as per normal standard of care at 3 monthly clinic visits.

4.7 Method

This is a single centre, real-world clinical evaluation of a model of care utilising both longitudinal and retrospective clinical data, prospectively collected patient reported outcome measures and validated psychological surveys.

Consent for participation in the study will be taken by the research fellow who is not involved in routine clinical care of the patient during their scheduled clinical appointments to the hospital. Following consent, the participant will be provided with a unique study number which will be used on data collection instruments in place of identifying information.

4.7.1 Clinical Pathway to AHCL therapy

Per section 4.2, patients with newly diagnosed T1D will progress through the newly diagnosed diabetes model of care. Newly diagnosed T1D patients who meet inclusion criteria will be identified by the clinical and study teams and approached for study inclusion.

AHCL pathways will be explored with each individual per section 4.2. For those who are willing and eligible to start AHCL, provided there are no concerns from the clinical team, every effort will be made to complete pump education modules and start AHCL prior to 12 weeks post diagnosis.

4.7.2 Data collection

4.7.2.1 Routine clinical data collection

The WA Children's Diabetes Database (WACDD) stores clinical data from consenting individuals with T1D receiving care at PCH (see section 8.6 below for further details). This data includes clinical (anthropometric/glycaemic/insulin delivery) and sociodemographic data.

Consent for data sharing and research participation is sought from families at time of initial diagnosis of T1D (HREC Ref 2013051EP). Majority of the data proposed to be collected through this study are routinely collected at diagnosis and 3 monthly clinic visits and stored in WACDD.

Data which is routinely collected at these clinic visits will be exported (clinical data from WACDD, device information/insulin delivery/CGM data from proprietary software) at each of the timepoints below.

Of note while majority of the questionnaires planned for collection in this study are additional for study participants (see additional data collected below), Type 1 Diabetes and Life Measure (T1DAL) (parent, child >8 years) and Problem Areas in Diabetes (PAID) (parent and child versions) are already routinely collected clinical measures, also stored in WACDD.

4.7.2.2 Additional data collected

1. Questionnaires collecting information on general quality of life, sleep quality, anxiety, hypoglycaemia fear and diabetes treatment satisfaction will be additionally collected to address the aims of this study. For the questionnaires not routinely collected at clinic, participants will be emailed a link at the appropriate timepoints to be completed online using REDCap.

2. Parental level of education is not routinely collected at diagnosis presently, however is considered important regarding a participant and their families understanding of diabetes education. It will therefore be collected in addition to the baseline sociodemographic and clinical data which is routinely collected.

As majority of the data is already routinely collected at 3 monthly clinic visits, the burden on participants is minimal. There are no additional visits required for this study outside of routine clinical care, and questionnaire completion can be done at a time and in an environment that is convenient to the participants. This could include either at the clinic appointment while waiting to see their diabetes clinical team members or following the appointment at a time suitable for the individual/caregiver.

4.7.2.3 Specific data group collection

1. *Baseline sociodemographic and clinical data*
    - Date of birth
    - Gender
    - Address and postcode of residence of individual (including multiple if child lives between separate households)
    - Socioeconomic Indexes For Areas (SEIFA) Index Relative Socioeconomic Disadvantage (IRSD) quintile for address/postcode (17)
    - Parental level of education
    - Psychosocial Assessment Tool
    - Ethnicity
    - Date of diagnosis
    - HbA1c at diagnosis of T1D
    - Presentation in Diabetic Ketoacidosis (DKA): Yes/No
    - T1D antibody status
    - Medical comorbidities and medications
2. *Glycaemic measures*
    - HbA1c
    - CGM metrics
        - % time in range (TIR) 3.9-10.0 mmol/L

- % time in tight range (TITR) 3.9-7.8 mmol/L
- % time above range (TAR) >10 mmol/L
- % time below range (TBR) <3.9 mmol/L
- Glucose Management Indicator (GMI)
- Mean Sensor Glucose
- Glycaemic Variability: Standard Deviation and Coefficient of Variation

3. *Device information/Insulin Delivery*

- Type of CGM/Pump device
- Source of pump (self-funded, philanthropic, private-health insurance, other)
- Total daily dose of insulin; % of basal and bolus insulin
- % CGM sensor wear time: 2-weeks and 3-months wear
- % time spent in closed loop system
- CGM/pump use cessation date and reason

4. *Anthropometric data*

- Height, weight, Body Mass Index

5. *Significant clinical events*

- Number of severe hypoglycaemic episodes
- Number of DKA episodes

6. *Health service utilisation and sick day information*

Data is available from the WA Health Patient Administration System, webPAS, and will be accessed through the Business Intelligence Unit. In addition a health utilisation questionnaire will be provided through REDCap.

