Intermittently Scanned CGM Versus Usual Care With Diabetes Education and Feedback, in Adults with Non-Insulin Dependent Type 2 Diabetes (iCUDE) A Randomized Trial

Short Title: isCGM With Education and Feedback for Non-Insulin Dependent Type 2 Diabetes

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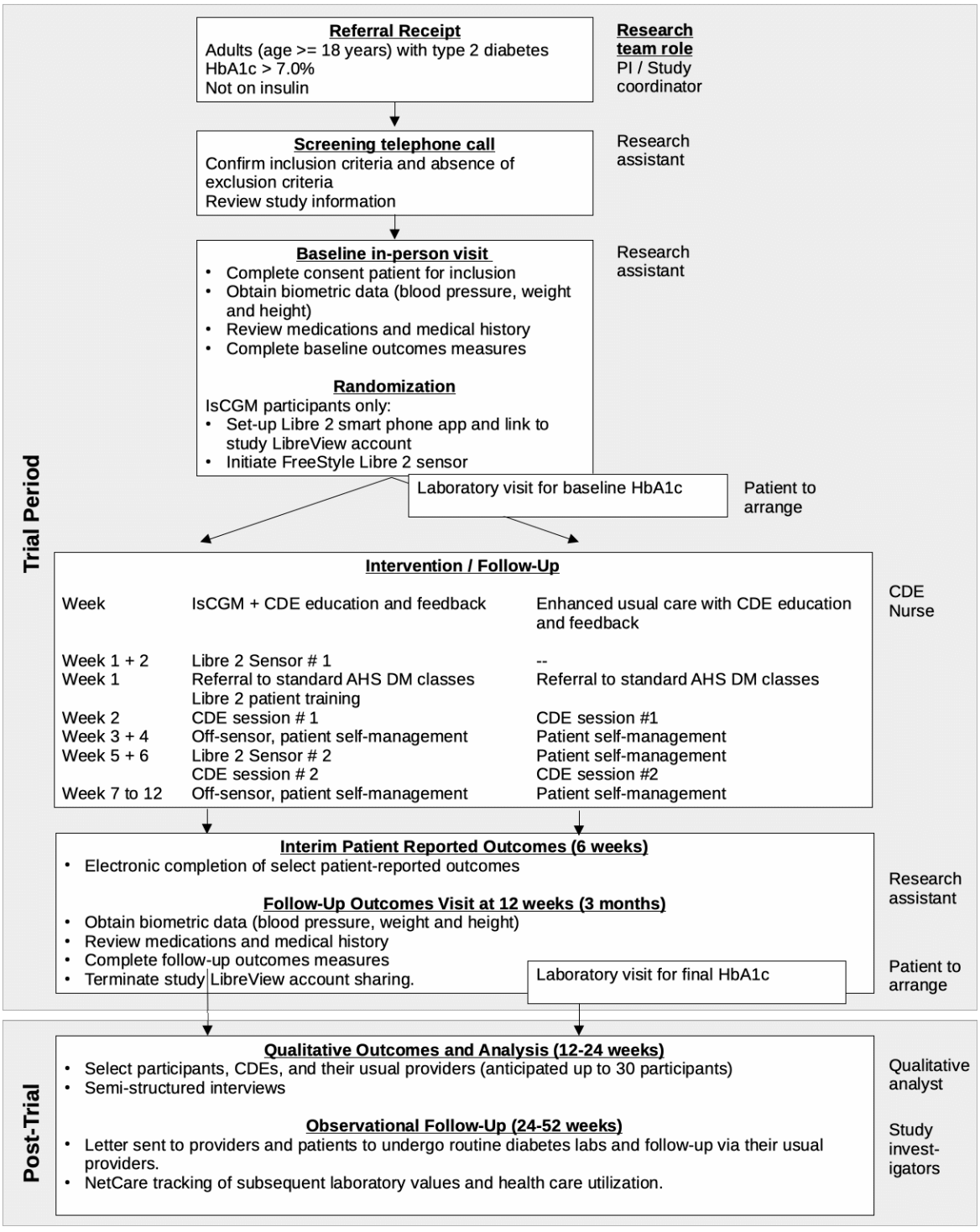
STUDY SYNOPSIS

Title	**Intermittently Scanned CGM Versus Usual Care With Diabetes Education and Feedback, in Adults with Type 2 Diabetes (iCUDE): A Randomized Trial**
Investigator(s)/center/study location	Edmonton, Alberta
Study Objectives	This trial will examine the effectiveness of intermittently-scanned continuous glucose monitoring (isCGM) when applied on an episodic basis and combined with diabetes education / feedback, in adults with type 2 diabetes on non-insulin therapy.
Study Design	The trial is an investigator-initiated prospective, single-center, open-label, randomized controlled trial.
Inclusion criteria:	1. Age >= 18 years with type 2 diabetes. 2. HbA1c > 7.0% within the last 6 months. 3. Non-insulin therapy. 4. Able to attend two in-person study visits. 5. English-speaking. 6. Community-dwelling. 7. In possession of a cell phone capable of accessing the internet and receiving FreeStyle Libre 2 sensor readings 8. Has a primary care provider who has been in contact with the patient for diabetes in the last 12 months.
Exclusion criteria:	1. Type 1 diabetes or diabetes clearly identified as having monogenetic etiology (e.g.: MODY). 2. Steroid-induced diabetes if steroid use is on-going or most recently taken within the last 3 months. 3. Pregnancy, plans to become pregnant within 6 months, or breast-feeding 4. Any use of insulin in the previous year. 5. Current or previous use of isCGM or rtCGM. 6. Cognitive dysfunction (SPMSQ score >= 5). 7. Symptoms of acute metabolic decompensation (extreme thirst, high urinary output, and weight loss, accompanied by acute fatigue or dyspnea). 8. Any terminal condition that would limit life expectancy to < 1 year. 9. Inability or refusal to use isCGM (e.g.: afraid of the device). 10. Inability or refusal to be reached by telephone. 11. Concurrent participation in another diabetes-related trial. 12. Has not already received two doses of a Health Canada-approved vaccine against SARS-CoV-2.
Evaluation criteria	**Primary Outcome:** Change in glycated hemoglobin (HbA1c) at 3 months compared to baseline. **Secondary Outcomes:** Feasibility of recruitment Blood pressure, body weight, waist circumference, and patient-reported outcomes, measured as change in continuous score at 3 months compared to baseline on validated instruments of: • Diabetes treatment satisfaction • Diabetes self-management empowerment • Diabetes-related distress • Diet • Physical activity

	Safety Outcomes: Any reported adverse events, major adverse events – hospitalization or ED visits. isCGM-related reactions (e.g.: skin reactions).
Treatment	Following informed consent, eligible adults will be randomly allocated to isCGM + education and feedback with a certified diabetes educator (CDE) or enhanced usual care with education and feedback using a 1:1 allocation ratio. The intervention (isCGM or enhanced usual care) will last 6-8 weeks. Those in the isCGM arm are free during the intervention or afterwards to obtain or fund their own supplemental isCGM sensors.
Randomization	Patients will be randomly assigned using a REDCAP based randomization system using variable block size. The computer-generated allocation table would be generated in a formal and secure manner.
Sample size	A target sample of 100 patients was chosen based on funding constraints, power / sample size considerations, and expected loss to follow-up of 20-30%. The minimum number of trial completers required to have 80% power to detect an HbA1c difference of 0.5% is 80.
Follow-up	Follow-up (week 5-6) CDE virtual education and feed-back session. 12-week bloodwork encounter at outpatient lab. 12-week in-person study encounter to complete study measurements. After conclusion of the 12 week trial period: Post-trial qualitative interviews with select consenting participants. Post-trial administrative linkage to examine outcomes at 24-52 weeks from randomization – no direct participant involvement.

1. OVERVIEW OF STUDY DESIGN

Figure 1: Overview of Study Design



2. INTRODUCTION AND RATIONALE

Glycemic control is an important treatment target for adults with diabetes.[1] Though rates of adults meeting glycated hemoglobin (HbA1c) targets of <= 7.0-7.5% have probably improved in the last decade, a large proportion of adults do not achieve their glycemic targets,[2-5] for a variety of reasons.[6]

Self-monitoring of blood glucose can help adults with type 2 diabetes (T2DM) progress towards their glycemic targets.[7] Continuous glucose monitoring (CGM), an alternative to traditional capillary blood glucose, uses a wearable sensor that continuously samples interstitial fluid glucose. Real-time CGM (rtCGM) continuously transmits blood glucose values, while intermittently scanned CGM (isCGM) requires scanning of the sensor to obtain the cumulated readings. CGM is painless, provides information on glucose trends, and has consistently demonstrated improved patient satisfaction compared to CBG, which tends to be limited by its "snap-shot" one-time perspective, and the inconvenience and discomfort associated with fingersticks.[8,9]

While rtCGM has demonstrated effectiveness in reducing HbA1c compared to traditional capillary blood glucose monitoring, in adults with T2DM on insulin,[10-13] the lower monthly cost of isCGM (FreeStyle Libre $180)[14] compared to rtCGM (Dexcom G6 $395)[15] makes isCGM an attractive alternative. However, the evidence for isCGM in T2DM is limited.[16] Several cohort studies have shown improved HbA1c in adults initiating isCGM, but these studies are limited by lack of relevant comparators.[17-20] Only two trials have examined isCGM in T2DM. In the REPLACE study of adults on insulin, no difference was detected in HbA1c between isCGM and CBG groups at 6 months, though isCGM participants had lower time in hypoglycemia and higher treatment satisfaction.[21] Yaron et al., randomized adults on prandial insulin and found a statistically significant 0.5% greater improvement in HbA1c in isCGM participants.[22] The reason for the contrasting results may be related to the absence of structured one-on-one diabetes educator interactions in REPLACE; a previous study of adults with type 1 and type 2 diabetes has shown the importance of education in potentiating the effect of isCGM.[23] Overall, the effectiveness of isCGM at reducing HbA1c in T2DM remains unresolved.

Adults with "earlier diabetes", i.e.: on non-insulin therapy only, comprise the majority of adults with T2DM. Yet, they are underrepresented in the current CGM literature.[24] Because their hypoglycemia risk and their opportunities for day-to-day medication adjustments are lower compared to adults on multiple daily doses of prandial insulin, it has been more challenging to demonstrate the value of glucose monitoring among these individuals.[25-27] However, capillary blood glucose studies have shown that glucose self-monitoring can improve lifestyle and accelerate medication intensification, leading to lower HbA1c compared to usual 3-monthly HbA1c-driven care, in those with diabetes not on insulin therapy.[28-31] Some trials of rtCGM have examined this sub-population of T2DM and found benefit.[10,12] For example, Vigersky et al. randomized adults with T2DM *not* on prandial insulin to intermittent use of rtCGM (2 weeks on, 1 week off) for 3 months versus CBG only. This trial showed reduced HbA1c in the intermittent rtCBG group at 3 months, that persisted up to 12 months, long after the intervention had stopped.[13] Given the expense of CGM, intermittent sensor deployment is an important cost-

savings measure applicable to the real world use of CGM. Neither of the two trials of isCGM in T2DM, above, have examined this subpopulation, leaving the effectiveness of isCGM in earlier T2DM largely unknown.

3. STUDY HYPOTHESIS

isCGM combined with nurse certified diabetes educator (CDE) education and feedback will improve glycemic control and patient self-management of diabetes compared to enhanced usual care with CDE education and feedback only.

4. STUDY OBJECTIVES

Primary Objective

To evaluate the effectiveness of isCGM with CDE education and feedback on glycemic control at 12 weeks, in adults with type 2 diabetes and uncontrolled HbAc (> 7.0%) not on insulin therapy.

Secondary Objectives

To determine the feasibility of recruiting adults with diabetes in Edmonton-area to a trial of glucose self-monitoring and education.

To determine the effectiveness of isCGM with CDE education and feedback on patient self-management of diabetes, measured using patient reported instruments for diabetes-related quality of life, diabetes treatment satisfaction, diabetes self-management empowerment, diet, and physical activity – at 6 weeks and at 12 weeks.

To determine the safety of isCGM with CDE education and feedback with respect to emergency department visits or hospitalizations, and isCGM-specific reactions (e.g.: skin reactions).

To understand the reasons *why* or *how* isCGM with CDE education is effective or ineffective from the perspective of involved participants and their providers.

To evaluate the effectiveness of isCGM with CDE education and feedback on glycemic control at 24-52 weeks (post-trial observational follow-up).

