**A Pilot Study Evaluating an Education Module Empowering People Living with Type 1 Diabetes to Understand their Continuous Glucose Monitoring Data: The Making Sense Program**

**HREC Study number:** TF

**ANZCTR number:** TF

**Short title:** A Pilot Study Evaluating CGM-User Education

**Intervention:** The Making Sense Program

**Protocol version:** 1.0

**Funding:** The Australian Centre for Accelerating Diabetes Innovations

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**1.0 BACKGROUND**

The Diabetes Control and Complications Trial (DCCT) showed with intensive insulin therapy, individuals with type 1 diabetes (T1D) should strive for a haemoglobin A1c (HbA1c) <7.0% to effectively reduce the risk of microvascular complications. (1) The recent Standards of Medical Care in Diabetes continue to suggest achieving an HbA1c target of <7.0% (53 mmol/mol) for adults with T1D, without significant hypoglycemia. (2) Conversely, attaining these glycaemic targets for individuals with T1D has been a challenge and this remains the case in the 21st Century.



A variety of technologies are available today including insulin pump therapy (IPT), glucose sensors (continuous glucose monitoring [CGM] or intermittently scanned glucose monitoring [ISGM]) and devices integrating IPT and CGM in conjunction with a control algorithm (e.g., closed loop systems). Improvements in glycaemic control have been apparent and associated with the rollout of these exciting new technologies. (3) Using CGM or ISGM metrics (e.g., ambulatory glucose profiles), studies suggest that glucose time-in-range (TIR) of >70%, with time below range <4% aligns with an A1c of ~7.0%. (4, 5) Recently access for people with T1D to CGM devices has increased with expansion of the National Disability Support Scheme (NDSS), and one may postulate that optimizing insulin therapy and achieving glycaemic targets should become easier to attain. However, a recent study by the United States based T1D Exchange Registry reported that only a minority of individuals living with T1D meet glycaemic targets despite the use of new technologies. In fact, average HbA1c values by year of age show that only approximately 20% of adults with T1D are meeting glycaemic targets. (6) **Figure 1**

(2)

Attainment of health outcomes (e.g., tight glycaemic control), improved quality of life, and fewer complications are correlated with consistent engagement in diabetes self-management. (7) Potential barriers to self-management are wide-ranging and include the dynamic and chronic nature of diabetes, financial burden, unrealistic demands, and patients’ lack of knowledge. (7) Following evaluation of the DCCT patients, it was found that one of five factors associated with lower HbA1c’s was whether individuals actually reviewed their glucose records and made insulin-dose adjustments based on pattern management and additional factors. (8) This review of data remains relevant despite the technological advances described above because while people living with T1D, their health care providers, and industry aspire for full automation of insulin delivery systems and reduced user burden, the most advanced closed loop systems still require a hybrid approach with between 40-60% of insulin-dosing determined and initiated by the user or their guardian. For example, even with the Medtronic Advanced Hybrid Closed Loop (AHCL) algorithm which incorporates an auto-bolus function that triggers in response to a rapidly rising glucose, glycaemia following a meal where a late bolus or no bolus is administered is inferior compared with a meal preceded by a user-initiated bolus of insulin (9). **(Figure 2)**



**Fig. 2:** Normal, missed and late bolus with Medtronic AHCL (9)

Typically, clinical patient education is centered around protocolized responses to specific situations (e.g., carbohydrate counting for meals; exercise; sickness; and treatment for hypo/ hyperglycaemia). However, the education curriculum usually does not address an individual’s understanding and comprehension, or the assessment and review of their glucose and insulin-dosing data. For example, most individuals proficient in assessing the carbohydrate content of their meal administer insulin accordingly, but do not review their data to assess post-prandial glucose levels and are even less likely to modify their pump settings, diet, or timing of the pre-meal bolus considering this information. We conducted a survey of 138 consecutive outpatients with T1D who were attending diabetes specialists at St Vincent’s Hospital Melbourne and using either IPT, a glucose sensor or both showed that while the majority had downloaded their device data, they did not look at their insulin delivery or glucose sensor data. (10) The most common reason was that they would not understand the information. Almost all expressed a strong interest in an education program that would enable them to understand the information provided by these devices so that they could be more involved in management decisions (**Table 1**).



