PROTOCOL TITLE: Assessment of a Decision Support Tool in Participants with Type 1 Diabetes

STUDY SITE:	Oregon Health Science University 3181 SW Sam Jackson Park Rd Portland, OR 97639
FUNDING: **PRINCIPAL INVESTIGATORS:**	Helmsley Charitable Trust Jessica R. Castle MD; Peter Jacobs PhD
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Background:

Type 1 diabetes (T1D) is a complex disease with a high risk of both hyper- and hypoglycemia which can lead to severe acute and chronic complications. The burden and complexity of managing T1D results in the majority of people not reaching adequate glycemic control. Our team has developed a smartphone based application, DailyDose, that combines continuous glucose monitoring data and insulin data to provide decision support for subjects with type 1 diabetes taking multiple daily injections (MDI).

DailyDose provides on-demand, real-time dosing recommendations for insulin doses prior to meals and to correct hyperglycemia. DailyDose analyzes glucose patterns and provides weekly recommendations to the patient on insulin settings including carbohydrate ratios and correction factors. As needed, DailyDose will make weekly recommendations to change basal insulin. Due to the ultra long-acting effects of Tresiba and Toujeo, DailyDose will only make recommendations to change these types of basal insulin every 2 weeks for safety. For subject safety, study investigators will set constraints on settings for short and long acting insulin during the onboarding process. DailyDose will not be able to recommend insulin dose changes above or below the set safety thresholds. DailyDose also provides recommendations on carbohydrate intake for exercise and includes hypoglycemia and hyperglycemia alarms.

Primary Objectives

- To test the performance of the OHSU DailyDose MDI decision support tool as measured by percent of time with sensed glucose between 70-180 mg/dl as compared to CGM-augmented MDI therapy.
- To assess the usability of the OHSU DailyDose MDI decision support tool.

Secondary Objectives

- To test the performance of the OHSU DailyDose MDI decision support tool as measured by percent of time with sensed glucose less than 70 mg/dl as compared to CGM-augmented MDI therapy.

- Assess cognitive, emotional and behavioral characteristics of the subjects and their response to DailyDose.

Study Hypothesis:

- The study hypothesis is that the OHSU DailyDose MDI decision support tool will increase time in range and decrease time in hypoglycemia as compared to the 14 day run-in period using CGM-augmented MDI therapy.

Primary Endpoint

- Percent of time with sensed glucose between 70 – 180 mg/dl based on the Dexcom G6 CGM data.

Secondary Endpoints:

- Mean sensed glucose based on the Dexcom G6 CGM data.
- Percent of time with sensed glucose <70 mg/dl based on the Dexcom G6 CGM data.
- Percent of time with sensed glucose <54 mg/dl based on the Dexcom G6 CGM data.
- Percent of time with sensed glucose >180 mg/dl based on the Dexcom G6 CGM data.
- Percent of time with sensed glucose >250 mg/dl based on the Dexcom G6 CGM data.
- Coefficient of variation of sensor glucose based on the Dexcom G6 CGM data.
- Evaluate cognitive, emotional and behavioral characteristics of the subjects and their response to DailyDose using validated surveys, including Clarke Hypoglycemia Awareness Scale, Hypoglycemia Fear Survey, Diabetes Distress Scale, Confidence in Diabetes Self-Care, Hypoglycemia Confidence Scale, Insulin Delivery Satisfaction Survey, Global Physical Activity Questionnaire and System Usability Scale.
- Documentation and reporting of all adverse events including device/system-related events

Study Type

This is a single center, one treatment, pilot study designed to access the glucose control resulting from the use of the OHSU DailyDose MDI decision support tool.

Study Population

Study population will be adults with type 1 diabetes, ages 18 – 60 years of age. Older subjects are excluded due to higher risk of unrecognized coronary artery disease. Younger subjects are excluded as it is appropriate to assess safety and efficacy first in the adult population. Twenty five subjects will be recruited to participate in studies.