5. isCGM (INTERMITTENTLY SCANNED CONTINUOUS GLUCOSE MONITOR) – DESCRIPTION OF TECHNOLOGY

Technology – The only isCGM on the market at this time is the FreeStyle Libre 2 system produced by Abbott. FreeStyle Libre 2 sensors use a subcutaneous, wired enzyme glucose-

sensing technology, factory-calibrated to detect glucose levels in *interstitial* fluid by way of a thin filament implanted under the skin. The sensors are water-proof, affix to the skin by medical adhesive, last 14 days each, and are roughly the size of two stacked quarters. They measure interstitial glucose every minute, with readings stored in 15-minute intervals. Patients can scan sensors on-demand, using either a near-field communication-enabled smart phone or the FreeStyle Libre 2 Reader, to receive a glucose result along with historic results for the preceding 8 hours. The FreeStyle Libre 2 system is fully marketed in Canada; in 2020, it's predecessor, the similar FreeStyle Libre flash glucose monitoring system, had over 2 million users internationally.[32]

Market Access / Licensing – The Libre 2 flash glucose monitoring system has been licensed by Health Canada since November 30, 2020 (No. 105518) for measuring interstitial fluid glucose levels in children aged 4 years and older and adults with diabetes mellitus.[33,34]

Accuracy – Compared to reference venous blood glucose measurements, Libre 2 sensors had a mean absolute relative difference (mARD) of 9.2%, with over 78% of values within +/- 15% of reference values, and over 88% of values within +/- 20% of reference values, across the physiologic range of blood glucose.[35] These values are improved from the preceding Libre flash glucometer system, which demonstrated mARD 11.4% (overall 85% of values within +/- 20% of reference).[36] An error analysis of the preceding Libre flash glucometer system showed that the difference between Libre glucose readings and capillary blood glucose measurements would lead to a difference in treatment in < 1% of readings.[36] Based on these data, interstitial glucose values can be used interchangeably with capillary blood glucose measurements, though users should be aware that interstitial glucose may lag behind venous blood glucose by 2.4 +/- 4.6 minutes.[35]

Reliability – Simultaneous tests of paired sensors yielded blood glucose results with a coefficient of variation of 5.7%, indicating good agreement between sensors.[35]

Data presentation – Upon scanning the sensor, the current glucose result is displayed for the patient, along with arrows indicating current glucose trends (i.e.: rising quickly, rising, changing slowly, falling, falling quickly) based on the rate of glucose change. Historic results are displayed in the "daily graph" as a line plot, providing a visual reference for the day's glucose peaks and valleys.

Remote patient telemonitoring – Internet-enabled smart phones can be configured to automatically push glucose data to LibreView, an online portal for patients and providers to review glucose data. Similar functionality using the Libre 2 Reader requires users periodically to connect their reader to a computer via USB. Providers can set up a LibreView account for their clinics, allowing access to glucose reports for multiple enrolled patients. LibreView provides sophisticated glucose reports, including glucose statistics and ambulatory glucose profiles (median and inter-quartile range), in addition to daily glucose profiles.

6. STUDY DESIGN

This trial is an investigator-initiated prospective, single-center, open-label, randomized controlled trial of isCGM with CDE education and feedback. All participants will receive standard treatment at the discretion of their physicians.

Setting

- Tertiary care ambulatory referral clinic in Alberta, Canada, with recruitment of patients from urban primary care practices.

Intervention – isCGM + CDE Education and Feedback

- *Short Term Use of isCGM* – Participants will be given three FreeStyle Libre 2 sensors during the study period. Each sensor, once worn, provides glucose measurements for 14 days. The three sensors will provide 6 weeks of isCGM. Participants will *not* be encouraged to use FreeStyle Libre 2 sensors outside of the intended study periods, but neither will they be discouraged from doing so if they choose to of their own accord. The first sensor will be initiated with the assistance of a study team member, who will also set up the Libre 2 smart phone app and link it to the study LibreView account during the baseline visit. Subsequent sensors will be participant-initiated. Should participants encounter difficulty with sensor placement, replacement sensors will be made available, and participants will be referred to their local retail pharmacist to assist with sensor initiation. A small number of FreeStyle Libre 2 Readers will be available for those with unforeseen technical difficulties. Patients using the readers will be asked to upload their data to LibreView online via USB adapter connection to their computers, on a weekly basis.
- *Initial Patient isCGM Training* – Participants will be provided multimedia materials (written booklet and link to bespoke introductory videos) to help them understand and trouble shoot the Libre 2 system, and to help them understand their glucose readings and act on them. These materials will be designed with patient and CDE-input using a human-centred design process via the University of Alberta's Physician Learning Program (in process), and may also include multimedia resources produced by Abbott, the manufacturer of the Libre 2 isCGM. Additionally, participants will be referred to Alberta Health Service's standard diabetes education group classes and advised to register according to their interest and motivation. Diabetes Canada and Alberta Health Services-concordant advice and handouts will be provided to isCGM participants on recognizing and managing hypoglycemia (https://www.albertahealthservices.ca/assets/mha/diabetes/mha-diabetes-hypoglycemia-the-basics.pdf).
- *CDE Education and Feedback* – A CDE nurse will assess the participant and review her/his LibreView data. The CDE nurse will provide general diabetes education and advice on using isCGM, and individualized recommendations on lifestyle (diet and physical activity) changes to improve glycemic control. Two encounters will take place with the CDE nurse. The first will occur during weeks 1-2, and the second during weeks 5-6,. During the second encounter, CDE nurses may also consider sending recommendations to participants' usual care providers for medication titration, if appropriate. CDE nurses will provide education and advice according to their usual training and practices. General guidance on incorporating isCGM readings into

individualized advice for participants and their care providers will be provided in the form of a clinical algorithm, which will also be designed with patient and CDE-input using a human centred design process via the University of Alberta's Physician Learning Program (in process). CDE encounters will take place either in-person, or virtually, over Zoom.

Control – Enhanced Usual Care With CDE Education and Feedback Only

- *No specific monitoring of glucose* – Participants will be discouraged from accessing FreeStyle Libre 2 glucometers or other CGM during the study period. They will be free to use capillary blood glucose monitoring according to their own interest and motivation, or as directed by the CDE nurse. Advice and handouts will be provided to isCGM participants on recognizing and managing hypoglycemia.
- *Alberta Health Services Diabetes Education Group Classes* – Participants will be referred to Alberta Health Service's standard diabetes education group classes and advised to register according to their interest and motivation.
- *CDE Education and Feedback* – A CDE nurse will assess the participant. The CDE nurse will provide general diabetes education, and individualized recommendations on lifestyle (diet and physical activity) changes to improve glycemic control. Two encounters will take place with the CDE nurse. The first will occur during weeks 1-2, and the second during weeks 5-6. CDE nurses will provide education and advice according to their usual training and practices. CDE encounters will take place either in-person, or virtually, over Zoom.

Study period – The trial period will be 12 weeks. From 12 weeks onwards, select participants will be approached to participate in semi-structured qualitative interviews. Linkage of participant information to Alberta administrative health care data may occur up to 3 years after trial completion to allow examination of diabetes outcomes on an observational basis up to 52 weeks from randomization.

Blinding

- This trial is open-label. Neither patients, investigators, nor statistical analysts will be blinded to treatment allocation.

Post-Trial Observational Follow-Up – Patients will be reviewed on NetCare for laboratory values and health care utilization at 24 and 52 weeks following randomization. NetCare data accrued up to 64 weeks post-randomization will be reviewed to identify nearest lab values for the 52-week time point.

Post-Trial Qualitative Study of Experiences Using isCGM – Consenting patients and providers will be contacted after the 12 week study period to participate in semi-structured interviews exploring their experiences using isCGM or managing their blood glucose without isCGM.

7. STUDY POPULATION

Adults (age >= 18 years) with type 2 diabetes an uncontrolled blood sugars, defined as HbA1c > 7.0%, not on insulin therapy.

Inclusion Criteria:

1. Age >= 18 years with type 2 diabetes.
2. HbA1c > 7.0% within the last 6 months.
3. Non-insulin therapy.
4. Able to attend two in-person study visits.
5. English-speaking.
6. Community-dwelling
7. In possession of a cell phone capable of accessing the internet and receiving FreeStyle Libre 2 sensor readings
8. Has a primary care provider who has been in contact with the patient for diabetes in the last 12 months.

Exclusion Criteria:

1. Type 1 diabetes or diabetes clearly identified as having monogenetic etiology (e.g.: MODY).
2. Steroid-induced diabetes if steroid use is on-going or most recently taken within the last 3 months.
3. Pregnancy; plans to become pregnant within 6 months; breast-feeding.
4. Any use of insulin in the previous year.
5. Current or previous use of isCGM or rtCGM.
6. Cognitive dysfunction (SPMSQ score >= 5).
7. Symptoms of acute metabolic decompensation (extreme thirst, high urinary output, and weight loss, accompanied by acute fatigue or dyspnea).
8. Any terminal condition that would limit life expectancy to < 1 year.
9. Inability to use isCGM (e.g.: afraid of the device).
10. Inability to be reached by telephone.
11. Concurrent participation in another diabetes-related trial.
12. Has not already received two doses of a Health Canada-approved vaccine against SARS-CoV-2.

8. RECRUITMENT STRATEGIES

A multifaceted recruitment strategy will be deployed to identify patients meeting study criteria from the following sources:

1. Kaye Edmonton Clinic (KEC) General Internal Medicine (3D), Endocrinology (3B), and Family Medicine (1A) clinics.
2. Regional Diabetes Program (RDP) clinics
3. C-ENDO, a multi-site privately administered endocrinology and internal medicine clinic in Edmonton

4. Primary Care Networks (PCN) and family medicine clinics, including Covenant Health sites.
5. Participant self-referral

For sources (1) through (4), above, outreach efforts will involve

- Identification of site "champions" to promote with recruitment – most likely to involve non-physician personnel (diabetes educators, dieticians).
- Presentations to clinic providers (physicians, diabetes educators, and dieticians) at staff/business meetings or divisional meetings.
- Dear Provider Letters – Appendix 1.
- Brochures featuring large graphics placed in exam and waiting rooms (with permission) – Appendix 2.
- Social media advertising via Facebook, Twitter, and study landing page, and through recruitment networks such as Bethecure.ca

We will ask providers – both physicians and non-physicians – to refer interested patients to study investigators for the study team to contact and screen. In our recruitment materials, we emphasize the potential benefit to participants being access to FreeStyle Libre 2 sensors on a trial basis with linkage to personalized CDE advice; regardless of randomization group, participants will be remunerated for the time and inconvenience of study participation (including labwork) with a honoraria consisting of gift cards (Walmart or Safeway or similar grocery store) of $40 CAD upon receipt of baseline and 12-week follow-up HbA1c measurements, and will have their parking fees paid. Study investigators will not enroll their own patients.

9. PARTICIPANT CONSENT

Following a screening phone call, eligible patients will attend a baseline visit to complete consent for participation and randomization, as well as completion of baseline measures. For the initial screening, verbal consent (Appendix 3.1) will be obtained from potential study participants to access their provincial NetCare electronic medical records and confirm that they meet the HbA1c inclusion criteria.

A study investigator or research assistant will review the nature of the clinical trial, and the anticipated risks and benefits. An electronic trial information sheet and consent form will be created by EpiCore Centre (Appendix 3.2). The trial consent form will be signed by the patient either using a touch-interface (e.g.: iPad or similar device) or using a mouse to draw a signature (desktop computer), and witnessed by the study investigator or research assistant. The patient's email address will be collected, and once the consent is signed, a copy will be emailed to the participant. In the event of technical difficulties, a participant without email access, or a participant that refuses electronic signing, paper copies of both the trial information sheet and consent forms will be available. An additional paper copies of the consent form, in that case, will be signed and given to the participant to take home.

Select providers (referring physicians / educators / dieticians and the study CDE nurse) will be approached and consented for semi-structured interviews to contribute their perspective on the use of isCGM. A specific information package and consent form for the qualitative sub-study (providers only – patients are covered by the full trial consent package) has been developed (Appendix 3.3).

Patients will be free to withdraw consent / withdraw from the study at any time, and will be given written instructions on termination of Libre 2 data sharing as part of the study information package (Appendix 4).

10. STUDY OUTCOMES AND VARIABLES

Case report forms are provided in Appendix 5. These will be translated into electronic documents to be completed by participants via a password protected webportal (EpiCore).

Primary Outcome:

- Change in HbA1c at 12 weeks compared to baseline.