A subsequent national survey (unpublished data) led by people living with T1D of 3,414 adults with the condition who use pumps and / or sensors to manage their glucose levels revealed that respondents perceived those important matters in supporting their use of technology included:

1. How to read and understand monitoring trace graphs and patterns
2. How to adjust insulin for out-of-range glucose levels
3. How to deliver insulin for what one eats
4. How to understand information that has been uploaded from your device
5. How to use and troubleshoot devices

Information regarding the operation of and troubleshooting of insulin pumps and glucose sensors is usually device specific and provided by the manufacturer. In addition, information regarding insulin dosing for meals and correction of elevated glucose levels has been resourced in advantaged countries by established structured education programs such as Dose Adjustment For Normal Eating (OzDAFNE) provided through consumer representative bodies such as Diabetes Victoria. (11, 12) However, there remains a gap in service provision regarding education focusing on the understanding of downloaded CGM data and its interpretation by the user in the light of their insulin dosing, and behavior which include dietary choices, emotional state, and physical activity. The Australian survey also showed that dissatisfaction with diabetes technology related education provision was associated with device discontinuation.

With the universal subsidy of CGM for people living with T1D in Australia we anticipate the need for education support will increase substantially as will the demand for the training and education to comprehensively cover all facets of the knowledge requirements to use these devices successfully.

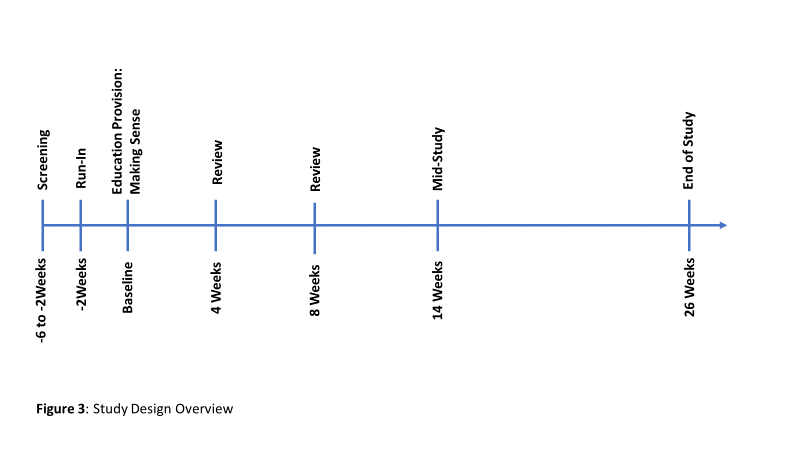
**2.0 HYPOTHESIS AND AIMS**

Our overarching hypothesis is that for adults living with T1D who use CGM, a curriculum educating the user to assess their device generated data will improve glycaemia and patient reported outcomes. The overall assessment of feasibility will be based on feasibility of recruitment, retention, adherence to the protocol, suitability of the tools used to collect outcomes, and timeline for implementation. Effect estimates for clinical outcomes will inform the design of subsequent later phase comparative randomized clinical trials, in particular in terms of participant numbers needed to achieve desired statistical power levels.

**3.0 STUDY DESIGN AND METHODS**

**3.1 Study Design Overview (Figure 3)**

This study will recruit 62 adults from three metropolitan hospital sites (St. Vincent’s Hospital Melbourne, The Austin Hospital, The Royal Melbourne Hospital) with T1D who are established CGM users (50% MDI and 50% insulin pump). Following baseline assessments, which will include at least two weeks of CGM, and person reported outcome data, all participants will receive the pilot education intervention implemented by Diabetes Victoria over two weeks with access to education resources for the duration of the study. All participants will then be followed for 26 weeks after they have received education provision with the assessments performed at baseline repeated at 14 weeks and end of study. The protocol will be conducted in accordance with the Declaration of Helsinki. HREC approval will be sought, and the study registered. All participants will provide written informed consent.



**3.2 Eligibility**

A record log will be made of all individuals approached to participate in the study. The reasons provided by those who declined will be recorded.