Power Analysis

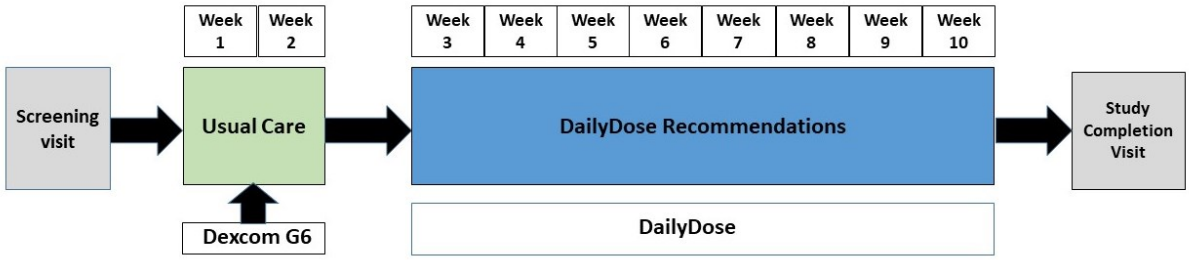
We estimate that 20 subjects provide 90% power to detect a paired difference in time in euglycemia of 10% or more on the absolute scale between the first and final 14 days of the study, assuming a standard deviation (SD) of 13% and a two-sided test with alpha = 0.05. The SD of 13% is the upper limit of a 60% confidence interval for the SD of the difference between measurements taken 2-3 weeks apart in unpublished pilot data (n=24), using percent time in euglycemia during one week. It is also consistent with published findings [1, 2] if we assume a

correlation between paired measurements of 0.6 to 0.7. Sample size calculations were performed using Stata version 15.

Protocol Summary:
Subjects will be on study for 10 weeks. Subjects will begin the study with a training visit on the Dexcom G6 CGM system and the InPen and Clipsulin smart insulin pens. Subjects will use these devices for the next 14 days at home. Subjects will return to OHSU at the end of the 14 days for a training on using the DailyDose system. Subjects will then return home to use the DailyDose system for 8 weeks. Sensor glucose, exercise, insulin and meal data will be collected during the DailyDose portion of the study in order to produce recommendations for insulin dosing. Subjects will wear the Dexcom G6 and an Apple Watch physical activity monitor for the entire study. Insulin data will be collected using the InPen for aspart insulin and Clipsulin for the long acting insulin. Subjects will complete a 30 minute aerobic exercise video at home once per week. Subjects will also be asked to complete two additional exercise sessions on their own at home, one aerobic session and the other whatever type of exercise they would normally do (aerobic, resistance etc.). Subjects will use the bolus calculator within the DailyDose app. Subjects will be instructed to test capillary blood glucose (CBG) after exercise, for symptoms of hypoglycemia or hypoglycemia alerts and again 15 minutes after rescue carbohydrate treatment until CBG >70 mg/dl. See **Figure 1** below for a diagram of the study flow.

The study investigators retain the authority to modify any aspects of the protocol at his/her discretion if he/she believes the subject's safety is a concern.

Figure 1: Study Flow Design



Subject Criteria
Inclusion Criteria:

1. Diagnosis of type 1 diabetes mellitus for at least 1 year.
2. Male or female subjects 18 to 60 years of age.
3. Physically willing and able to perform 30 min of exercise (as determined by the investigator after reviewing the subject's activity level).
4. Use of multiple daily insulin injections (MDI) for at least 4 weeks at time of screening visit.
5. A1C 7.0-10.0% at the time of screening.
6. Willingness to follow all study procedures, including attending all clinic visits.
7. Willingness to sign informed consent and HIPAA documents.

Exclusion Criteria:

1. Female of childbearing potential who is pregnant or intending to become pregnant or breast-feeding, or is not using adequate contraceptive methods. Acceptable contraception includes birth control pill / patch / vaginal ring, Depo-Provera, Norplant, an IUD, the double barrier method (the woman uses a diaphragm and spermicide and the man uses a condom), or abstinence.
2. Any cardiovascular disease, defined as a clinically significant EKG abnormality at the time of screening or any history of: stroke, heart failure, myocardial infarction, angina pectoris, or coronary arterial bypass graft or angioplasty. Diagnosis of 2nd or 3rd degree heart block or any non-physiological arrhythmia judged by the investigator to be exclusionary.
3. Renal insufficiency (GFR < 60 ml/min, using the MDRD equation as reported by the OHSU laboratory).
4. Liver failure, cirrhosis, or any other liver disease that compromises liver function as determined by the investigator.
5. History of severe hypoglycemia during the past 6 months prior to screening visit or hypoglycemia unawareness as judged by the investigator. Subjects will complete a hypoglycemia awareness questionnaire. Subjects will be excluded for four or more R responses.
6. Any active infection.
7. Known or suspected abuse of alcohol, narcotics, or illicit drugs.
8. Seizure disorder.
9. Active foot ulceration.
10. Peripheral arterial disease.
11. Major surgical operation within 30 days prior to screening.
12. Use of an investigational drug within 30 days prior to screening.
13. Chronic usage of any immunosuppressive medication (such as cyclosporine, azathioprine, sirolimus, or tacrolimus).
14. Allergy to aspart insulin.
15. Current administration of oral or parenteral corticosteroids.
16. Any life threatening disease, including malignant neoplasms and medical history of malignant neoplasms within the past 5 years prior to screening (except basal and squamous cell skin cancer).
17. Current use of any medication intended to lower glucose other than insulin (ex. use of liraglutide).
18. Vision impairment which in the opinion of the investigator would preclude the use of the smart phone application.
19. A positive response to any of the questions from the Physical Activity Readiness Questionnaire (see Appendix A) with one exception: subject will not be excluded if he/she takes a single blood pressure medication that doesn't impact heart rate and blood pressure is controlled on the medication (blood pressure is less than 140/90 mmHg).
20. Any clinically significant disease or disorder which in the opinion of the Investigator may jeopardize the subject's safety or compliance with the protocol.