Secondary Outcomes:

- Feasibility of recruitment
  - Participant referral, screening, and randomization rates over time
  - Reasons for inclusion / exclusion of all participants referred.
- Change in scores at 6 and 12 weeks compared to baseline, on the patient-reported outcomes shown in Table 1, below.
- isCGM participants only – change in time-in-target range, coefficient of variation, and glucose management indicator at 12 weeks compared to baseline.

Table 1: Patient-Reported Outcomes

Outcome	Instrument	Number of items
Diabetes treatment satisfaction – Status score	Diabetes Treatment Satisfaction Questionnaire (DTSQs)[37] (weeks 6 and 12)	8
Diabetes treatment satisfaction – Change score	Diabetes Treatment Satisfaction Questionnaire (DTSQc) (week 6 only)	
Self-management empowerment	Diabetes Empowerment Scale – Short Form (DES-SF) [38] (weeks 6 and 12)	8
Diabetes-related distress	Problem Areas in Diabetes (PAID) Questionnaire[39]	20
Diet	UK Diabetes and Diet Questionnaire (UKDDQ)[40] (weeks 6 and 12)	25
Physical activity	International Physical Activity Questionnaire (IPAQ) short form[41,42] (weeks 6 and 12)	7
Health status	Euroqol EQ-5D-5L (weeks 6 and 12)	5

* In addition to collection at baseline.

Safety outcomes at 12 weeks:

- Any adverse events (serious and non-serious) occurring from baseline to 12 weeks will be identified and tracked at the 12 week study visit by patient interview, and reviewed

by study investigators to determine whether clinically attributable to diabetes, diabetes management, or isCGM. isCGM issues (e.g.: skin reactions) will be specifically sought.
- Emergency department visits or hospital admission for any reason, identified from patient interview and from NetCare review.

Qualitative Outcomes: Semi-structured interviews will undergo thematic analysis using constant comparative methods. The starting point will be the participant and provider experience with isCGM or enhanced usual care, with a particular focus on barriers and enablers of effectiveness (see Appendix 6, interview guides). Semi-structured interviews will take place for participants after trial completion (from 12-24 weeks).

24-52 Week Post-Trial Observational Follow-up: After the trial ends, we will send out reminder letter to all participants and their providers encouraging them to have routine diabetes assessments, including laboratory measures, done. We will ascertain the effect of the intervention on HbA1c at 24 and 52 weeks, by review of NetCare. NetCare data up to 64 weeks post-randomization may be reviewed to assign the nearest lab value to the 52 week time point.

Other Quantitative Variables Measured:
Case report forms are provided in Appendix 5.

11. MITIGATION OF ANTICIPATED MINOR RISKS

Skin reaction to the device may occur, namely local dermatitis or allergy-type reactions (redness, itching, localized swelling, blisters, oozing). This reaction is usually due to a contact allergy to a component of the adhesive, e.g.: isobornyl acryate. Systemic reactions have not been described with the device. If sufficiently bothersome or severe, skin reactions can be managed with topical steroid cream or ointment. We will refer participants to their usual providers for assessment. Subsequent sensor placement can be facilitated (if the participant remains willing) by placing a barrier product (i.e.: 3M Cavilon no sting barrier film, Tegaderm Advanced barrier, or hydrocolloid blister patch) prior to initiating a sensor.

12. MITIGATION STRATEGIES FOR COVID-19 RISKS

1. Study personnel interacting with participants face-to-face will complete and document the Alberta Health Services COVID-19 Assessment for Healthcare Workers and Workers in High Risk Settings daily (https://myhealth.alberta.ca/journey/covid-19/Pages/HWAssessLanding.aspx).
2. Both participants and research personnel will be required to wash hands with alcohol-based hand sanitizer and don masks during the interaction.
3. Participant-facing spaces will be disinfected with a hard surface cleaner with a broad-spectrum virucidal claim or a virucidal claim against coronaviruses, approved by Health Canada. Alcohol-based handwash will be available.

4. A brief screening call will take place ahead of the baseline study visit to ensure that all participants have received at least 2 doses of a Health Canada-approved vaccine against COVID-19.
5. Participants will be asked to reschedule their in-person encounters if they have any symptoms of COVID-19, or any close contact with an individual newly diagnosed with COVID-19 in the previous 10 days. Participants will have infrared surface temperature screening for fever at the beginning of the visit (screening form included under Documentation).

In Alberta, the current recommended isolation period for an individual with COVID-19 is 5 days (fully immunized) or 10 days (not fully immunized). Although our participants will all be fully immunized, out of an abundance of caution we will reschedule their visit for >= 10 days from symptom onset (or exposure to a COVID-19 case), as long as symptoms by then have improved and the participant is afebrile for >= 24 hours.

13. TREATMENT-EMERGENT ADVERSE EVENTS

Included participants belong to a population (adults with type 2 diabetes and are not on insulin) that does not typically experience hypoglycemia, and do not typically measure their glucose levels. No serious adverse events are expected. However, this protocol has several features to identify unexpected adverse events during the study.

- All emergency department visits and hospitalizations occurring from randomization to week 12 will be reviewed and adjudicated (see Appendix 5.6 for adverse event reporting forms) by study investigators. If a serious adverse event occurred because of the trial or trial intervention, study protocols will be reviewed and amended to mitigate the harm.
- We are performing in-person visits with participants to measure BP and weight. There is the possibility that we detect extremely abnormal physical parameters (e.g.: severe hypertension >= 180/110 mmHg, severe hypotension SBP < 90 mmHg). A study investigator will be paged if a result this extreme is detected and the participant will be advised to attend the emergency department.
- For emotional or psychological distress disclosed during a study visit or interview, the interviewer will offer supportive listening, remind participants of their right to withdraw from the trial, offer to connect the participant with a study investigator, and refer participants back to their usual care provider.

14. STATISTICAL AND ANALYTICAL METHODS

Our sample size calculation was intended to detect an HbA1c difference of 0.5%, presuming a standard deviation of HbA1c values at 3 months of 0.78% based on a recent similar trial of capillary blood glucose monitoring. To have 80% power to detect this HbA1c difference at a type 1 error rate of 5%, we would need 40 trial-completers in each arm. Given expected loss-to-follow-up rates of 20% or more, our enrollment target will be 100 participants.

Data will be analyzed according to intention-to-treat principles. Patients will be kept in the study group to which they were randomized, and efforts will be taken to ascertain outcome events in all patients randomized. Discontinuation of study treatment (isCGM) or no-show to CDE encounters are not equivalent to withdrawal from the study, and efforts will be made to contact study participants for HbA1c measurements and patient-reported outcomes at 12 weeks regardless.

Outcomes (HbA1c and patient-reported outcomes) are continuous scores – the difference at 12 weeks from baseline will be presented using simple means and standard deviations. On change in HbA1c, our primary outcome, we will test for a difference between intervention and enhanced usual care arms using linear regression with adjustment for age and sex. Secondary outcomes and diabetes-related distress will be analyzed in similar fashion, including follow-up values for patient-reported outcomes obtained at 6 and 12 weeks. Safety outcomes are dichotomous (e.g.: ED visits), and differences between trial arms will be assessed using Fisher's exact test. The primary outcome will be considered statistically significant at $p < 0.05$. Secondary and safety outcomes are considered hypothesis-generating and will also be considered statistically significant at $p < 0.05$. No correction for multiple comparisons is planned *a priori*. If the primary outcome is statistically significant at $p < 0.05$, the Benjamini-Hoochberg procedure will be performed on secondary outcomes targeting a false discover rate of 20%, if requested by reviewers.

Secondary analyses are planned, and include:

- Post-hoc analysis of outcomes in clinically relevant groups, e.g.: by sex, baseline self-management empowerment, etc., using the above methods.
- Partitioning participants into those who improved their HbA1c by 0.5% or more, and examining predictors of improvement using logistic regression with simultaneous incorporation of other explanatory variables.

For the post-trial cohort study, the relationship between outcomes (HbA1c and health care utilization) and study allocation will be examined using linear (log-transformed or un-transformed) and logistic regression models with simultaneous adjustment for multiple other variables, selected using a mixed purposeful / stepwise method.

For the qualitative sub-study, semi-structured interviews will be transcribed verbatim, anonymized, and will undergo thematic analysis using constant comparative methods. Co-investigators will interview transcripts independently and meet to develop a coding manual. The qualitative research associate will then code the remaining transcripts line by line. Team members will meet periodically to review and refine codes using a constant comparison method, with further sampling guided by emerging themes until content saturation is achieved.

15. TRIAL ORGANIZATION

This study will be conducted in Edmonton through the University of Alberta. The study staff consist of:

- A research assistant (roughly support staff grade 4-6 [per University of Alberta-Non-Academic Staff Association support staff wage scales]), who will have Alberta NetCare access through Alberta Health Services.
- CDE nurses, one or more community-based practitioners with active CDE practice and experience.
- A qualitative research associate (roughly support staff grade 8) with a graduate degree and previous experience in semi-structured interviews or focus group and thematic analyses.

Study staff will be hired by the principal investigator (Division of General Internal Medicine, Department of Medicine). The Epidemiology Coordination and Research (EPICORE) Centre (Division of Cardiology, Department of Medicine – www.epicore.ualberta.ca) provide study database, secure online database access, computerized participant allocation, and statistician services.

16. DATA MANAGEMENT

Study data, including the generation and maintenance of electronic case report forms, will be managed by EPICORE. The data will be housed on EPICORE's secure servers hosted at the University of Alberta Faculty of Medicine and Dentistry. Data access is limited to authorized EPICORE and study personnel, who will be provided with unique credentials. Study personnel will use the REDCap interface to complete electronic data entry; the collected data will be accessible via encrypted virtual private network.

As an innovation, EPICORE has designed a patient portal in REDCap to enable self-completion of patient-reported outcomes. While the baseline and follow-up visits will still be in-person, participants may choose to finish filling in patient-reported outcomes from home, on their computers or smart phones.

A copy of the locked and final study data will be stored on the principal investigator's secure server. This server space is hosted by the Data Analytics and Research Core (DARC) at the University of Alberta's Faculty of Medicine and Dentistry, and is also only accessible to authorized personnel via virtual private network. This will facilitate compliance with university policies on data retention, as well as satisfy the secondary analyses and the follow-up observational study once EPICORE's services are complete.

17. FEASIBILITY AND LIMITATIONS

Feasibility of the trial:

The trial is small, features a short follow-up period, and deploys existing (licensed and marketed) technologies, which have demonstrated benefits in other sub-populations of adults with diabetes. Trial needs are relatively straightforward.

The EPICORE Centre has extensive experience in clinical trials, supporting numerous investigators, with a lengthy list of completed and on-going projects (https://www.epicore.ualberta.ca/home/). They will provide data base and analysis support.

The team of study investigators is small, but collectively covers formal expertise in clinical epidemiology and sophisticated statistical analyses, diabetes care from both specialist and primary care lenses, and significant experience with clinical trials and qualitative / mixed methods evaluations in the context of primary care quality improvement.[43] The more experience study investigators are well established in local and regional clinical care organizations, and we expect to leverage their interpersonal contacts to enable participant recruitment.

Limitations and Design Issues:

- *Episodic and short-term use of isCGM.* We have designed the intervention to test the effectiveness of *episodic* isCGM, recognizing that, in the current cost and insurance coverage environment, many patients will only be able to afford isCGM on an episodic basis. Our results may not generalize to continuous or longer duration use of isCGM, or to a longer, more continuous CDE education and feedback.
- *Enhanced usual care control group does not formally feature support for capillary blood glucose monitoring*. Our control group is usual care enhanced with CDE education and feedback, which may include CDE recommendation that patients undergo self-monitoring of blood glucose with capillary blood glucose monitors, but not on a protocolized or formal basis. There is variable evidence that capillary blood glucose monitoring can improve glycemic control in this population, but a formal test of isCGM compared to capillary blood glucose monitoring is beyond the scope of the present trial.
- *Limited trial period of 12 weeks*. There is the possibility that insufficient time may have elapsed by the 12 week study HbA1c to see the effect of the intervention, since the 12 week HbA1c may be influenced by blood glucose exposure early in the trial period, before isCGM-based changes are made. Additionally, the 12 month outcome will not be able to speak to the sustainability of any isCGM benefits detected. We have designed a post-trial observational follow-up to address the longer term outcomes of episodic isCGM, recognizing that the follow analysis will no longer benefit from the expected confounder balance of randomization, as participants who consent to data linkage and who have HbA1c measurements post-trial will represent a non-random subset of those initially randomized.
- *Limited support to titrate anti-hyperglycemic medications.* The presumptive mechanism for any improvement in glycemic control is improved diet and lifestyle modification in adults randomized to isCGM. An alternative mechanism may be more rapid medication titration based on isCGM data, instead of HbA1c measurements, which are recommended at intervals no less than 90 days. While the

CDE algorithm (currently under development) may have a role for CDE-to-provider suggestions for medication changes, the intervention is not intended to provide further support or practice change related to provider prescribing (e.g.: decision support, alternate prescribers, provider training).