*Inclusion criteria*: T1D (diagnosis consistent with American Diabetes Association Classification of Diabetes Mellitus [13]); Age >18Y; HbA1c <9.5%; Fluent in English; using carbohydrate counting; >3 months On MDI or IPT and safely operating an RT-CGM or ISGM device; Willing and able to download and review device data; Living in an area with internet and cellular phone coverage; English speaking. Recruitment will be stratified approximately 1:1 MDI and IPT and at least 40% of all participants will be on either RT-CGM or ISGM. At least 10 days of CGM data between screening and the baseline visit.

*Exclusion criteria:* Pregnant or planning pregnancy; Using open-source artificial pancreas system (so-called ‘do-it-yourself’ (DIY) technology); Use of any non-insulin glucose-lowering agent within the past 3 months; Oral or injected steroid use within the past 3 months; active significant nondiabetic illness impacting glucose management (e.g. coeliac disease, thyroid disease, myocardial ischaemia) or any severe or unstable medical or psychological condition which, in the opinion of the investigator, would compromise the ability to meet protocol requirements.

**3.3 Visit Schedule (Table 2)**

***Visit 1 (Screening; eligibility; informed consent):***Plain language information sheets will be provided in advance to adults with T1D who potentially fit eligibility criteria and express an interest in participating. Following written informed consent, those who are interested in participating in the study will be assessed to determine if they meet the eligibility criteria listed above. Baseline participant data to be collected will include:

1. General demographic characteristics
   1. Date of birth
   2. Sex
   3. Highest education degree
   4. Postcode
   5. Country of birth
2. Clinical characteristics
   1. Date of diabetes diagnosis
   2. Insulin delivery method, MDI and for IPT: pump start date, pump type
   3. Insulin formulation and dose (total daily basal; total daily bolus; insulin to carbohydrate ratios)
   4. Glucose monitoring method(s): Device(s) used, start date, Frequency of use over last month e.g. for blood glucose meter-frequency of fingerstick measurements, for RT-CGM/ISGM percentage of time worn based upon upload and self-reported estimate of the number of times they check it each day
   5. Type of glucose monitoring device and percentage time worn
   6. Diabetes-related complications
   7. History of severe hypoglycaemia (as per study definition)
   8. Single-item Gold score and 5-item HypoA-Q
   9. History of diabetic ketoacidosis and other diabetes-related hospitalisations past 12 months
   10. Medical history, other medications
   11. Weight, height, blood pressure and general examination

A urine pregnancy test will be performed in women of childbearing age. Blood will be drawn for HbA1c to be performed at a centralized DCCT aligned laboratory and electrolytes.

Psychological questionnaires will be administered (see **Section 3.5**).

All participants will be requested to wear their glucose sensor continuously for the next two weeks. Training will be provided to ensure that the participants can ensure either the automatic or manual upload of their devices.

The time taken to complete the visit will be recorded.

***Visit 2 (Run-in Visit)****:* A visit will be scheduled with the participant two weeks following screening. Pathology and uploaded CGM data and insulin dosing information will be reviewed, and study eligibility confirmed. Changes to insulin dosing will not be recommended unless there are safety concerns (e.g. severe hypoglycaemia or ketosis). Those participants meeting criteria for inclusion in the study will be scheduled to receive the education intervention.

Using the diary provided at this visit, participants will be asked to commence recording details of all symptomatic hypoglycaemic episodes, and time spent reviewing their device uploads. For the three days prior to education provision meals will be recorded. All will wear their glucose sensor continuously in the two weeks prior to education provision. Diaries will be returned to the study team by registered post.

Participants on MDI will be provided with and educated on the use of the smart insulin pen (Inpen, Medtronic, Northridge, CA) which they will use to administer rapid acting insulin for the duration of the study. (see **Section 3.7**)

The time taken to complete the visit will be recorded.

***Visit 3 (Education Provision/ Baseline):*** The education module itself will be implemented by Diabetes Victoria and will include an initial on-line introductory group session, on-line education modules and a final face-to-face group review session after two weeks. (See **Section 3.4**) Diaries to be completed at mid will be provided. Time taken to complete the visit will be recorded.