Subject Recruiting:
Subjects will be recruited from OHSU clinics, from flyers to be posted in approved places at OHSU or posted on the web to the clinical trials page for the OHSU Schnitzer Diabetes Clinic, to the Clinic's facebook group, ads on facebook, electronic newletter or from the OHSU Subject Recruitment website. The T1D Exchange will send out approved recruitment emails to Glu community users in the Portland/Vancouver area. Handouts may also be made available to faculty at Providence, Tuality, Kaiser and Legacy. Records from OHSU Schnitzer Diabetes Clinic subjects may be screened to find potential subjects. Subjects will also be recruited from a list of subjects who participated in past OHSU studies who have agreed to be contacted regarding future studies, from the OHSU diabetes research registry and/or www.clinicaltrials.gov. Non-English speaking subjects will not be recruited since this protocol would require the use of medical devices and mobile software that do not have non-english versions available.

Up to 50 subjects may be screened in this study. Goal enrollment is 25 subjects.

Withdrawal Criteria
The subject may withdraw at will at any time or at the discretion of the Investigator.

A subject must be withdrawn if the following applies:
1. Hypoglycemia during the treatment period posing a safety problem as judged by the investigator.
2. Hyperglycemia during the treatment period posing a safety problem as judged by the investigator.
3. Protocol deviation having influence on efficacy or safety data as judged by the Investigator.
4. Substantial and repeated non-compliance with trial procedures.
5. Pregnancy.
6. Intention of becoming pregnant.

Visit Procedures
Staff will confirm participant and household do not have COVID-19 or symptoms of COVID-19 prior to conducting any face-to-face visits. In order to minimize face to face contact with participants per OHSU Covid-19 policy, there is the option to complete some visits virtually.

Screening (Visit 1)
All screening visits will take place at OHSU's Oregon Clinical Translational Research Institute (OCTRI) outpatient clinic or at the Harold Schnitzer Diabetes Health Center. The subject will be sent the consent form prior to the screening by email so that they can have time to read it fully at their leisure and prepare any questions they might have. Upon arrival at the clinic and prior to any procedures, study staff will explain the study, give the subject ample time to ask questions and consider participation, and ensure that subject voices understanding of the informed consent and study requirements. To minimize the possibility of coercion and to ensure that subject is signing the appropriate version of consent, an informed consent checklist will be used by study staff. After the subject has signed the consent, a copy of the consent/authorization form will be given to the subject. The original will be kept for the source document.

A capillary blood glucose (CBG) will be obtained and measured by a Contour Next glucose meter and recorded after consenting. Prior to measurement of any blood samples, the meter will undergo quality control testing with two different glucose levels, one high and one low, and both values must fall within the accepted range for a meter to be used.

Study personnel will review medical history, and medications. Height, weight, pulse, and blood pressure will be obtained. A study investigator will perform a physical examination, excluding breast and pelvic exams. Females of child-bearing potential will take a urine pregnancy test, which must be negative to participate. A venous blood sample will be taken for the following tests: hemoglobin A1C, complete blood count, complete metabolic set (including creatinine, liver set, and electrolytes). An EKG will be completed.

A study investigator will assess inclusion/exclusion criteria and review the subject's medical record for clarification as needed. A three-digit subject ID number will be assigned to the subject. Subjects will complete several questionnaires, one on physical activity readiness and one on hypoglycemia unawareness. This visit will take approximately 1 ½ hours.

When the risk of Covid-19 is considered to be significant and OHSU is on modified operations, only one staff member will be in the room with the participant at a time and the only time staff will have to be within 6 feet of the participant is when the study investigator is completing the physical exam and when research staff is completing the EKG and drawing blood for screening labs.