- *Sample size still has a 20% risk of type 2 error* – Our study is powered to detect a 0.5% difference in HbA1c at a power of 80%. The type 2 error rate (failure to detect a difference on such a difference truly exists) is still 20%, though may be slightly lower if loss-to-follow-up is minimized and recruitment approaches the full 100 participants.

18. ETHICAL CONSIDERATIONS

The study will be conducted in accordance with the Tri-Council Policy Statement.[44]

Informed Consent of the Patient - Patients who meet all inclusion criteria and none of the exclusion criteria are deemed eligible. Before being enrolled into the clinical study, the patient must provide written consent to participate in the study after the nature, scope and possible consequences of the clinical study have been explained both orally and in writing.

Approval of the Study Protocol - Before the start of the study, the study protocol and the informed consent form used at the site and other appropriate documents must be submitted to and approved by the local Ethics Committee or Institutional Review Board (REB) and the appropriate regulatory authorities in accordance with local legal requirements.

Maintenance of Records - The Investigator agrees to obtain a correctly completed informed consent form for each patient included in the study. The investigator will maintain a personal list of patient numbers and patient names to enable records to be found at a later date. As per University policy data will be kept for 5 years from completion of the study. The REDCap database will be maintained for a period of 25 years from study completion.

Generation and Sharing of Remote Patient Data – isCGM data will automatically be shared with the clinic LibreView account to facilitate CDE nurse education and feedback, via internet-capable smart phones. Participants will be provided with written, graphic instructions on terminating data sharing. Data sharing will be terminated by study personnel during the 12 week in-person visit, or by special appointment if participants wish to terminate data sharing earlier and are unable to do so themselves.

19. STUDY MONITORING

We will adhere to the Data and Safety Monitoring Board Guidance for University of Alberta Sponsored PI-Initiated Studies.[45] Because the completed PI-Initiated Study Risk Assessment Worksheet identifies this trial as being low overall risk (Appendix 7), the data safety and monitoring will be undertaken by the principal investigator, who will provide an annual

review of the data and safety information to Quality Management in Clinical Research, a research oversight department at the University of Alberta.

20. ADMINISTRATIVE RULES

Curriculum vitae - An updated copy of the curriculum vitae for each Investigator and co-Investigator will be provided to the principal investigator prior to the beginning of the study.

Confidentiality agreement - All goods, materials, information (oral or written) and unpublished documentation provided to the Investigators, inclusive of this protocol and the patient case report forms are the exclusive property of the Division of General Internal Medicine, University of Alberta.

They may not be given or disclosed by the Investigator or by any person within his authority either in part or in totality to any unauthorized person without the prior written formal consent of the PI.

It is specified that the submission of this protocol and other necessary documentation to the Ethics Research Committee is expressly permitted, the Ethics Committee members having the same obligation of confidentiality.

The Investigator shall consider as confidential and shall take all necessary measures to ensure that there is no breach of confidentiality in respect of all information accumulated, acquired or deduced in the course of the trial, other than that information to be disclosed by law.

Record retention in investigating center(s) - The Investigator must maintain all study records, patient files and other source data for the maximum period of time permitted by the institution.

21. OWNERSHIP OF DATA AND USE OF THE STUDY RESULTS

The investigators of the study have ownership of all data and results collected during this study. Full publication rights of the study data solely reside with the investigators.

22. PUBLICATIONS

All study presentations and/or publication of the results will be based on clean, checked and validated data in order to ensure the accuracy of the results. The responsibility for presentations and/or publications belongs to the investigators. The final content of the manuscript is the responsibility of the investigators. Publication of the main findings of this study will be authored based on the contributions of the individuals to the overall study.

23. POTENTIAL IMPACT OF STUDY

This trial will estimate the effectiveness of episodic isCGM paired with CDE education and feedback on glycemic control and a number of patient-reported constructs relevant to patient self-management of diabetes. Post-trial investigations will shed light on barriers and facilitators of isCGM, participant experience with isCGM, and factors mediate the effectiveness (if any) of isCGM. This sub-population of adults with diabetes is relatively un-studied, and the results will not only contribute new knowledge to guide clinical application of isCGM, but may also have implications for public insurance funding policies. The results will be disseminated in peer-reviewed journals. The intervention package (patient education materials and CDE management algorithms), being developed using a human-centred design process, will be revised post-trial and made available for use regionally. The results of the trial will also feed into local policy and prioritization efforts related to improving the care of adults with diabetes in Alberta.

24. REFERENCES

1. Imran SA, Agarwal G, Bajaj HS, Ross S. Targets for Glycemic Control. *Can J Diabetes.* 2018;42 Suppl 1:S42-s6.
2. Leiter LA, Berard L, Bowering CK, et al. Type 2 diabetes mellitus management in Canada: is it improving? *Can J Diabetes.* 2013;37:82-9.
3. Bodoarca R, Yeung RO, Lau D. New Diabetes Guidelines: Impact on Eligibility for SGLT-2 Inhibitors and GLP-1 Receptor Agonists in Canada (unpublished manuscript). 2021.
4. Fang M. Trends in Diabetes Management Among US Adults: 1999-2016. *J Gen Intern Med.* 2020;35:1427-34.
5. NHS Digital. *National Diabetes Audit, 2016-17. Care Processes and Treatment Targets: Short report*. Leeds, UK: NHS Digital; 2017.
6. Leiter LA, Cheng AYY, Ekoé JM, et al. Glycated Hemoglobin Level Goal Achievement in Adults With Type 2 Diabetes in Canada: Still Room for Improvement. *Can J Diabetes.* 2019;43:384-91.
7. Cheng AYY, Feig DS, Ho J, Siemens R. Blood Glucose Monitoring in Adults and Children with Diabetes: Update 2021. *Can J Diabetes.* 2021;45:580-7.
8. Moström P, Ahlén E, Imberg H, Hansson PO, Lind M. Adherence of self-monitoring of blood glucose in persons with type 1 diabetes in Sweden. *BMJ Open Diabetes Res Care.* 2017;5:e000342.
9. Heinemann L. Measuring glucose concentrations: daily practice, current and future developments. *J Diabetes Sci Technol.* 2008;2:710-7.
10. Martens T, Beck RW, Bailey R, et al. Effect of Continuous Glucose Monitoring on Glycemic Control in Patients With Type 2 Diabetes Treated With Basal Insulin: A Randomized Clinical Trial. *Jama.* 2021;325:2262-72.
11. Yoo HJ, An HG, Park SY, et al. Use of a real time continuous glucose monitoring system as a motivational device for poorly controlled type 2 diabetes. *Diabetes Res Clin Pract.* 2008;82:73-9.

12. Ehrhardt NM, Chellappa M, Walker MS, Fonda SJ, Vigersky RA. The effect of real-time continuous glucose monitoring on glycemic control in patients with type 2 diabetes mellitus. *J Diabetes Sci Technol.* 2011;5:668-75.
13. Vigersky RA, Fonda SJ, Chellappa M, Walker MS, Ehrhardt NM. Short- and long-term effects of real-time continuous glucose monitoring in patients with type 2 diabetes. *Diabetes Care.* 2012;35:32-8.
14. Lau D. Personnal communication with Costco Pharmacy (2616 91 St NW, Edmonton, AB) regarding FreeStyle Libre 2 sensor pricing on Oct 1, 20212021.
15. Connected in Motion. Costs of Type 1 Diabetes in Canada: Product Highlight: Dexcom G6 Subscription. 2020; https://www.connectedinmotion.ca/blog/costs-of-type-1-diabetes-in-canada-product-highlight-dexcom-g6-subscription/. Accessed 2021 Oct 05.
16. Castellana M, Parisi C, Di Molfetta S, et al. Efficacy and safety of flash glucose monitoring in patients with type 1 and type 2 diabetes: a systematic review and meta-analysis. *BMJ Open Diabetes Res Care.* 2020;8.
17. Wright EE, Jr., Kerr MSD, Reyes IJ, Nabutovsky Y, Miller E. Use of Flash Continuous Glucose Monitoring Is Associated With A1C Reduction in People With Type 2 Diabetes Treated With Basal Insulin or Noninsulin Therapy. *Diabetes Spectr.* 2021;34:184-9.
18. Miller E, Brandner L, Wright EE, Jr. 84-LB: HbA1c Reduction after Initiation of FreeStyle Libre System in Type 2 Diabetes Patients on Long-Acting Insulin or Noninsulin Therapy. *Diabetes.* 2020;69.
19. Elliott T, Beca S, Beharry R, Tsoukas MA, Zarruk A, Abitbol A. The impact of flash glucose monitoring on glycated hemoglobin in type 2 diabetes managed with basal insulin in Canada: A retrospective real-world chart review study. *Diab Vasc Dis Res.* 2021;18:14791641211021374.
20. Kröger J, Fasching P, Hanaire H. Three European Retrospective Real-World Chart Review Studies to Determine the Effectiveness of Flash Glucose Monitoring on HbA1c in Adults with Type 2 Diabetes. *Diabetes Ther.* 2020;11:279-91.
21. Haak T, Hanaire H, Ajjan R, Hermanns N, Riveline JP, Rayman G. Flash Glucose-Sensing Technology as a Replacement for Blood Glucose Monitoring for the Management of Insulin-Treated Type 2 Diabetes: a Multicenter, Open-Label Randomized Controlled Trial. *Diabetes Ther.* 2017;8:55-73.
22. Yaron M, Roitman E, Aharon-Hananel G, et al. Effect of Flash Glucose Monitoring Technology on Glycemic Control and Treatment Satisfaction in Patients With Type 2 Diabetes. *Diabetes Care.* 2019;42:1178-84.
23. Hermanns N, Ehrmann D, Schipfer M, Kröger J, Haak T, Kulzer B. The impact of a structured education and treatment programme (FLASH) for people with diabetes using a flash sensor-based glucose monitoring system: Results of a randomized controlled trial. *Diabetes Res Clin Pract.* 2019;150:111-21.
24. Jackson MA, Ahmann A, Shah VN. Type 2 Diabetes and the Use of Real-Time Continuous Glucose Monitoring. *Diabetes Technol Ther.* 2021;23:S27-S34.
25. Davis WA, Bruce DG, Davis TM. Is self-monitoring of blood glucose appropriate for all type 2 diabetic patients? The Fremantle Diabetes Study. *Diabetes Care.* 2006;29:1764-70.

26. Malanda UL, Welschen LM, Riphagen, II, Dekker JM, Nijpels G, Bot SD. Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin. *Cochrane Database Syst Rev.* 2012;1:Cd005060.
27. Machry RV, Rados DV, Gregório GR, Rodrigues TC. Self-monitoring blood glucose improves glycemic control in type 2 diabetes without intensive treatment: A systematic review and meta-analysis. *Diabetes Res Clin Pract.* 2018;142:173-87.
28. Durán A, Martín P, Runkle I, et al. Benefits of self-monitoring blood glucose in the management of new-onset Type 2 diabetes mellitus: the St Carlos Study, a prospective randomized clinic-based interventional study with parallel groups. *J Diabetes.* 2010;2:203-11.
29. Polonsky WH, Fisher L, Schikman CH, et al. Structured self-monitoring of blood glucose significantly reduces A1C levels in poorly controlled, noninsulin-treated type 2 diabetes: results from the Structured Testing Program study. *Diabetes Care.* 2011;34:262-7.
30. Polonsky WH, Fisher L, Schikman CH, et al. A structured self-monitoring of blood glucose approach in type 2 diabetes encourages more frequent, intensive, and effective physician interventions: results from the STeP study. *Diabetes Technol Ther.* 2011;13:797-802.
31. Parsons SN, Luzio SD, Harvey JN, et al. Effect of structured self-monitoring of blood glucose, with and without additional TeleCare support, on overall glycaemic control in non-insulin treated Type 2 diabetes: the SMBG Study, a 12-month randomized controlled trial. *Diabet Med.* 2019;36:578-90.
32. Abbott Laboratories. New Real-World Data Show That Abbott's FreeStyle Libre System Delivers Positive Health Outcomes for People with Type 1 and Type 2 Diabetes. Madrid, Spain: PRNewswire; 2020.
33. Health Canada Health Products and Food Branch, Medical Devices Directorate. Active licence listing by company (ABBOTT DIABETES CARE LTD. 134918). *https://health-products.canada.ca/* 2022; https://health-products.canada.ca/mdall-limh/information.do?companyId_idCompanie=134918&lang=eng. Accessed Feb. 22, 2022, 2022.
34. Bayshore Specialty Rx Ltd.. FreeStyle Libre 2 Sensor. *https://libre.myfreestyle.ca* 2022; https://libre.myfreestyle.ca/freestyle-libre-2-sensor-i200010.
35. Alva S, Bailey T, Brazg R, et al. Accuracy of a 14-Day Factory-Calibrated Continuous Glucose Monitoring System With Advanced Algorithm in Pediatric and Adult Population With Diabetes. *J Diabetes Sci Technol.* 2022;16:70-7.
36. Bailey T, Bode BW, Christiansen MP, Klaff LJ, Alva S. The Performance and Usability of a Factory-Calibrated Flash Glucose Monitoring System. *Diabetes Technol Ther.* 2015;17:787-94.
37. Bradley C, Lewis KS. Measures of psychological well-being and treatment satisfaction developed from the responses of people with tablet-treated diabetes. *Diabet Med.* 1990;7:445-51.
38. Anderson RM, Fitzgerald JT, Gruppen LD, Funnell MM, Oh MS. The Diabetes Empowerment Scale-Short Form (DES-SF). *Diabetes Care.* 2003;26:1641-2.
39. Welch GW, Jacobson AM, Polonsky WH. The Problem Areas in Diabetes Scale. An evaluation of its clinical utility. *Diabetes Care.* 1997;20:760-6.