***Visit 4 (Week 4 /Post-Education Review 1)*:** Two weeks after completion of the education module the participant will review their uploaded data in the presence of a member of the study team. While the education program helps to identify where an individual is not meeting their glycaemic targets and may inform lifestyle changes it does not aim to teach participants when and how to make insulin adjustments. However, we recognize the prerogative of the person living with type 1 diabetes to adjust their own insulin dosing regimen. The study team member will only intervene if there is a significant risk. The visit may be conducted face-to-face or remotely as determined by the study team. Time taken to complete the visit will be recorded.

***Visit 5 (Week 8/ Post-Education Review 2)*:** Six weeks after completion of the education module the participant will review their uploaded data in the presence of a member of a study team member. If the participant deems their glycaemic control unsatisfactory, they can suggest changes to address these. These changes may encompass lifestyle and insulin dosing. However, we recognize the prerogative of the person living with type 1 diabetes to adjust their own insulin dosing regimen. The study team member will only intervene if there is a significant risk. The visit may be conducted face-to-face or remotely as determined by the study team. Time taken to complete the visit will be recorded.

***Visit 6 (Week 14/ Mid-Study Visit):*** Two weeks prior to the mid-study visit all participants will be contacted to remind them that they will need to wear their CGM devices for the next fourteen days and commencing keeping the study diary which will include a record of their meals in the three days prior to the mid-study visit. All participants will visit the study site for the mid-study visit. A clinical assessment will be performed as per the screening visit, blood collected for HbA1c, and questionnaires implemented. If the participant deems their glycaemia control unsatisfactory, they can suggest changes, which may encompass lifestyle and insulin dosing, to address these. The study team member will only intervene if there is a significant risk. Time taken to complete the visit will be recorded. Completed diaries will be collected and new ones provided. Data from the smart pens will be uploaded to a computer. The time taken to complete the visit will be recorded.

***Visit 7 (Week 26 End of Study Visit):***Two weeks prior to the mid-study visit all participants contacted to remind them that they will need to wear their CGM devices for the next fourteen days and commencing keeping the study diary which will include a record of their meals for the three days prior to the visit. All participants will visit the study site for the end-of-study visit. Study diaries will be collected at the study visit. Smart pens will be collected, and data uploaded. A clinical assessment will be performed as per the screening visit, blood collected for HbA1c, and questionnaires implemented. A recorded interview will be conducted by the study team with scripted open-ended questions to explore the acceptability and feasibility of the education and participants’ recommendations for further refinements. Time taken to complete the visit will be recorded.

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| **Study Visit** | **1** | **2** | **3** | **4** | **5** | **6** | **7** |
| **Weeks from commencing education intervention** | **-4** | **-2** | **0 - 2** | **4** | **8** | **14** | **26** |
| **Clinical assessment** | **X** |  |  |  |  |  | **X** |
| **HbA1c** | **X** |  |  |  |  | **X** | **X** |
| **Urine Pregnancy test** | **X** |  |  |  |  |  |  |
| **Psychosocial Questionnaires** | **X** |  |  |  |  | **X** | **X** |
| **Smart Pen Provision** |  | **X** |  |  |  |  |  |
| **Smart Pen Upload** |  |  |  |  |  | **X** | **X** |
| **Study Diary Provision** |  | **X** | **X** |  |  |  |  |
| **Study Diary data collection\*** |  |  | **X** |  |  | **X** | **X** |
| **CGM data required\*** | **X** | **X** |  |  |  | **X** | **X** |
| **‘Making Sense’ provision** |  |  | **X** |  |  |  |  |
| **Clinical Review** |  |  |  | **X** | **X** | **X** |  |
| **Semi-Structured Interview** |  |  |  |  |  |  | **X** |

**Table 2:** Visit schedule. \*Prior two weeks data mandated.

**3.4: Participant Safety**

All participants will continue to be followed by their usual health care professional team. In addition, a telephone help line will be provided enabling access to a study clinician should this be required. Device uploads from all participants will be reviewed remotely by the study team on a fortnightly basis to ensure safety. All participants will be advised to inform the study team of any changes to insulin dosing that they may want to initiate prior to implementation of these changes.