Start of 14 day Run-in (Visit 2):

This visit will take place within 12 weeks of the screening visit. This visit will take place at OHSU's Oregon Clinical Translational Research Institute (OCTRI) outpatient clinic, the Biomedical Engineering Point of Care (BME POC) Laboratory or at the Harold Schnitzer Diabetes Health Center. This visit will take approximately 60 minutes, depending on subject experience.

Subjects will receive training on how to use the Dexcom G6 CGM system including changing out the sensor every 10 days. The wire glucose sensor is sterile and commercially available from Dexcom™ and will be used for single use only as directed by the manufacturer. Subjects will be trained to insert the sensor into the subcutaneous tissue of the abdomen after appropriate preparation of the abdominal skin as per the manufacturer's directions. Subjects will be trained how to pair the Dexcom G6 transmitter to the Dexcom G6 app on a provided study iPhone, start and stop a new sensor session, and how to enter calibrations. The Dexcom G6 does not require calibrations. As part of the training, the study staff will review with the participants that Dexcom G6 values can be inaccurate. In the event that the participant's symptoms (such as symptoms of hypoglycemia or hyperglycemia) are discrepant with the G6 CGM reading, then the participants will be instructed to perform a CBG and use this CBG value to make treatment decisions and use the CBG value to calibrate the Dexcom G6 device. Participants will be provided with a copy of the Dexcom G6 user guide.

The CGM alerts will be set at 70 mg/dL and 250 mg/dL with user able to adjust. Subjects will be given a Contour Next meter for measuring their CBG and Precision Xtra meter for measuring

ketones. Subjects will be instructed to test CBGs after exercise, for symptoms of hypoglycemia or hypoglycemia alerts and again 15 minutes after rescue carbohydrate treatment until CBG >70 mg/dl. Subjects will be instructed to enter rescue carbohydrate treatment into the Dexcom G6 mobile app before/during and after exercise. When the CGM ≥ 300 mg/dl for over 2 hours or > 400 mg/dl, subjects will be instructed to check a capillary blood glucose and serum ketones. If ketones are 0.6-1.4 mM, subjects will be instructed to take a correction bolus. If ketones are 1.5-3 mM, subjects will call the study investigator right away for further instructions. If ketones are > 3mM, subjects will be instructed to go directly to the nearest emergency room and to contact the study investigator.

Subjects will be provided with Novolog insulin cartridges for use in the InPen smart insulin pen. Subjects will be instructed to not use the InPen smartphone application for bolus calculation but to continue with their usual insulin care calculating insulin doses based on their usual insulin carbohydrate and correction factor ratios. If the subject was using a different type of insulin, the doses will be reviewed by a study investigator but will generally be kept the same given short-acting insulin formulations such as Humalog, Admelog, and Apidra are equivalent to Novolog. Subjects will use the Clipsulin smart insulin pen with their normal long acting insulin. In the event that the long-acting insulin used by the subject will not work with the Clipsulin device, the subject will be provided with Basaglar, Lantus Solostar or Tresiba insulin pens and the study investigator will review insulin dose with the subject. Subjects will be given an Apple Watch to wear that will be paired with the study iPhone. Subjects will be asked to announce exercise to the Apple Watch. Subjects will be instructed on the use of these devices.

Subjects will complete 6 surveys, listed below. All surveys are located in Appendices D-J.

- Confidence in Diabetes Self-Care Scale [3]
- Diabetes Distress Scale [4]
- Hypoglycemia Fear Survey [5]
- Hypoglycemia Confidence Scale [6]
- Insulin Delivery Satisfaction Survey [7]
- Global Physical Activity Questionnaire

When the risk of Covid-19 is considered to be significant and OHSU is on modified operations: there is the option to complete this visit via Webex with the study devices delivered to the participant via a courier and study staff virtually connecting with participants for training on the devices, going over responses to questionnaires and study procedures while they are at home.

The goal will be for this visit to run for 14 days with subjects immediately beginning the 8 week DailyDose visit after completion. To allow for scheduling issues, this visit can go over, but must be completed within 20 days. If the run-in visit is longer than 14 days, we will use the later 14 days of data for analysis. If there is not 14 days of CGM data collected during the run-in period due to sensor issues etc, the run-in may be extended to a total of 24 days in order to capture 14 days of data for analysis.