40. England CY, Thompson JL, Jago R, Cooper AR, Andrews RC. Development of a brief, reliable and valid diet assessment tool for impaired glucose tolerance and diabetes: the UK Diabetes and Diet Questionnaire. *Public Health Nutr.* 2017;20:191-9.
41. Ekelund U, Sepp H, Brage S, et al. Criterion-related validity of the last 7-day, short form of the International Physical Activity Questionnaire in Swedish adults. *Public Health Nutr.* 2006;9:258-65.
42. Duclos M, Dejager S, Postel-Vinay N, di Nicola S, Quéré S, Fiquet B. Physical activity in patients with type 2 diabetes and hypertension--insights into motivations and barriers from the MOBILE study. *Vasc Health Risk Manag.* 2015;11:361-71.
43. Manca DP, Fernandes C, Grunfeld E, et al. The BETTER WISE protocol: building on existing tools to improve cancer and chronic disease prevention and screening in primary care for wellness of cancer survivors and patients - a cluster randomized controlled trial embedded in a mixed methods design. *BMC Cancer.* 2018;18:927.
44. Canada Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council. *Tri-Council Policy Statement. Ethical Conduct for Research Involving Humans*. Ottawa, ON: Secretariat on Responsible Conduct of Research (Government of Canada); 2018.
45. Nothern Alberta Clinical Trials + Research Centre. Data and Safety Monitoring Board (DSMB) Guidance for University of Alberta PI-Initiated Studies. 2012; https://www.ualberta.ca/research/media-library/quality-management-in-clinical-research/qmcr-templates-and-tools/qmcrdataandsafetymonitoringboard.doc. Accessed Feb. 25, 2022.

APPENDIX 1: Dear Provider Trial Letter

Separately attached.

APPENDIX 2: Brochure for waiting room and exam rooms – for hand-out to patients and for provider information

Separately attached.

APPENDIX 3: Consent Information Package and Form

Appendix 3.1: Verbal Consent for NetCare Access to Screen for Study Eligibility

Separately attached.

Appendix 3.2: Consent for patients with diabetes participating in the trial

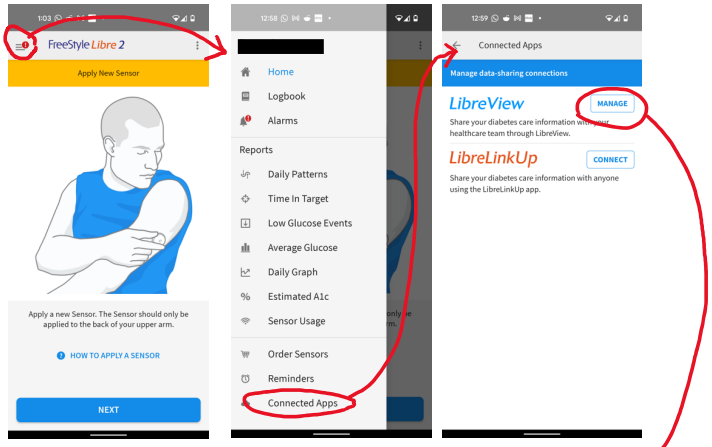
Separately attached.

Appendix 3.3: Consent for diabetes providers for qualitative interviews

Separately attached.

APPENDIX 4: Instructions to Terminate LibreView Data Sharing

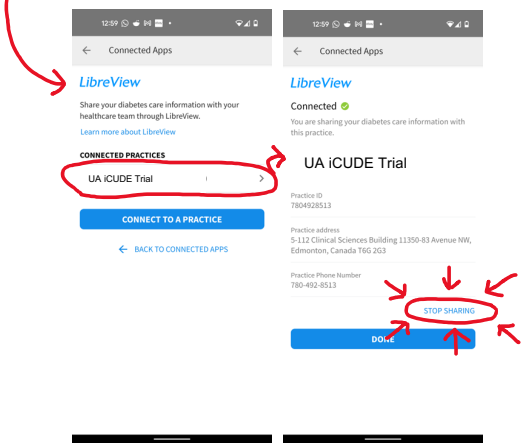
Terminating Libre 2 Glucose Data Sharing With the iCUDE Study Team
Instructions



Open the Libre 2 app.
Open the menu.

Select "Connected Apps".

Select "Manage" next to LibreView.



Select the "UA iCUDE Trial" connected practice.

Press STOP SHARING.

APPENDIX 5: Case Report Forms

Electronic case report forms with the following content

Appendix 5.1: Screening and Randomization Form

Screening

Patient study ID
Patient name
Patient health care number
Patient date of birth
Screening date
Inclusion Criteria

1. Age >= 18 years with type 2 diabetes.
2. HbA1c > 7.0%.
3. Non-insulin therapy.
4. Able to attend two in-person study visits.
5. English-speaking.
6. Community-dwelling
7. In possession of a cell phone capable of accessing the internet and receiving FreeStyle Libre 2 sensor readings
8. Has a primary care provider who has been in contact with the patient for diabetes in the last 12 months.

Exclusion Criteria

1. Type 1 diabetes or diabetes clearly identified as having monogenetic etiology (e.g.: MODY).
2. Steroid-induced diabetes if steroid use is on-going or most recently taken within the last 3 months.
3. Pregnancy; plans to become pregnant within 6 months; breast-feeding.
4. Any use of insulin in the previous year.
5. Current or previous use of isCGM or rtCGM.
6. Cognitive dysfunction (SPMSQ score >= 5).
7. Symptoms of acute metabolic decompensation (extreme thirst, high urinary output, and weight loss, accompanied by acute fatigue or dyspnea).
8. Any terminal condition that would limit life expectancy to < 1 year.
9. Inability to use isCGM (e.g.: afraid of the device).
10. Inability to be reached by telephone.
11. Unwillingness to participate.
12. Has not already received two doses of a Health Canada-approved vaccine against SARS-CoV-2.

Consent completion (yes / no)
Patient address
Patient telephone numbers

- Primary
- Secondary
- Best time to call

Patient alternate contact name
Patient alternate contact phone number
Patient email address
Patient's usual diabetes provider name
Patient's usual diabetes provider phone number

Randomization
Patient study ID
Randomization date
Randomization group

Appendix 5.2: Baseline visit

Patient study ID
Baseline visit date
Patient demographics

- Age
- Sex
- Ethnicity (White, Asian, Black, Latin American, Arab, Indigenous (including Metis or First Nations))
- Marital status
- Income quintile (pre-tax: < $36,500, $36,500-<$62,000, $62,000-<$92,000, >=$92,000, refuse answer)
- Smoking status

Medical conditions

- Hypertension
- Dyslipidemia
- Heart disease
- Heart attack
- Heart failure
- Atrial fibrillation
- Stroke or TIA
- Peripheral artery disease
- COPD
- Asthma

Diabetes-related quantities

- Duration of diabetes
- Retinopathy (problem with the back of your eye that you were told was due to diabetes?)
- Diabetic nerve disease (problem with loss of sensation or with nerve pain that you were told was due to diabetes?)
- Foot infection without ulcer (an infection in your foot that you were told was due to diabetes?)
- Foot ulcer (a wound or hole in your foot that you were told was due to diabetes?)
- Amputation
- Chronic kidney disease (defined as eGFR <= 60 mL/min/1.73m^2 or UACR >= 3 mg/mmol or UPCR >= 15 mg/mmol or semi-quantitiative urine dipstick >= 1+)
- Most recent eGFR on NetCare (date)
- Most recent proteinuria indicator on NetCare (date)
    - UACR
    - UPCR
    - Semi-quantitative urine dipstick proteinuria
- Previous use of fingerstick blood sugar measurement

Physical parameters

- BP
- Height (cm)

- Weight (kg)
- BMI (kg/m^2)

Medication list

- Medication names, total daily dose
- Medication compliance: Frequency of missed doses (0%, 1-20%, 21-50%, > 50%)

Health care utilization

- ED visits in the last 6 months
- Hospital admission in the last 6 months
- Family physician visits in the last 6 months
- Diabetes specialist visits in the last 6 months

Appendix 5.3: Follow-up visit

Patient study ID

Follow-up visit date

Diabetes-related quantities

- Retinopathy (problem with the back of your eye that you were told was due to diabetes?)
- Diabetic nerve disease (problem with loss of sensation or with nerve pain that you were told was due to diabetes?)
- Foot infection without ulcer (an infection in your foot that you were told was due to diabetes?)
- Foot ulcer (a wound or hole in your foot that you were told was due to diabetes?)
- Amputation
- Most recent eGFR on NetCare since baseline visit (date)
- Most recent proteinuria indicator on NetCare since baseline visit (date)
    - UACR
    - UPCR
    - Semi-quantitative urine dipstick proteinuria
- Use of fingerstick blood sugar measurement since baseline visit
    - Number of weeks using fingerstick blood sugar measurement
    - Number of fingerstick blood sugar measurements per day while using it
- Use of isCGM
    - Number of sensors since baseline visit
    - Number of scans per day (self-report) while sensor active

Adverse events

- Any adverse event that might be related to diabetes, diabetes treatment, or glucose monitoring (open adverse event reporting form)
- Skin reactions related to CGM
    - Type of skin reaction: Hives, dermatitis, bleeding
    - Able to continue using CGM?
    - Any treatment applied?
        - Barrier film
        - Steroid cream
        - Other

CDE compliance

- Number of CDE education and feedback sessions attended

Medications

- Medication names, total daily dose
- Any medication changes since baseline?
    - Number of new medications since baseline
    - Number of medications with dose increase since baseline
    - Number of discontinued medications since baseline
    - Number of medications with dose decrease since baseline
- Medication compliance: Frequency of missed doses (0%, 1-20%, 21-50%, > 50%)

Health care utilization

- ED visits since last study visit

- Hospital admission since last study visit
- Family physician visit since last study visit
- Diabetes specialist visit since last study visit

Appendix 5.4: Patient-reported outcomes forms

isCGM Use
Follow-up time: 6 weeks, 12 weeks

In the last 6 weeks, have you used a continuous glucose monitoring sensor?
If yes, please indicate how many?

In the last 6 weeks, have you measured your blood sugars by finger prick?

Diabetes Treatment Satisfaction Questionnaire Status (DTSQs)
Follow-up time: Baseline, 6 weeks, 12 weeks
Date completed

Customized prompt: The following questions are concerned with the treatment for your diabetes (including blood glucose measurement, if applicable, and tablets and/or diet) and your experience over the past few weeks. Please answer each question by circling a number on each of the scales.

Diabetes Treatment Satisfaction Questionnaire: DTSQs

The following questions are concerned with the treatment for your diabetes (including insulin, tablets and/or diet) and your experience over the past few weeks. Please answer each question by circling a number on each of the scales.