**3.5: Study Outcomes of Interest**

*Primary Outcome:* The proportion of the number of participants (n=62) who complete the study per-protocol. The intervention will be deemed feasible if this proportion is at least 0.75.

*Process Outcomes*: To assess the feasibility of those processes that will be key to the successful implementation of a definitive large randomized-control study aimed at evaluating the ‘Making Sense’ education program. In addition to those specific outcomes listed below, upon completion of the study, teams at the study sites will be interviewed to elicit their input about matters for improvement regarding study processes which will include:

Clarity and suitability of the eligibility criteria

Recruitment rates

Retention rates

Proportion of participants who successfully complete the education program.

A better understanding of data collection tools and outcomes including unanticipated responses to questionnaires.

*Resource Outcomes*: To assess resources that will be required for the conduct of the study. In addition to those specific outcomes listed below at the end of the study staff will be interviewed to elicit their input about matters for improvement regarding study resourcing.

1. Determining the time taken for each study site visit

(ii) Determining the time taken to implement the education program (Stage 1 and Stage 3 group sessions as well as time spent by participants on the on-line modules [Stage 2]).

(iii) Determining qualification and capacity issues regarding human resources (lived experience and RN-CDE) available to implement the education program

(iv) Determining if the on-line platforms for Stages 1 and 2 of the education program perform as expected

*Scientific Glycaemic Outcomes:* CGM data collected over the final two weeks of the study will be examined according to standardised criteria described by Battelino et al. (14) CGM metrics for 24 h/day, day [06:00–00:00] and night [00:00–06:00],

(i) Proportion of time spent 3.9–10.0 mmol/L

(ii) Proportion of time spent <3.0 mmol/L

(iii) Proportion of time spent <3.9 mmol/L

(iv) Proportion of time spent >10.0 mmol/L

(v) Proportion of time spent >13.9 mmol/L

(vi) Glucose variability: coefficient of variation (CV)

(vii) Mean glucose (mmol/L)

(viii) HbA1c

*Scientific Psychological Outcomes:* Validated measures will be completed via a Qualtrics survey administered via an iPad. These will include:

Perceived satisfaction with diabetes management experience (22-item DME-Q), which includes three subscales: perceived effectiveness, convenience, intrusiveness)

Diabetes-specific positive well-being (a 4-item scale from the W-BQ28)

User engagement with the education module (including interest, attention, flow)

Brief study-specific rating scales

Problem Areas In Diabetes (PAID) questionnaire

Open-ended questions to explore the acceptability and feasibility of the education and participants’ recommendations for further refinements.

*Safety Outcomes:*

1. Hospitalisations for diabetic ketoacidosis (n)
2. Severe hypoglycaemia (n) defined as requiring third party assistance.
3. Symptomatic hypoglycaemia (n)

*Behavioural Outcomes Relating to Data Access and Review:*

(i) Time spent reviewing data (minutes)

(ii)Number of changes to insulin dosing (n)

(iii) Frequency and duration of exercise

(iv) Missed meal boluses / injections

**3.6: Education Intervention**

The education intervention, *‘The Making Sense Program’* was designed based on and in the light of ongoing input by people living with diabetes and an expert reference group consisting of endocrinologists, diabetes educators, industry, dieticians, psychologists, community engagement and education specialists. The education intervention will be conducted over a period of two weeks. Participants will attend in groups of approximately eight. It will be implemented as a combination of teleconferencing, on-line, and face-to face sessions. The time required to implement each stage of the education intervention will be recorded.

**Stage 1:** All participants have had a 90-minute introductory group session where they will be provided with an overview of the program. The virtual group session will be facilitated by a peer (a person living with T1D experienced in the use of technology who has undertaken the facilitator training day). The peer facilitator is supported by a registered nurse-credentialled diabetes educator (RN-CDE) who has also participated in the facilitator training day. During this session participants will meet one another and have an opportunity to identify their expectations for the program. They will also be provided with instructions on how to move through the program including the on-line education modules.