- Emergency department attendances
- Hospital admissions (related and unrelated to T1D)
- Number of out-of-clinic telephone, telemedicine and face-to-face visits with PCH Diabetes clinical team
- Other health professional attendances (GP, mental health professional attendance, other specialist teams, etc)
- Sick days resulting in missed education/occupation (parent and child)

7. Questionnaires

Psychological measures

Participants will be emailed a link for the following surveys to be completed online using REDCap.

- Anxiety: GAD-7 (parent, child >12 years) (18)
- Pittsburgh Sleep Quality Index (parent, child >12 years) (19)
- Diabetes Treatment Acceptance and Satisfaction Questionnaire (DTSQ) (DTSQ-Teen, DTSQ-Parent) (21)*
- DTSQ Change (DTSQc) (DTSQc-Teen, DTSQc-Parent) (21)
- Hypoglycaemic Fear Survey (Child version) (22)

Type 1 Diabetes and Life Measure (T1DAL) (parent, child >8 years) (23) and Problem Areas in Diabetes (PAID) (Parent and Child Versions) (24) questionnaires are collected as part of routine clinical care at the PCH Diabetes Clinic.

Health-economic measures

- Child Health Utility Instrument (CHU-9D) (parent of child <5 years, child >5 years) (20)

4.7.3 Timeline of data collection:

Timeline outlining when each of the data/questionnaires will be collected is listed in the below table. Of note the data collection may not fall precisely at 3 month time-frames post pump start, but given routine follow-up occurs 3 monthly, would be expected to be at 3 monthly intervals +/- 6 weeks based on when the routine clinical appointment occurs.

Blue shade indicates data that is routinely collected through the PCH diabetes service and green shade indicates additional for this study.

	Baseline/ Consent	Pump start	3m	6m	9m	12m	15m	18m	21m	24m
Consent	X									
Sociodemographic and clinical data	X									
Sociodemographic and clinical data: Parental level of education	X									
Glycaemic measures		X	X	X	X	X	X	X	X	X
Device information/Insulin Delivery		X	X	X	X	X	X	X	X	X
Anthropometric data	X	X	X	X	X	X	X	X	X	X

	Baseline/ Consent	Pump start	3m	6m	9m	12m	15m	18m	21m	24m
Significant clinical events		X	X	X	X	X	X	X	X	X
Health Service utilisation & sick day information		X	X	X	X	X	X	X	X	X
Questionnaires										
T1DAL						X				X
PAID						X				X
GAD7		X				X				X
Pittsburgh Sleep Quality Index		X				X				X
DTSQ (and if participant withdraws with permission)		X				X				X
DTSQ (Change)						X				
Hypoglycaemia Fear Survey						X				X
CHU-9D		X				X				X

4.8 Project Duration/Schedule

This study will be completed within 36 months. Participants will be enrolled in the study for 24 months, as detailed in Section 4.6.

5 Treatment of Participants

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

There are no new treatments or interventions in this study.

This project is considered to be low burden on the participant and family as much of the data is already being collected clinically as highlighted in the table above. The additional measures including psychosocial questionnaires will be collected using REDCap, allowing participants to respond in an environment which is convenient for them.

5.2 Permitted medications/treatments

Participants will continue their usual medications and treatments for the duration of the study including insulin and emergency hypoglycaemia management as prescribed by their diabetes team.

6 Assessment of Efficacy

6.1 Outcomes

Glycaemic control will be measured by HbA1c measured every 3 months utilising the DCA Vantage HbA1c analyser.

6.2 Efficacy assessment

A lower regression adjusted mean difference in HbA1c in the contemporary cohort as compared to historical control at 6, 12 and 24 months will be the primary efficacy assessment.

7 Assessment of Safety

7.1 Risks and Benefits

This is a low risk, non-invasive study. There are no invasive or painful procedures anticipated.

Foreseeable risks include the potential for psychological distress from responding to the psychological questionnaires, some of which are routinely collected in the clinical setting. In the case where the additional measures collected through REDCap result in any psychological distress, study participants will have access to a Child and Adolescent Health Care Practitioner and study investigators to discuss their distress or aid them in seeking other avenues for mental health support (eg: GP review for mental health care plan where individuals can access free/subsidised sessions with a mental health professional in the community).