1. How satisfied are you with your current treatment?
   very satisfied 6 5 4 3 2 1 0 very dissatisfied

2. How often have you felt that your blood sugars have been unacceptably high recently?
   most of the time 6 5 4 3 2 1 0 none of the time

3. How often have you felt that your blood sugars have been unacceptably low recently?
   most of the time 6 5 4 3 2 1 0 none of the time

4. How convenient have you found your treatment to be recently?
   very convenient 6 5 4 3 2 1 0 very inconvenient

5. How flexible have you found your treatment to be recently?
   very flexible 6 5 4 3 2 1 0 very inflexible

6. How satisfied are you with your understanding of your diabetes?
   very satisfied 6 5 4 3 2 1 0 very dissatisfied

7. Would you recommend this form of treatment to someone else with your kind of diabetes?
   Yes, I would definitely recommend the treatment 6 5 4 3 2 1 0 No, I would definitely not recommend the treatment

8. How satisfied would you be to continue with your present form of treatment?
   very satisfied 6 5 4 3 2 1 0 very dissatisfied

Please make sure that you have circled one number on each of the scales.

Diabetes Treatment Satisfaction Questionnaire Change (DTSQc)
Follow-up time: 6 weeks only, following DTSQs
Date completed

Customized prompt: For the past 6 weeks you have been taking part in a diabetes treatment study. At the start of the study, you may have had a change of treatment. Today we would like to know your experience with your current treatment (including blood sugar measurement, if applicable, and medication and diet) has changed from your experience with your treatment before the study began. Please answer each question by circling a number on each of the scales to indicate the extent to which you have experienced changes. If you have experienced no changes, please circle "0".

Diabetes Treatment Satisfaction Questionnaire (change): DTSQc

For the past 6 weeks you have been taking part in a diabetes treatment study. At the start of the study you may have had a change of treatment. Today we would like to know how your experience with your current treatment (including medication and diet) has changed from your experience with your treatment before the study began. Please answer each question by circling a number on each of the scales to indicate the extent to which you have experienced changes. If you have experienced no change, please circle "0".

1. How satisfied are you with your current treatment?

much more satisfied now	3	2	1	0	-1	-2	-3	much less satisfied now

2. How often have you felt that your blood sugars have been unacceptably high recently?

much more of the time now	3	2	1	0	-1	-2	-3	much less of the time now

3. How often have you felt that your blood sugars have been unacceptably low recently?

much more of the time now	3	2	1	0	-1	-2	-3	much less of the time now

4. How convenient have you found your treatment to be recently?

much more convenient now	3	2	1	0	-1	-2	-3	much less convenient now

5. How flexible have you found your treatment to be recently?

much more flexible now	3	2	1	0	-1	-2	-3	much less flexible now

6. How satisfied are you with your understanding of your diabetes?

much more satisfied now	3	2	1	0	-1	-2	-3	much less satisfied now

7. How likely would you be to recommend your present treatment to someone else with your kind of diabetes?

much more likely to recommend the treatment now	3	2	1	0	-1	-2	-3	much less likely to recommend the treatment now

8. How satisfied would you be to continue with your present form of treatment?

much more satisfied now	3	2	1	0	-1	-2	-3	much less satisfied now

Please make sure that you have circled one number on each of the scales.

Diabetes Empowerment Scale – Short Form (DES-SF)
Follow-up time: Baseline, 6 weeks, 12 weeks
Date completed

In general, I believe that I:

1. know what part(s) of taking care of my diabetes that I am dissatisfied with. (DESSF1)
   5 – Strongly Agree. 4 – Somewhat Agree. 3 – Neutral. 2 – Somewhat Disagree. 1 – Strongly Disagree.
2. am able to turn my diabetes goals into a workable plan. (DESSF2)
   5 – Strongly Agree. 4 – Somewhat Agree. 3 – Neutral. 2 – Somewhat Disagree. 1 – Strongly Disagree.
3. can try out different ways of overcoming barriers to my diabetes goals. (DESSF3)
   5 – Strongly Agree. 4 – Somewhat Agree. 3 – Neutral. 2 – Somewhat Disagree. 1 – Strongly Disagree.
4. can find ways to feel better about having diabetes. (DESSF4)
   5 – Strongly Agree. 4 – Somewhat Agree. 3 – Neutral. 2 – Somewhat Disagree. 1 – Strongly Disagree.
5. know the positive ways I cope with diabetes related stress. (DESSF5)
   5 – Strongly Agree. 4 – Somewhat Agree. 3 – Neutral. 2 – Somewhat Disagree. 1 – Strongly Disagree.
6. can ask for support for having and caring for my diabetes when I need it. (DESSF6)
   5 – Strongly Agree. 4 – Somewhat Agree. 3 – Neutral. 2 – Somewhat Disagree. 1 – Strongly Disagree.
7. know what helps me stay motivated to care for my diabetes. (DESSF7)
   5 – Strongly Agree. 4 – Somewhat Agree. 3 – Neutral. 2 – Somewhat Disagree. 1 – Strongly Disagree.
8. know enough about myself as a person to make diabetes care choices that are right for me. (DESSF8)
   5 – Strongly Agree. 4 – Somewhat Agree. 3 – Neutral. 2 – Somewhat Disagree. 1 – Strongly Disagree.

Scoring
DES-SF score (average of the 8 items) (DESSFscore).

Problem Areas in Diabetes Questionnaire
Follow-up time: Baseline, 6 weeks, 12 weeks
Date completed

Items PAID01 – PAID20, scored 0-4 as below.

Problem Areas In Diabetes (PAID) Scale

Instructions: Which of the following diabetes issues are **currently** a problem for you? Tick the box that gives the best answer for you. Please provide an answer for each question.

		Not a problem	Minor problem	Moderate problem	Somewhat serious problem	Serious problem
1	Not having clear and concrete goals for your diabetes care?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
2	Feeling discouraged with your diabetes treatment plan?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
3	Feeling scared when you think about living with diabetes?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
4	Uncomfortable social situations related to your diabetes care (e.g. people telling you what to eat)?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
5	Feelings of deprivation regarding food and meals?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
6	Feeling depressed when you think about living with diabetes?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
7	Not knowing if your mood or feelings are related to your diabetes?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
8	Feeling overwhelmed by your diabetes?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
9	Worrying about low blood glucose reactions?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
10	Feeling angry when you think about living with diabetes?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
11	Feeling constantly concerned about food and eating?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
12	Worrying about the future and the possibility of serious complications?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
13	Feelings of guilt or anxiety when you get off track with your diabetes management?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
14	Not accepting your diabetes?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
15	Feeling unsatisfied with your diabetes physician?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
16	Feeling that diabetes is taking up too much of your mental and physical energy every day?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
17	Feeling alone with your diabetes?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
18	Feeling that your friends and family are not supportive of your diabetes management efforts?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
19	Coping with complications of diabetes?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
20	Feeling burned out by the constant effort needed to manage diabetes?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4

Scoring
Sum of for each item PAID01-PAID02 multiplied by 1.25 (PAIDscore).

UK Diabetes and Diet Questionnaire (UKDDQ)
Follow-up time: Baseline, 6 weeks, 12 weeks
Date completed

Items UKDDQ01-25, scored A-F as below.

Name:_____ Date:_____

Think about your diet over the last MONTH. Circle the answer that best applies to you . Put the letter score in the ovals.

1. How often did you eat a portion of vegetables?
Include fresh, tinned and frozen vegetables and pulses like lentils and kidney beans.

Never or very rarely (F)	Once a week or less often (E)	2- 4 times a week (D)	5 - 6 times a week (C)	1 - 2 times a day (B)	3 or more times a day (A)	Score:

2. How often did you eat a portion of fruit? Include fresh, frozen, tinned and dried fruit. Do not count fruit juices.

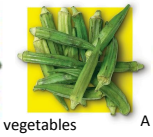
Never or very rarely (F)	Once a week or less often (E)	2- 4 times a week (D)	5 - 6 times a week (C)	1 - 2 times a day (B)	3 or more times a day (A)	Score:

A portion of vegetables or fresh, frozen or tinned fruit is 80g (2.9oz) or about a handful. These are some examples:


2 florets



3 heaped tablespoons of cooked vegetables



A dessert bowl of salad


7 cherry tomatoes


1 medium fruit


2 small fruits


10 chunks


A handful


A 5cm slice


A tablespoon of dried fruit (30g or 1/2 handful)

3. How often did you eat a cake, a sweet pastry like a Danish pastry, a donut or a sweet biscuit?

Never or very rarely (A)	Once a week or less often (B)	2- 4 times a week (C)	5 - 6 times a week (D)	1 - 2 times a day (E)	3 or more times a day (F)	Score:

4. How often did you eat sweets, chocolate or sugary foods like gulab jamun, halva or sweet popcorn?

Never or very rarely (A)	Once a week or less often (B)	2- 4 times a week (C)	5 - 6 times a week (D)	1 - 2 times a day (E)	3 or more times a day (F)	Score:

5. How often did you drink sugary drinks? Include non-diet fizzy drinks, squashes, mixers, energy drinks, fruit juices, sweetened milk drinks or coffee, tea or other hot drinks with sugar or flavoured syrups.

Never or very rarely (A)	Once a week or less often (B)	2- 4 times a week (C)	5 - 6 times a week (D)	1 - 2 times a day (E)	3 or more times a day (F)	Score:

6. How often did you use butter, full-fat margarine, ghee, lard or coconut oil or palm oil on your bread, potatoes or vegetables or in cooking?

Never or very rarely (A)	Once a week or less often (B)	2- 4 times a week (C)	5 - 6 times a week (D)	1 - 2 times a day (E)	3 or more times a day (F)	Score:

7. How often did you eat oily fish? Think about fresh or tinned salmon, trout, sardine, mackerel, pilchards, herring, red mullet, or fresh tuna.

Never (F)	Less than once a week (E)	Once a week (B)	Twice or more per week (A)	Score:

8. How often did you drink alcohol?

Never or very rarely (A)	Once a week or less often (A)	2- 4 times a week (B)	5 - 6 times a week (C)	1 - 2 times a day (E)	3 or more times a day (F)	Score:

Turn over to answer questions on page 2

 Version 3 26/01/2017 self scored Page 1

Think about your diet over the last MONTH. Circle the answer that best applies to you . Put the letter score in the ovals

9. How often did you eat full-fat cheese? Include cheese in sandwiches, on biscuits, in sauces and when used as a topping. Include hard cheeses like cheddar, blue cheeses and soft cheeses like brie, cream cheese, pannier or full-fat goat cheeses.

Never or very rarely (A)	Less than once a week (B)	1 - 2 times a week (C)	3 - 5 times a week (D)	Nearly every day or daily (E)	Twice or more per day (F)	Score:

10. How often did you eat processed meat? Include processed meat in sandwiches, ready meals and if eaten as a snack. Processed meat includes foods like bacon, ham, spam, sausages, salami or chorizo.

Never or very rarely (A)	Less than once a week (B)	1 - 2 times a week (C)	3 - 5 times a week (D)	Nearly every day or daily (E)	Twice or more per day (F)	Score:

11. How often did you eat savoury foods like crisps, corn chips, corn puffs, salted nuts or Bombay mix?

Never or very rarely (A)	Less than once a week (B)	1 - 2 times a week (C)	3 - 5 times a week (D)	Nearly every day or daily (E)	Twice or more per day (F)	Score:

12. How often did you eat a savoury pastry? Think about food like pies, pasties, samosas, sausage rolls, patties or vol-au-vents.

Never or very rarely (A)	Less than once a week (B)	1 - 2 times a week (C)	3 - 5 times a week (D)	Nearly every day or daily (E)	Twice or more per day (F)	Score:

13. How often did you eat 'fast foods' from a take-away or in a restaurant?
Think about foods like burgers, fish and chips, fried chicken, donor kebabs, pizza, fried rice or curries with cream or ghee.

Never or very rarely (A)	Less than once a week (B)	1 - 2 times a week (C)	3 - 5 times a week (D)	Nearly every day or daily (E)	Twice or more per day (F)	Score:

14. How often did you eat pudding or dessert, apart from fruit, with your meals?

Never or very rarely (A)	Less than once a week (B)	1 - 2 times a week (C)	3 - 5 times a week (D)	Nearly every day or daily (E)	Twice or more per day (F)	Score:

15. How often did you have 3 or more regular meals in a day?
Include light meals like a sandwich, a soup and roll or something on toast. Don't include snack times when you ate only a biscuit or cake or a piece of fruit or vegetable sticks or a packet of crisps or piece of cheese.

Never or very rarely (F)	Less than once a week (E)	Once a week (D)	2 - 4 times a week (C)	5-6 times a week (B)	Every day (A)	Score:

16. How often did you eat breakfast (more than just a drink or one or two sweet biscuits) within about 2 hours of waking?