**Stage 2:** The three training modules are hosted on a web-based platform. (EdApp [edapp.com]) which provides flexibility and may be completed at the person’s convenience. The platform can be accessed from a desktop or laptop computer, smartphone, or tablet. People may leave a module and return to it later. The training modules are:

1. Making the most of glucose monitoring technology (CGM and Flash): An Introduction
2. Making the most of glucose monitoring technology (CGM and Flash): Interpreting your Data
3. Making the most of glucose monitoring technology (CGM and Flash): An Introduction to Insulin Pumps and Hybrid Closed Loop Systems

Modules 1 and 3 may be optional as determined by the study team. Module 1 provides basic information that the experienced device user may be already familiar with. Module 2 provides core information and is to be completed by all participants. Module 3 can only be attempted after completing Module 2 and will not be applicable to those participants using MDI.

Each module comprises a series of lessons and a ‘Briefcase’ feature with supporting material.

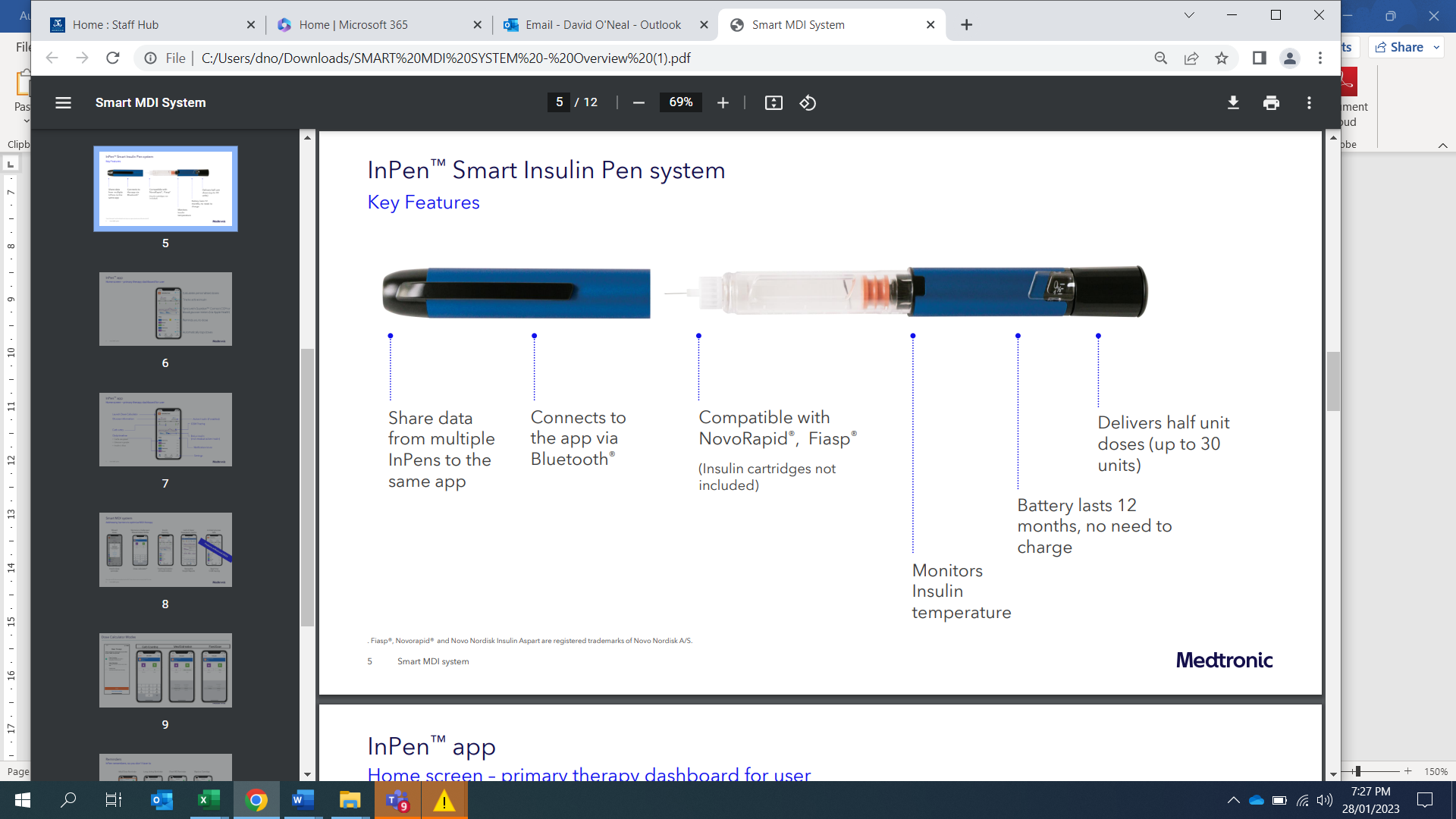
The lessons within each module are to be completed sequentially. Apart from the first lesson, each subsequent lesson can only be attempted after an earlier lesson is completed. Each lesson starts with a title page and then a dot point summary of the information to be covered by the lesson. There are videos embedded within each lesson expanding on specific points. There are also quiz questions during each lesson whose sole purpose is to reinforce important study points and they will not be used to determine a “pass” or “fail”. At the end of each quiz question, the person will be provided with a “correct” or a “not quite” message and reinforcing information will then be provided. Upon completion, a lesson can be repeated, or the person can go on to the next lesson in the module.