It will be explained to the participant that their involvement in the study is entirely voluntary and that they can withdraw from the project at any stage without affecting their relationship with the health professionals or researchers at Perth Children's Hospital. When a participant withdraws a follow-up phone call will be made to ascertain the reason for withdrawal, complete the exit DTSQ and to refer him/her to other services if required.

Benefits to the participant include the following:

- Participants will be able to be involved as consumer advocates for children, adolescents, families and caregivers living with T1D and improved access to diabetes technology.

- Participants may benefit from the reflection that follows answering the types of questions asked in the study.

7.2 Safety

Adverse events are unlikely, however if any participant experiences distress, they will be offered the opportunity to not answer questions, or to discontinue their involvement in the study. At all clinical visits a diabetes social worker is available to support families experience high diabetes distress or experiencing other adverse wellbeing.

Participants will have full access to their usual diabetes clinical triage line and diabetes on-call service outside of office hours if they need to discuss diabetes management, or to be referred for psychological assistance as deemed necessary by the clinical team. After hours psychological assistance in the community is available. This information will be provided in hard copy and included will be the contact details needed to access the services.

7.3 Adverse events reporting

Given this study involves standard diabetes treatment, and the treatments being used have been used in previous studies and standard clinical care, the risk of Adverse and/or Serious Adverse Events are unlikely in this low risk, non-invasive study. If they do occur, they will be reported to the HREC according to local procedure.

7.4 Follow-up of Adverse Events

The type of follow-up required after an adverse event will be determined by the CPI and PI's on the study team according to clinical and/or psychological need.

8 Data Management, Statistical Analysis and Record Keeping

8.1 Statistics and Interim Analysis

The cohort newly diagnosed with T1D in the 12 months following study start (the contemporary cohort) will be compared to a historical control (the cohort newly diagnosed between March 2022 and March 2023). Routine clinical data for both cohorts will be extracted from WACDD. Descriptive statistics (mean/SD, median/IQR, or frequency/% as appropriate) will be presented for key demographic and clinical measures. The 24-month HbA1c in the contemporary cohort will be compared to the historical control through multivariable regression model adjusting for potential imbalances in clinical/sociodemographic characteristics. The adjusted mean difference along with 95% confidence intervals will be calculated. A sensitivity analysis using an inverse probability of treatment weighted regression based on propensity score will also be conducted.

Interim analyses employing similar models examining HbA1c difference between the cohorts at 6 and 12 months will be conducted. Further exploratory analyses presenting mean HbA1c over various clinical factors (e.g. urban/remote postcode/SEIFA, insurance status, age at diagnosis, timing of HCL commencement, etc) will also be conducted. Subanalysis reviewing mean HbA1c on those commencing on AHCL within 12 weeks from diagnosis will similarly be examined.

Device uptake and attrition will be presented as frequencies and proportions along with 95% confidence intervals. Bivariate predictors of device use at uptake will be presented through simple contingency tables of device use by clinical and sociodemographic factors (Age group (≤12 years, >12 years), gender, socioeconomic indices for areas quintile (lowest quintile, other 4 quintiles), DKA at diagnosis.

Simple descriptive statistics (mean/SD, median/IQR, or frequency/%) will be presented for CGM metrics and psychosocial measures at each of the follow-up points for the contemporary cohort. Where appropriate, mixed models or non-parametric Friedman tests will be conducted to assess within person change over time.

A cost-effectiveness analysis of the new model of care compared to the previous model of care from a health care system perspective will be led by a co-investigator from Monash university with expertise in health economics. The main outcome of interest will be the incremental cost-effectiveness ratio which captures the mean differences in health outcomes and costs. Health outcomes will be measured by quality-adjusted life years (QALYs), calculated from the CHU-9D instrument. Data will be captured during the trial for the intervention (new model of care) group. The comparator (historical cohort) will not have CHU-9D data available as it was not historically captured. Therefore, we will use CHU-9D data collected on children with diabetes from the Longitudinal Study of Australian Children (LSAC) for quality of life in the comparator group. This is suitable given that LSAC data was collected under the previous model of care which exists in most states/territories (with limited access to AHCL). Other outcomes such as the number of significant events (including hospitalisations) averted will also be explored. Costs include the cost to deliver the new model of care, and the cost of health care services used by participants during the time horizon of the trial (including hospitalisations and emergency department attendances) costed using standard Australian unit prices. Standardised economic evaluation techniques including bootstrapping to determine confidence intervals will be employed. The results of our analysis will also be used to do a budget impact analysis to estimate the financial consequences of adopting the new model of care.

Final analysis will occur after the final study participant has completed the 24 month data collection, however interim analyses will occur approximately 6 monthly from initial pump start in the contemporary cohort.