Never or very rarely (F)	Less than once a week (E)	Once a week (D)	2 - 4 times a week (C)	5-6 times a week (B)	Every day (A)	Score:

17. How often did you 'snack' or 'pick' on high-fat or high-sugar foods between meals? Think about food like biscuits, chocolate, cakes, crisps, nuts and cheese.

Never or very rarely (A)	Less than once a week (B)	Once a week (C)	2 - 4 times a week (D)	5-6 times a week (E)	Every day (F)	Score:

Now answer the questions on page 3

Name: _____ **Date:** _____

Think about your diet over the last MONTH. Circle the answer that best applies to you . Put the letter score in the ovals.

Each photo is a serving or portion. Use them to help work out how many servings you eat each week or day.

3 tablespoons cereal or porridge (about 30g or 1oz)

Breads (about 28g or 1oz)

2-3 tablespoons cooked rice, cooked pasta or noodles (about 80g or 2.9oz)

18. How often did you eat a portion of bread? Include bread in sandwiches and wraps.
A portion of bread is 1 small slice of bread, a bread roll, half a baguette, a bagel, a pikelet a tortilla wrap, a small naan, a chapatti or a paratha.

Circle the answer that applies. There is no score because there is no most healthy or least healthy choice. Use this question with question 19 to see if bread could be an important source of fibre for you.

Never or very rarely	Once a week or less than once a week	2- 6 times a week	1 – 2 times a day	3 – 4 times a day	More than 4 times a day

19. When you ate bread did you choose higher fibre breads?
Breads that are high in fibre include wholemeal, granary or wholegrain wheat and rye breads. If you follow a gluten free diet include high fibre gluten free breads.

All of the time (A)	Most of the time (B)	About half the time (C)	Less than half the time (D)	Never (E)	I did not eat bread (no score)	Score:

20. How often did you eat a bowl of breakfast cereal, porridge or muesli?

Circle the answer that applies. There is no score because there is no most healthy or least healthy choice. Use this question with question 21 to see if cereal could be an important source of fibre for you.

Never or very rarely	Less than once a week	Once a week	2 – 5 times a week	Nearly every day or daily	Twice or more per day

21. When you ate cereal did you choose higher fibre cereals?
Cereals that are high in fibre include porridge, muesli, Weetabix, Shredded Wheat, multi-grain cereals and wheat or oat bran cereals.

All of the time (A)	Most of the time (B)	About half the time (C)	Less than half the time (D)	Never (E)	I did not eat cereal (no score)	Score:

22. How often did you eat a serving of rice, pasta or noodles? A serving is 2-3 tablespoons cooked rice, cooked pasta or noodles.

Circle the answer that applies. There is no score because there is no most healthy or least healthy choice. Use this question with question 23 to see if rice, pasta or noodles could be an important source of fibre for you.

Never or very rarely	Less than once a week	Once a week	2 – 5 times a week	Nearly every day or daily	Twice or more per day

23. When you ate rice, pasta or noodles did you choose brown rice or wholegrain pasta / noodles?

All of the time (A)	Most of the time (B)	About half the time (C)	Less than half the time (D)	Never (E)	I did not eat rice / noodles / pasta (no score)	Score:

24. And finally, what type of milk did you usually use, if any?

Full fat (cow, goat or sheep) (F)	Semi-skimmed (cow, goat or sheep) (B)	Skimmed (cow, goat or sheep) (A)	Sometimes full fat, sometimes skimmed or semi skimmed (D)	Soya, oat, rice or other non-dairy milk (A)	None (A)	Score:

Now go to page 4 for scoring

25. Are you concerned about your weight?

I am not concerned about my weight	I am a little concerned about my weight	I am moderately concerned about my weight	I am very concerned about my weight

26. How important is it to you to change your diet?

Not at all important 0 3 5 7 10 Extremely important

27. How confident are you that you could change your diet?

Not at all confident 0 3 5 7 10 Extremely confident

Notes:

Fruit: Be aware that large portions of fruit in one go MAY contribute to raised blood glucose levels. Spread fruit out evenly through the day.

Oily fish: Contains essential omega-3 fatty acids. For vegetarians, or people who dislike oily fish, the best alternate sources are walnuts, ground linseeds (flaxseeds) and linseed oil. Other sources are rapeseed oil (commonly vegetable oil), walnut oil, chia seeds and edamame (cooked soy beans) and tofu. If appropriate consider foods fortified with omega-3s, such as omega-3 eggs.

Alcohol: Scoring for alcohol does not take into account binge drinking. Drinking more than 14 units of alcohol a week exceeds guidelines. A unit is half a pint beer, a small glass of wine or a single shot of spirits.

Milk: If you drink soya, oat, rice or other non dairy milk or no milk try to include other sources of calcium such as calcium fortified foods and drinks, tofu set with calcium salts, tinned fish with bones, broccoli and spring greens.

Summary scores

UKDDQ_AB – Total number of questions answered A or B.
UKDDQ_CD – Total number of questions answered C or D.
UKDDQ_EF – Total number of questions answered E or F.
UKDDQscore – Converted A = 5, B = 4, C = 3, D = 2, E = 1, F = 0; sum of scores from UKDDQ01-UKDDQ24 *omitting UKDDQ18 and UKDDQ20*.

International Physical Activity Questionnaire (IPAQ)
Follow-up time: Baseline, 6 weeks, 12 weeks
Date completed

Note that IPAQ hours and IPAQ minutes should be automatically calculated from each other – if a respondent enters 1.5 hours, it should automatically input 90 minutes; and vice versa.

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the last 7 days. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the vigorous activities that you did in the last 7 days. Vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?
   _____ days per week (IPAQ1days)
   ☐ No vigorous physical activities → Skip to question 3. (IPAQ1none; if checked, set IPAQ1days and IPAQ2mins to 0)

2. How much time did you usual spend doing **vigorous** physical activities on one of those days?
   _____ hours per day (no specific variable name – auto-fills IPAQ2mins)
   _____ minutes per day (IPAQ2mins)
   ☐ Don't know / Not sure (IPAQ2dk; if checked, set IPAQ2mins to -9)

Think about all the moderate activities that you did in the last 7 days. Moderate activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.
   _____ days per week (IPAQ3days)
   ☐ No moderate activities → Skip to question 5. (IPAQ3none; if checked, set IPAQ3days and IPAQ4mins to 0)

4. How much time did you usual spend doing **moderate** physical activities on one of those days?
   _____ hours per day (no specific variable name – auto-fills IPAQ4mins)
   _____ minutes per day (IPAQ4mins)
   ☐ Don't know / Not sure (IPAQ4dk; if checked, set IPAQ4mins to -9)

Think about the time you spent walking in the last 7 days. This includes at work and at home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?
   _____ days per week (IPAQ5days)
   ☐ No walking → Skip to question 7. (IPAQ5none; if checked, set IPAQ5days and IPAQ6mins to 0)

6. How much time did you usually spend **walking** on one of those days?
   _____ hours per day (no specific variable name – auto-fills IPAQ6mins)
   _____ minutes per day (IPAQ6mins)
   ☐ Don't know / Not sure (IPAQ6dk; if checked, set IPAQ6min to -9)

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend sitting on a week day?
   _____ hours per day (no specific variable name – auto-fills IPAQ7mins)
   _____ minutes per day (IPAQ7mins)
   ☐ Don't know / Not sure (IPAQ7dk; if checked, set IPAQ7mins to -9)

Summary scores

Treat responses of -9 as 0.
Walking MET-minutes / week (metmin_walk) = 3.3 * IPAQ5days * IPAQ6mins
Moderate MET-minutes / week (metmin_mod) = 4.0 * IPAQ3days * IPAQ4mins
Vigorous MET-minutes / week (metmin_vig) = 8.0 * IPAQ1days * IPAQ2mins
Total MET-mins / week (metmin_tot) = metmin_walk + metmin_mod + metmin_vig.

Summary categories

IPAQhepa = 1 if (IPAQ1days >= 3 & metmin_tot >= 1500) or ((IPAQ5days + IPAQ3days + IPAQ1days) >= 7 & metmin_tot >= 3000); else IPAQhepa = 0.

IPAQminactive = 1 if (IPAQ1days >= 3 & IPAQ2mins >= 20) or (IPAQ3days >= 5 & IPAQ4mins >= 30) or ((IPAQ5days + IPAQ3days + IPAQ1days) >= 5 & metmin_tot >= 600); else IPAQminactive = 0.

IPAQinactive = 1 if IPAQhepa = 0 & IPAQminactive = 0; else IPAQinactive = 0.

Health-Related Quality of Life – EQ-5D-5L
Follow-up time: Baseline, 6 weeks, 12 weeks
Date completed
Sample worksheet shown below.
Items named MO, SC, UA, PD, AD, each taking a value between 1 and 5.

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about	☐	
I have slight problems in walking about	☑	1 ☐ 2 ☑ 3 ☐ 4 ☐ 5 ☐ Level = 2
I have moderate problems in walking about	☐	
I have severe problems in walking about	☐	
I am unable to walk about	☐	

SELF-CARE

I have no problems washing or dressing myself	☑	
I have slight problems washing or dressing myself	☐	1 ☑ 2 ☐ 3 ☐ 4 ☐ 5 ☐ Level = 1
I have moderate problems washing or dressing myself	☐	
I have severe 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 doing my usual activities	☑	
I have slight problems doing my usual activities	☐	1 ☑ 2 ☐ 3 ☐ 4 ☐ 5 ☐ Level = 1
I have moderate problems doing my usual activities	☐	
I have severe problems doing my usual activities	☐	
I am unable to do my usual activities	☐	

PAIN / DISCOMFORT

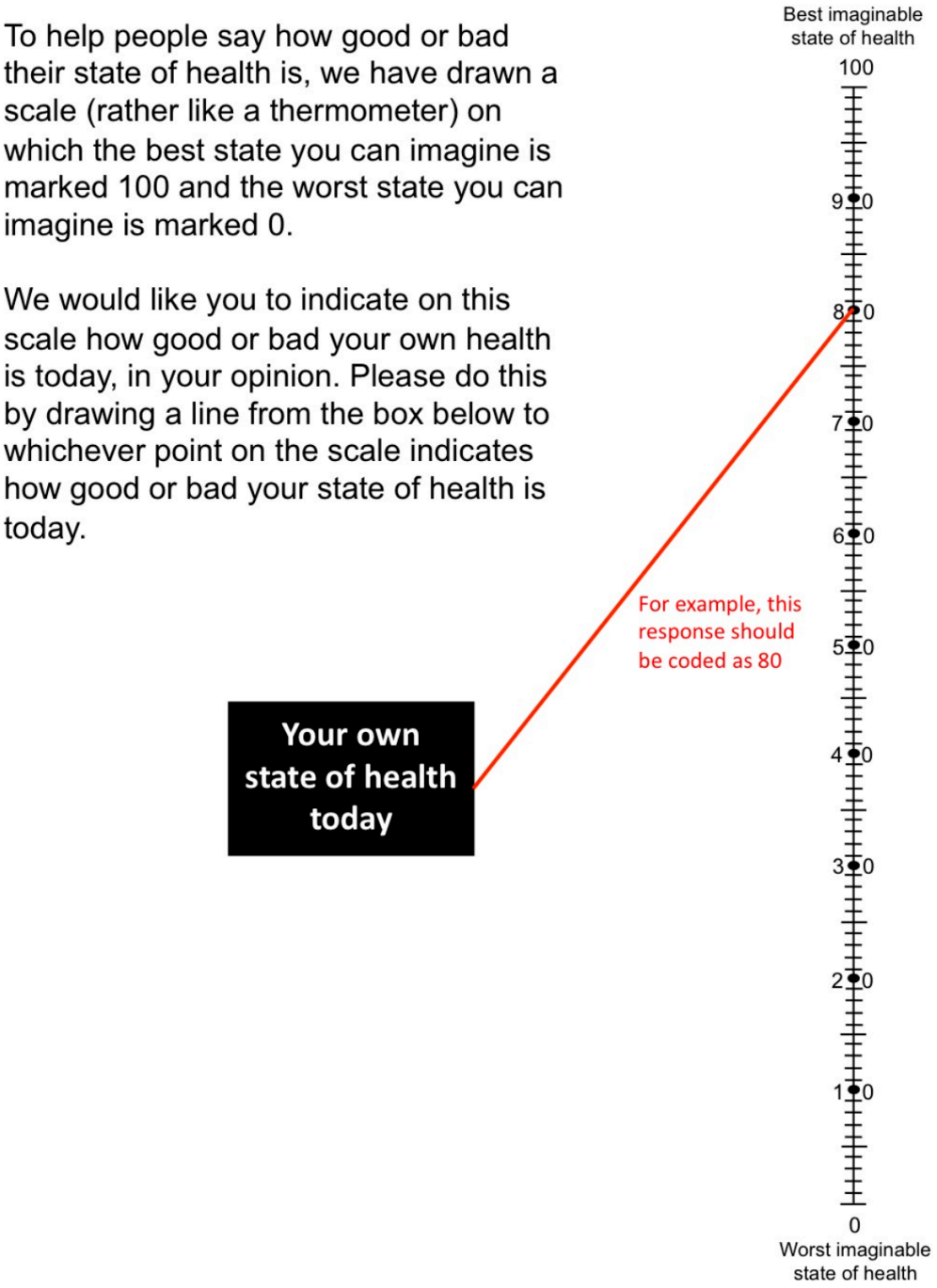
I have no pain or discomfort	☐	
I have slight pain or discomfort	☐	1 ☐ 2 ☐ 3 ☑ 4 ☐ 5 ☐ Level = 3
I have moderate pain or discomfort	☑	
I have severe pain or discomfort	☐	
I have extreme pain or discomfort	☐	

ANXIETY / DEPRESSION

I am not anxious or depressed	☐	
I am slightly anxious or depressed	☐	1 ☐ 2 ☐ 3 ☐ 4 ☑ 5 ☐ Level = 4
I am moderately anxious or depressed	☐	
I am severely anxious or depressed	☑	
I am extremely anxious or depressed	☐	

Levels of perceived problems are coded as follows

Health state 21134



Scoring

Health utility value from EQ-5D-5L responses will be calculated by investigators using Canadian valuation data. Stata / SAS / excel code available at: https://apersu.ca/eq-5d-scoring-algorithms/.