Start of 8 week use of DailyDose (Visit 3):
This visit will take place at the OHSU OCTRI outpatient clinic, the Biomedical Engineering Point of Care (BME POC) Laboratory or Harold Schnitzer Diabetes Health Center clinic. At this

visit, subjects will go through the onboarding process with the DailyDose app. This process will occur with the study investigator and involve:

1. Training on using the Dexcom G6 CGM within the DailyDose app.
2. Entering subject choices for meals, either entering carbohydrate amount or selecting preset meal size.
3. Entering long and short acting insulin types along with dose, frequency and correction and insulin carbohydrate ratios.
4. Setting up alerts for low and high blood glucose alerts.
5. Training on the app including bolus calculator, alerts, accepting/declining recommendations, logging exercise, using the insights tab/settings/logbook. Training will include that the bolus calculator is a suggestion and that participants should use their judgement on what insulin dose to take as the bolus calculator is not aware of certain circumstances such as illness or alcohol use.
6. The study investigator setting safety constraints for changing insulin dosing for both short and long acting insulin.

The study investigator will use the glucose and insulin data from the 14 day run in period to determine the optimal settings for each participant at the start of the 8 week intervention period.

Subjects will continue to use Novolog cartridges for use in the InPen smart pen and their own long-acting insulin (with the exception of those subjects that were given Basaglar, Lantus, or Tresiba as described above).

DailyDose has glucose alerts for safety. The G6 CGM alerts in DailyDose will be set at 70 mg/dL and 250 mg/dL with user able to adjust. There is a very low glucose alert (<55 mg/dL) that cannot be adjusted. Subjects will be able to set an alert time before bed if a night time low glucose is predicted by the system. There is also an alert when glucose is predicted to go low within 30 minutes. Subjects will continue to follow instructions to check ketones as during the run-in period. Subjects will also be given recommendations with regards to adjusting insulin doses and ingestions of carbohydrates if applicable before and after exercise as outlined below.

This visit will take approximately 3-4 hours, depending on subject experience. Subjects will go home and use the DailyDose system for the next 8 weeks.

Study staff will follow-up with subject by phone within the first 4 days of using DailyDose, after 7-11 days of using DailyDose, after 21-25 days, and after 41-45 days. Study staff may contact subjects via text message or phone call at other times at the investigator's discretion. For an additional safety review, a study investigator will review the Dexcom G6 data for each subject every 7-10 days on study. If the CGM < 70 mg/dl more than 10% of the time or < 54 mg/dl more than 4% of the time, the investigator will call the participant and review the subject's insulin dosing and adjust accordingly and confirm the participant is comfortable with changes in insulin doses prior to making the adjustments. There will be a cloud-based portal where the study investigator can input new insulin settings for the user. The user's study phone would have to be connected to the internet to upload the new settings. The period of the day in which the changes to insulin dosing would be implemented potentially would not roll around for another 24 hours,

which would be sufficient time for the phone to connect to the internet. If the physician is inputting changes to settings that would need to be implemented quickly (i.e. for an upcoming meal), study staff will text the patient to ensure that the phone is connected to the internet to receive the new settings. DailyDose shall alert investigators if the user's recommended settings reach the maximum or minimum insulin limits. The investigator will update the minimum and maximum settings if appropriate on the portal on the next business day. Subjects will have the ability to accept or decline recommendations, change their insulin settings and to contact study staff.

DailyDose will present up to 7 recommendations to the user every 7 days. The app will not provide recommendations if less than 4 out of 7 days of CGM data is available. For safety, subjects will be instructed to only use the bolus calculator to calculate meal amounts and not for calculating insulin correction doses for 3 hours if they notice the InPen didn't capture a dose or the dose didn't appear in DailyDose app. Due to the ultra long-acting effects of Tresiba and Toujeo, DailyDose will only make recommendations to change these types of basal insulin every 2 weeks for safety. Participants will be instructed to alert investigators if they receive "Insulin pen not sending data" alert on two subsequent days despite attempts to repair the Inpen device with the smartphone.

When the risk of Covid-19 is considered to be significant and OHSU is on modified operations, there is the option to complete this visit via Webex with study staff virtually connecting with participants for training. A study investigator will enter the minimum and maximum insulin settings for the study into the Physician Portal.

At-home Exercise Sessions:
During the 14 day run-in and 8 week DailyDose visits, subjects will be asked to complete at-home aerobic exercise sessions using a 30 minute exercise video once per week. Subjects will be asked to complete an additional two exercise sessions each week, one aerobic session and the other with an activity of their choice. Subjects will be instructed to check a CBG after exercise (as soon as possible after exercise but no later than 15 minutes after the completion of exercise) to ensure safety.