8.2 Sample Size

Over a 12-month period at PCH there are 130-150 children newly diagnosed with T1D depending on annual variation. With a similar sized historical cohort, we expect sufficient power (>80%) to detect moderate effects (greater than 0.35%) in our primary analysis.

With regard to the prospectively collected data, we expect at least 80% uptake of this study, resulting in approximately 105-121 patients to be consented to make up the contemporary cohort.

8.3 Study Power and Significance

P values of <0.05 will be used to determine statistical significance and 2-sided P-values will be reported. Corrections for multiple comparisons will not be employed.

8.4 Statistical plan deviations

Any deviations to the original statistical plan will be reported to relevant ethics and governance committees, and in the manuscript.

8.5 Selection of participants for analyses

Fully detailed in section 4.3. All participants newly diagnosed with T1D in the 12 months following study commencement along with historical controls identified from WACDD, will be included in the primary analysis.

Data for the historical cohort is available on WACDD. Parents of PCH patients and PCH patients aged over 16 years of age are provided with an information sheet and consented to have their health information recorded in the PCH component of the shared database (WACDD, HREC Ref 2013051EP), for clinical, audit and research purposes.

8.6 Data Management

Any information collected in connection with this project will remain confidential. All project-related information will be stored securely. Following consent, the participant will be provided with a unique study number which will be used on data collection instruments in place of identifying information to protect participant confidentiality.

Consent and questionnaire data will be collected using CAHS REDCap which is a secure web platform hosted on the CAHS network. Sociodemographic and clinical data will be extracted from the Western Australian Children's Diabetes Database (WACDD – 2013051EP) . This database is located on a secure Department of Health server at Perth Children's Hospital accessible only by authorised users.

Pump and CGM data will be extracted from the Department of Endocrinology and Diabetes Glooko, Dexcom Clarity and Carelink accounts. Patients attending clinics will be familiar with these systems and there are no study specific requirements above what participants would normally do for clinic visits.

Data will be extracted by staff trained in the use of the above-mentioned databases and for the purposes of this study will be stored in restricted access files on password protected computers accessible by the research team. Data will be retained indefinitely.

Deidentified data will be shared with the study team at Telethon Kids Institute, Monash and Macquarie Universities for data analysis and publication of the project outcomes.

8.7 Procedure for accounting for missing, unused, and spurious (*false*) data.

Multiple imputation by chained equations (MICE) using predictive mean matching will be used to account for missing data in regression models.

9 Monitoring / Audit

9.1 Monitoring, Audit and Regulatory Inspections Statement

The project investigators/institutions will permit project-related monitoring, audits, and regulatory inspections, providing direct access to source data/documents.

9.2 Procedures for Monitoring and auditing

There are no external monitors for this study. The Coordinating Principal Investigator will collate information on participant recruitment, data collection and adverse events at regular intervals. This information will be presented to the wider diabetes research team consisting of medical professionals, scientists, a biostatistician and a community involvement coordinator with experience and training in research to monitor study progress and safety.

As the data for interstitial glucose is downloaded from proprietary software and collated it will be monitored by the research team to ensure data integrity.

10 Quality Control And Quality Assurance

10.1 Compliance statement

The study will be conducted in compliance with the protocol. All staff involved in this study will have Good Clinical Practice (GCP) certification and will be well-versed in the study protocol including the consent process, adverse event management, and data collection. The project will be supervised by the principal investigator(s) to ensure it is conducted in compliance with the protocol, GCP and regulatory requirements. Information on participant recruitment and retention, participant safety and data collection will be collated and reviewed on a regular basis.

10.2 Quality control

All staff will be trained to ensure appropriate data collection in accordance with ICH-GCP guidelines.

Data will be cleaned by trained staff to ensure quality and data checks will be completed. Statistical tools will be used to assess data completeness. Data completeness will be ensured by using mandatory fields in online survey tools.

The data will be presented at a multi-disciplinary team meeting throughout the duration of the study.

11 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. Consent will be obtained from the participants and their guardian prior to study commencement, and they will be informed that they are able to withdraw at any point.

12 Budget, Financing, Indemnity And Insurance

This is an investigator led project. All investigators and study personnel are indemnified by their employing institutions.

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13 Publication

The results of this study will be disseminated in a peer reviewed manuscript, presented at local and international conferences, shared with all participants and the general T1D community via email, the Children's Diabetes Centre patient newsletter and the T1D Collaborator (aimed at stakeholders, researchers and collaborators nationally and internationally) and social media, and Diabetes Community organisations.

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