Appendix 5.5: HbA1c and Time in Range Form

HbA1c Report Form

Research assistant to complete
Patient study ID
Follow-up time: Baseline, 12 weeks
HbA1c value
Date of HbA1c

isCGM Time-in-Range Report Form

Research assistant to complete
Patient study ID
Follow-up time: 12 weeks
For adults randomized to the isCGM group only

Date of first sensor start:
Date of second sensor start:
Date of third sensor start:

Referring to the first two weeks of isCGM sensor use:

- Start date:
- Time-in-range (3.9-10.0 mmol/L) (%):
- Time-above-range (>10.0 mmol/L and <= 13.9 mmol/L):
- Time-above-range – severe (> 13.9 mmol/L):
- Time-below range (sum of < 3.9 mmol/L and < 3.0 mmol/L):
- Glucose Management Indicator (GMI) (%):
- Coefficient of variation (CV):

Referring to the last two weeks of isCGM sensor use:

- Start date:
- Time-in-range (3.9-10.0 mmol/L) (%):
- Time-above-range (>10.0 mmol/L and <= 13.9 mmol/L):
- Time-above-range – severe (> 13.9 mmol/L):
- Time-below range (sum of < 3.9 mmol/L and < 3.0 mmol/L):
- Glucose Management Indicator (GMI) (%):
- Coefficient of variation (CV):

Appendix 5.6: Adverse events report form

Patient study ID

Adverse event

- Diagnosis, if available
- Patient-report

Start date

Setting: Managed in the community, required EMS, required ED, required hospital admission.

Event details:

- Enclose ED chart or discharge summary if ED or hospital admission required
- Patient description of event

Investigator Review:

- Relationship to study treatment (definitely, possibly, not related)
- Outcome (resolved, persistent, death)
- Expected (yes, no)
- Serious (yes, no)

Definitions for adverse events form.

An Adverse Event (AE) is defined as any untoward medical occurrence, including an exacerbation of a pre-existing condition, in a patient in a clinical investigation who received a pharmaceutical product. The event does not necessarily have to have a causal relationship with this treatment.

A Serious Adverse Event (SAE) is defined as any AE which results in death, is immediately life-threatening, results in persistent or significant disability / incapacity, requires or prolongs patient hospitalization, is a congenital anomaly / birth defect, or is to be deemed serious for any other reason representing a significant hazard, which is comparable to the aforementioned criteria.

Relationship to study treatment will be determined in the medical judgement of a study investigator.

Appendix 6: Qualitative Sub-Study Interview Guides

Interview Guide (Group 1: Trial Patients Randomized to Intervention)

I would like to start by thanking you for participating in this interview. I am interested in your perspectives regarding the FreeStyle Libre 2 continuous glucose monitor and your visits with the diabetes educator. Before we start our interview, I would like to ask you not to use names of people or institutions that may identify them. We will also remove all identifying information from the transcripts.

1. Did you have any thoughts or expectations about what using the FreeStyle Libre 2 would be like before you started it?

2. Can you tell me about your experience using the Libre 2 for the first time?
   Probes: Was it easy or difficult to start using? What do you think about being able see your blood sugar on your cell phone? What did you think of your blood sugars the first day you measured them? How did they make you feel? Did you know what to make of them, or what to do about them?

3. What changes did the Libre 2 lead to in terms of what you eat or what you do during the day? How difficult was it to make those changes?
   Probes: Can you think of anything that helped you make those changes? Anything that might have made it harder to make those changes?

4. Has the Libre 2 changed how you think or feel about your diabetes?

5. What kind of support or resources did you have to help with your diabetes before this trial?

6. Can you tell me about the kind of impact meeting with the diabetes educator had on you?
   Probes: How long was the encounter? How did it feel talking to the diabetes educator? What did you learn during the encounter? Did you make a plan? What did you like best about the encounter? What would you like to be different?

7. Can you tell me about the kind of impact meeting with the diabetes educator had on your ability to use the Libre 2? To look after your diabetes?
   Probes: How about in terms of changes to your diet and activity?

8. Was the second educator encounter different from the first?
   Probes: Were there things you learnt that were different in the second encounter, from the first? What would the perfect number of encounters be? How far apart should they be?

9. Is the FreeStyle Libre 2 something you'd consider using again in the future? Why or why not?

10. Do you have goals for your diabetes moving forward?
    Probes: Can you describe your goals? What do you think about these goals? How optimistic are you that you will be able to follow through with your goals?

11. Is there anything else you would like to share about using the Libre 2 or meeting the diabetes educator?

Thank you very much for speaking with me. We would be pleased to offer you a small amount of money ($20) in appreciation for your time. You can expect it in the mail – please let us know if you don't receive it.

Interview Guide (Group 2: Trial Patient Randomized to Enhanced Usual Care)

I would like to start by thanking you for participating in this interview. I am interested in your perspectives about looking after your diabetes and your visits with the diabetes educator. Before we start our interview, I would like to ask you not to use names of people or institutions that may identify them. We will also remove all identifying information from the transcripts.

1. Do you know how well your diabetes was looked after before you met the educator? How did you feel about your diabetes before you met the educator?
   Probes: Were you doing anything in particular to make your diabetes better, or to keep it from getting worse? What kind of support or resources did you have to help with your diabetes?

2. Can you tell me about the kind of impact meeting with the diabetes educator had on you?
   Probes: How long was the encounter? How did it feel talking to the diabetes educator? What did you learn during the encounter? Did you make a plan? What did you like best about the encounter? What would you like to be different?

3. Was the second educator encounter different from the first?
   Probes: Were there things you learnt that were different in the second encounter, from the first? What would the perfect number of encounters be? How far apart should they be?

4. Did you start measuring your blood sugars at any time during the trial? Do you feel that measuring your blood sugars could have been useful?

5. Do you have goals for your diabetes moving forward?
   Probes: Can you describe your goals? What do you think about these goals? How optimistic are you that you will be able to follow through with your goals?

6. Is there anything else you would like to share about meeting the diabetes educator?

Thank you very much for speaking with me. We would be pleased to offer you a small amount of money ($20) in appreciation for your time. You can expect it in the mail – please let us know if you don't receive it.

Interview Guide (Group 3: Providers)

I would like to start by thanking you for participating in this interview. I am interested in your perspectives regarding looking after adults with early diabetes – those who are not on insulin, but who need additional blood sugar lowering to get to target. Specifically, I want to talk about using the FreeStyle Libre 2 continuous glucose monitor with these patients. Before we start our interview, I would like to ask you not to use names of people or institutions that may identify them. We will also remove all identifying information from the transcripts.

1. What is your previous experience looking after patients using the Libre or Libre 2 CGM?

2. What difference did the Libre 2 make for our trial patients who were not on insulin? Would you consider the Libre 2 useful or not useful, in this population? Why or why not?
   Probe: (If not useful, then what would the Libre 2 being useful look like?)

3. Are there patient factors that determine whether the Libre 2 is useful for an individual or not? What are they?
   Probe: Are they related to knowledge? Skill? Motivation? Supports? Environment? Diet? Activity? Are there other factors you'd like to mention?

4. Can you tell me about your encounters with patients using the CGM?
   Probes: How long was the encounter? How did it feel from your perspective? Is there anything you'd like to highlight as working particularly well? Anything you would think about doing differently during these encounters?

5. Were you able to relate the Libre 2 results to things going on in the patients' lives? Were you able to build plans of action with your patients using Libre 2 results?
   Probe: How challenging did you find this? What kind of plans did you typically leave with? Did patients need a lot of convincing to take these steps?

6. Do you feel you have the right training or resources to help patients at this stage of their diabetes, to use the CGM and improve their diabetes?

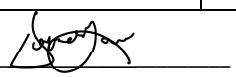
7. Is there anything else you would like to share about help adults with diabetes who are not on insulin use the Libre 2?

Thank you very much for speaking with me. We would be pleased to offer you a small amount of money ($20) in appreciation for your time. You can expect it in the mail – please let us know if you don't receive it.

APPENDIX 7: PI-Initiated Study Risk Assessment Worksheet

Appendix C: PI-Initiated Study Risk Assessment Worksheet

Use this table to assess the risks of the study's procedures, experimental treatments, and population vulnerability to derive an estimate of the overall risk of the study. For each factor please **enter** the appropriate score and add up. **Please note, this assessment will simultaneously undergo a binding independent review through QMCR**. Once this form is completed please return it to Lori Anderson at QMCR.

Study Title: Intermittently Scanned CGM Versus Usual Care With Diabetes Education and Feedback, in Adults with Type 2 Diabetes (iCUDE) **PI: Darren Lau**			**ENTER SCORE**
I. Experimental Treatment			
Low Risk	No experimental treatment in study	1 point	
Moderate Risk X	Treatment effects documented from studies with similar and/or different populations and/or settings. No serious adverse events expected. Specific plans to monitor AE's detailed in DSMP	2 points	
High Risk	Experimental treatment. (e.g. investigational drug, device, or biologic)	4 points	2
II. Procedures, Measurements, and Data Collection Methods			
Low Risk X	Minimally invasive with low degree of emotional and/or physical discomfort. Probability of adverse events is low. Severity (magnitude) of adverse events is low. (Procedure may be rated low risk if probability of AE is moderate to high so long as the severity is low, as in the case of a bruise from phlebotomy) (e.g. procedures that meet IRB criteria for expedited review)	1 point	
Moderate Risk	Moderate degree of emotional and/or physical discomfort. Probability of adverse events is low. Severity of adverse events is moderate to high. (e.g. PET scan, lumbar puncture, arterial lines)	2 points	
High Risk	Moderate to high degree of emotional and/or physical discomfort. Probability of adverse events is moderate to high. Severity of adverse events is high. (e.g. heart muscle biopsy, insulin infusion)	4 points	1
III. Decision-making Capability			
Non-vulnerable X	Adult who 1) demonstrates decision-making capacity **and** 2) demonstrates no perception of undue influence or coercion to participate.	1 point	
Vulnerable	Any minor. Adult who 1) demonstrates limitations in decision-making capacity **and/or** 2) is prone to perception of undue influence or coercion to participate.	2 points	1
Review completed by: __Darren Lau_____ Signature:  **Date: Feb 27, 22**		**TOTAL:**	4

The Level of Overall Risk of the Study is:
Low: 3 or 4 points Moderate: 5 points High: 6 to 10 points
Monitoring Requirements:
3-5 points: may be monitored by the PI who provides an annual review of data and safety information.
6 points: may be monitored by the PI who provides a quarterly review of data and safety information.
7-10 points: must have an independent monitor or DSMB, who conducts a regular review of data and safety information.
Are there any concerns regarding scientific validity or the probability of obtaining reasonable results?

Yes X **No**

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