The DailyDose app will give instructions to the subject before and during exercise based on the published PEAK recommendations [8]. The PEAK guidelines include a set of standardized instructions for diabetes treatment based on the glucose level, insulin on board and type of exercise. Subjects will receive reminders via phone or text to complete their exercise and to monitor adherence to protocol.

Study Completion visit:
Subjects will return to OHSU after the completion of the 8 week DailyDose visit to end the study. This visit will be conducted in the Harold Schnitzer Diabetes Health Center, the Biomedical Engineering Point of Care (BME POC) Laboratory or the OCTRI outpatient research unit. At this visit, the iPhone, Clipsulin device, and Apple watch will be turned in. The study investigator will consult with the subject regarding appropriate insulin dosing for the remainder of the day. Subjects will complete 6 surveys, listed below.

- Confidence in Diabetes Self-Care Scale [3]
- Diabetes Distress Scale [4]
- Hypoglycemia Fear Survey [5]
- Hypoglycemia Confidence Scale [6]
- Insulin Delivery Satisfaction Survey [7]
- the System Usability Scale [9]

This visit will take approximately 60 minutes.

There is the option to complete this visit by Webex. Participants will be given shipping boxes for sending all devices back. Participants will be given a checklist of equipment to return. Participants will connect with study staff virtually to complete the visit and go over responses to questionnaires.

The Dexcom sensor will be removed from the subject. The sensor site will be inspected for signs of irritation or infection. In addition, the sensor will be inspected for the possibility of breakage or fracture. If there is any evidence of sensor breakage, it will be recorded. If an area of inflammation of 1 cm or greater exists around the point of insertion, a de-identified photograph will be taken of the area and the subject will return 1-3 days later for a follow-up visit. A capillary blood glucose value will be taken immediately prior to discharging the subject. Subjects will be given oral carbohydrate for values below 85 mg/dl, and will be instructed to give an injection of aspart insulin if deemed appropriate by the study investigator for values above 200 mg/dl.

If the 8 week DailyDose study period is paused for a period of time, such as due to technical problems, the participant may be asked if they can repeat that part of the study period with additional compensation provided. Problems that would qualify for extending the study time are 1) insufficient study supplies that require the participant to go off of DailyDose for a period of time (such as running out of CGM supplies), 2) issues with the smartphone such that DailyDose cannot be used/accessed (such as a due to a damaged phone), 3) issues with the CGM system or the capture of the CGM data by DailyDose such that DailyDose cannot generate recommendations due to insufficient CGM data, or 4) scheduling issues such that the participant is finished with the run-in period but their DailyDose start visit is delayed. Participants can complete up to 4 additional weeks to make up time the study was paused. The study team will track when participants extend their study time and the reason and this will be included in the annual report to the FDA.

Data Collection

In this study, we will be collecting de-identified physiologic data from people with type 1 diabetes. The following data will be collected from participants in this study:

- Glucose sensor data (Dexcom G6)
- Glucose meter data (Contour Next)
- Ketone meter data (Precision Xtra)
- Short-acting insulin data (InPen)

- Long-acting insulin (Clipsulin)
- Self-report food and exercise data logged by the participant
- Responses to surveys

To collect the data, each participant in the study will be given an Apple iPhone. The iPhone will have the following apps that will be used to collect data.

- The Dexcom G6 app and the DailyDose app will collect data from the Dexcom G6 glucose sensor.
- A Companion InPen commercial app will collect data from the short-acting insulin InPen.
- A Clipsulin commercial app will collect data from the Clipsulin long-acting insulin pen.
- A custom app developed by OHSU called DailyDose will also be installed on the iPhone. The DailyDose app has undergone a security review by OHSU IT and the results of this can be provided upon request.

The DailyDose app will serve as the 'data aggregator' on the phone and will perform the following functions:

- DailyDose app will collect self-report meal and exercise data from the participants.
- DailyDose app will aggregate all of the data collected from the glucose sensor, insulin pens and self-logged food and exercise data to be stored as de-identified data within the iCloud storage area of the phone. The data stored within iCloud is de-identified and does not contain any information from the 18 HIPAA designations of personally identifiable information. ITG has granted an Exception approval for using and storing data on the iCloud. Data stored on the iCloud will be deleted once the study is complete.