The ’Briefcase’ feature contains a list of resources relevant to the module. These may take the form of written pdf documents, links to on-line resources, or further activities

**Stage 3:** It is anticipated that participants will complete the on-line module(s) within two weeks. After this time, they will attend a 4-hour group session (virtual or face-to-face). The group session will be facilitated by the same peer who led the introductory session, and they will be supported by the same RN-CDE. During the final group session, participants will have an opportunity to consolidate their online learning and to practice their new skills in interpreting data from their glucose sensing device. They will be encouraged to provide examples of their own CGM data though this will not be mandatory.

**3.7: Smart Pen (Figure 4)**

A smart pen (Inpen, Medtronic, Northridge, CA) used to administer rapid acting insulin will be provided to all participants on MDI. These will be stand-alone devices with their own power supply which lasts 12 months. They record the number and dose of rapid acting insulin injections. The pens are approved by the Australian FDA.



**Figure 4:** Components and description of Inpen.

**3.8: Study Power and Data Analysis**

The primary outcome will be the overall feasibility of the proposed intervention. The intervention will be deemed feasible if this proportion is at least 0.9. As the aim of the study is of estimation (rather than of hypothesis testing), nature, we use precision-based (rather than power-based) approach to estimate the sample size. Recruiting 62 participants will provide the precision (half-width of 95% confidence interval) of 0.075, to estimate the underlying proportion of participants who complete the study per-protocol of 0.9.

To estimate observed within-participant effects for clinical, safety, and patient-reported outcomes, these outcomes will be compared pre- and 26 weeks post- education provision within mixed-effect general linear modelling framework. Continuous outcomes will be estimated using a general linear model, count outcomes using a Poisson or negative binomial regression, and binary outcomes using logistic regression modelling. Resulting effects will be reported with respective 95% confidence intervals.

The association between age, sex, education, and level of social disadvantage (as determined according to postcode) , as well as baseline insulin delivery mode and glycaemic outcomes will be estimated in exploratory analyses.

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No interim analyses for safety, efficacy, or futility are planned.

**4.0: STUDY MANAGEMENT**

The day-to-day management of the study will be the responsibility of the investigator at each center. The Principal Investigator and study project manager will maintain regular email correspondence with all investigators and study coordinators. The Principal Investigator, with the site lead investigators will assume responsibility for the progress of the study in accordance with agreed timelines and milestones with the study funders. The study project manager will liaise with the study teams in all centres to establish procedures and ensure that the study is carried out according to the protocol and to standards of GCP, with robust systems for reporting adverse events.

**5.0: DATA MANAGEMENT**

The study database and study project manager will be centralised to the University of Melbourne. At consent each participant will be assigned a unique identifying number based on their study site which will be used for data input to the database. Quality control checks will be performed to ensure accurate data entry. Data will be entered into the eCRF (electronic case record form) at each participant contact. Device upload information will be reviewed at each center by the study team, copied and de-identified before being filed. It is recognized that participants will be using devices from different manufacturers with differing web-based platforms (e.g. Glooko, Clarity, Carelink). All platforms provide standardised ambulatory glucose profile (AGP) metrics which will be directly entered into the eCRF.