We will install the OHSU Intelligent Hub on the iPhones. Upon enrollment, subjects will be assigned with a three-digit code that will be used instead of their name, medical record number or other personally identifying information. The key associating the code and the subjects personal identifying information will be restricted to the PI and study staff. The key will be encrypted and kept secure on a restricted OHSU network drive in a limited access folder as stated below. The iPhones will be registered to the study participants' unique study ID number and all of the data stored on the iPhone will be associated with this ID.

Subject privacy will be protected by using a three-digit identifying number to code paper study documents. Study staff will record data required by the protocol onto the Case Report Forms (CRF) during study visits. The CRFs and all surveys will be collected on paper. All DailyDose and survey data will be coded and uploaded after collection by study staff to an Oregon Clinical and Translation Research Institute (OCTRI) REDCap Cloud server. Investigators and research coordinators will verify that the procedures are conducted according to the approved protocol. All paper source documents will be kept in a locked cabinet for a minimum of five years. The CRFs will include:

1. Screening form
2. 7 Surveys
3. 14 day Run-in Visit

4. 8 week DailyDose Visit
5. Study Completion Visit
6. Physician CGM Review Form
7. Phone/Email Update Form
8. Adverse Event form
9. Serious Adverse Event form
10. Concomitant Medications

The Principal Investigators may authorize other personnel to make entries in the CRF.
The coded data will be stored in the OregonAPC repository according to IRB protocol 19858. The key to the code for this study will not be stored in the repository and only named study members on this project will have access to the key for this study. Researchers who request data from the repository will not receive any identifiers aside from date and we do not anticipate that the date will allow those researchers to re-identify the data. However, some of the researchers named on this project may use the data from the repository which would mean that the repository data will still be potentially identifiable to those who have access to the key as part of this project. During screening, all participants will sign the consent form to store their study data in the data repository.

Cleaning and Disinfecting
All devices will be cleaned and disinfected between subjects. Dexcom G6 transmitters will only be used for a single participant. The Apple iPhone, Clipsulin device and Apple Watch will be cleaned by study staff. Technicians who are disinfecting units will wash hands thoroughly and wear gloves. All items will undergo intermediate-level disinfection using Oxivir Tb Germicidal disposable wipes. The disinfectant will be applied and allowed to air dry. After disinfection, when the units are completely dry, they will be placed in a sealed bag labeled with subject information.

Statistical methods
CGM data from 14 day run-in period will be compared to the last 14 days while using DailyDose. Endpoints will be calculated as a summary measure per subject per time period. These include:

- Percent of time with glucose in the ranges
  - 70-180 mg/dL (primary outcome)
  - <70 mg/dL
  - <54 mg/dL
  - >180 mg/dL
  - >250 mg/dL
- Mean and CV of sensor glucose (secondary outcomes)

We anticipate that the primary outcome (percent of time in range 70-180 mg/dL) will be approximately normally distributed. We will review the appropriateness of this assumption using both goodness-of-fit tests and diagnostic plots, such as quantile-normal plots. If the normality assumption holds, possibly with a transformation of the outcome, we will test the difference between the initial and final 14 days using a paired t-test. In the case of mild departures from

normality or unequal variances at the two time points, we will re-analyze the primary outcome as the difference between the two time periods using bootstrapped standard errors, which avoid distributional assumptions. We will use two-sided tests at the 0.05 level of significance.

Secondary outcomes (with the exception of mean and CV of sensor glucose, for which we will use the same approach as for the primary outcome) are likely to have skewed distributions and will be presented as median (quartiles) and tested with two-sided non-parametricWilcoxon signed-rank tests at the 0.05 level. Because these are secondary outcomes and not independent of each other, we do not plan to adjust p-values for multiple comparisons.

Missing data: Participants contributing at least 72 hours in the baseline and final periods will be included. Missing sensed glucose values will be interpolated for up to 30 min segments. Longer periods of missing data will be omitted if they represent <3% of observation time (which will be truncated if a participant leaves the study early). If the missing data are >3% of observation time, we will use available CBG values to interpolate or impute using measurements from similar time periods on other observation days. In the case that >2 subjects fail to complete the study, we will analyze the primary outcome under multiple imputation using baseline values.

Confidentiality and Protection of Human Subjects

RISKS and BENEFITS

Risks: The risks of the protocol procedures are considered minor. There is a risk of hyperglycemia and hypoglycemia, but users are unlikely to experience severe low or high blood sugar because there are low and high glucose alerts available with the DailyDose app. Exercise may increase the risk of hypoglycemia.

Risks from exercise include falls, sprains, bruises, very low risk of bone fractures and head trauma. The likelihood of significant harm is quite low.