**6.0: ADVERSE EVENTS AND SAFETY REPORTING**

Each investigator has the responsibility to ensure arrangements are in place to record, notify, assess, report, analyse and manage adverse events in this study to comply with the Therapeutic Goods Administration (TGA) regulations and local Ethics requirements.

All serious adverse events should be reported withing 24 hours, or the next working day to investigators at the lead site (below)

|  |  |
| --- | --- |
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**6.1: Definitions**

**Severe hypoglycaemia** Any low glucose level requiring the assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions.

**Symptomatic hypoglycaemia** Symptoms consistent with hypoglycaemia confirmed by a finger-prick glucose level of less than 4.0 mmol/L.

**Adverse event** Any undesirable clinical occurrence in a participant whether it is 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 that is causally related to the device implantation procedure, the presence of the device, or the performance of the device system.

**Serious adverse event (SAE)** Any untoward medical occurrence in the study that:

* results in death.
* is life-threatening.
* requires in-patient hospitalisation or prolongation of existing hospitalisation.
* results in a persistent or significant disability/incapacity.
* is a congenital anomaly/birth defect
* is a medically important event or reaction
* is an episode of diabetic ketoacidosis or severe hypoglycaemia

All SAEs should be reported immediately to the Principal Investigator. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should be de-identified using participants’ unique code numbers assigned. The investigator should also comply with the applicable regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authorities and the HREC.

The Principal Investigator must inform the HREC and the TGA of all serious or unexpected adverse events that occur during the study and may affect the conduct of the study or the safety of the participants or their willingness to continue participation in the study.

The TGA require that all serious andunexpected adverse device events are reported to the Devices Clinical Section, Office of Blood, Devices and Tissues of the TGA in an expedited fashion (i.e. within 15 calendar days of first knowledge), or for fatal or life-threatening events, an initial or full report within 7 calendar days and a follow-up report if necessary within the 15 calendar day timeframe. All other adverse device reactions and adverse events are tabulated as per usual study protocols and produced on request.

**7.0: ETHICAL CONSIDERATIONS**

**7.1: Informed Consent**

Adults with T1D identified as eligible for the study who wish to take part will be asked to sign a consent form agreeing to the study. Consent will initially be obtained by an investigator, who is not directly involved in routine clinical care of the individual, to avoid any undue pressure to agree to participation. Written signed informed consent will be retained in the study site files.

**7.2: No Fault Liability**

All the investigators and research personnel will be indemnified for negligent harm based on local health service provision and personal investigators medical insurance provision.

**7.3: Ethical Committee Review:**

The study protocol is to be seen and approved by the appropriate ethical review committees at all study sites. Copies of the letters of approval will be filed in the study file.

**7.4: National Statement & ICH Good Clinical Practice**

The study is to be carried out in conformation with the spirit and the letter of the Declaration of Helsinki, and in accord with the National Statement on Ethical Conduct in Human Research (2007) and ICH Good Clinical Practice Guidelines.

**7.5: Confidentiality Protection**

All participants will be allocated a unique study identifier, and this will be used for the transfer of all data. Confidential data will be retained at the study sites in a secure study file. At all times the confidentiality of the participants will be maintained, and reports to meetings and publications will not include confidential or data identifying individuals.

**7.6: Changes to Protocol**

Any proposed protocol changes following initial HREC approval require the agreement of the Principal Investigator and JDRF and will be submitted for HREC approval or notification.

**7.7: Participant Withdrawal**

A participant may terminate participation in the study at any time without necessarily giving a reason and without any personal disadvantage. An investigator can stop the participation of a participant after consideration of the benefit/risk ratio. Possible reasons include:

1. Serious adverse event

2. Non-compliance

3. Technical grounds (e.g. participant moves away)

4. Early termination of the study at the request of the steering committee

**7.8: Ownership and Commercialisation of the Data**

Ownership of data and publication agreements as outlined in the Clinical Trial Research Agreement and Funding Agreements.

**References:**

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