Rarely, there can be allergic responses to insulin such as skin redness, hives, itching of the skin, swelling of the mouth, or breathing difficulties. These reactions are considered very unlikely.

There is a small risk of sensor fracture, and in such a case, a piece of the sensor could be left in the tissue after sensor removal. For this reason, the study investigator will inspect each removed sensor for the possibility of breakage or fracture. Any evidence of sensor breakage will be recorded and reported to FDA and the sensor company.

Benefits: The subject may not directly benefit from being in this study; however, their participation may help to advance automated insulin decision support software.

COSTS

Subjects will receive $700 for completion of all study visits. If subjects withdraw early from the study, compensation will be given as follows: $100 for the 14 day run in period and $75 per week for the 8 week DailyDose period. There is no compensation for the screening visit.

If a participant completes additional time on study to make up for time the study was paused due to technical issues, participants will receive an additional $75 per week. Additional reimbursement will be available for participants who complete protocol requirements to help compensate for their time. The payment amount will be specified in the informed consent form.

Monitoring Procedures

This investigation will be monitored by Jessica Castle, MD. Dr. Castle has no commercial interest in any of the companies which manufacture any of the devices used in this study.

This protocol is written in accordance with the principles established by the 18th World Medical Assembly General Assembly (Helsinki, 1964) and amendments and clarifications adopted by the 29th (Tokyo, 1975), 35th (Venice, 1983), 41st (Hong Kong, 1989), 48th (Somerset West, South Africa, 1996), 52nd (Edinburgh, 2000), 53rd (Washington, 2002), 55th (Tokyo, 2004), 59th (Seoul, 2008), and 64th (Brazil, 2013) General Assemblies. The investigator will ensure that the study described in this protocol is conducted in full conformance with those principles, the protocol, current FDA regulations, ICH Good Clinical Practices (GCP) guidelines, Good Laboratory Practices (GLP) guidelines, local ethical and regulatory requirements, including the Federal Food, Drug and Cosmetic Act, U.S. applicable Code of Federal Regulations (title 21), any IEC requirements relative to clinical studies.

Should a conflict arise, the investigator will follow whichever law or guideline affords the greater protection to the individual subject. The investigator will also ensure thorough familiarity with the appropriate use and potential risks of use of the study device, as described in this protocol, prior to the initiation of the study.

Unanticipated problems, including study, disease or device-related problems, will be detected by reviewing descriptions of known or foreseeable adverse events and risks in the IRB-approved research protocol and the current IRB approved consent form, any underlying disease or conditions of the subject experiencing the adverse event, a careful assessment of whether the adverse event is related or possibly related to the subject's participation in the study or if root cause or associations is with study devices.

Triggers for reporting unanticipated problems are seizure, hospitalization, death or any other occurrence considered serious by the PI. If ongoing monitoring of the studies reveals studies repeatedly being terminated because of unresponsive hyperglycemia or repeated serious hypoglycemia (resulting in altered mental status, loss of consciousness, or seizure), then the study will be discontinued immediately. If studies in two subjects are stopped for severe hypoglycemia or severe hyperglycemia, then the entire study will be halted. Severe hypoglycemia is defined as an event requiring the assistance of another person to administer carbohydrate, glucagon or resuscitative actions. Severe hyperglycemia is defined as capillary blood glucose that exceeds 300 mg/dl with serum ketones 3.0 mM or higher. In addition, if there is any unexpected event such as death or patient hospitalization, the studies will be stopped until the root cause is evaluated.

At all study visits, study staff will determine if any device, disease or study-related adverse events (AEs) have occurred. Any adverse event (AE) and/or unanticipated problem (UP) will be reported to the investigator monitor immediately by one of the investigators. All study, disease or device-related AEs or UPs will be monitored until adequately resolved or stable.

Information regarding all AEs that occur during the study will be entered into appropriate CRFs. Such information will include, at a minimum:

- Date of event

- Severity
- Outcome
- Resolution of event

Unanticipated Adverse Device Effect (UADE)

An unanticipated adverse device effect (UADE) is not expected to occur. An UADE is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by – or associated with – the device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan (including documents such as the protocol, the informed consent document, other study-related documents), or any other unanticipated serious problem associated with the device that relates to the rights, safety, or welfare of participants.

During the review of a reported SAE, if the Investigator determines the severity or extent of the event was not cited in this protocol or associated protocol materials, and the event was classified as, 'possibly related' to the device, the event will be documented as an UADE. If the event is classified as an UADE, the Investigator must notify the IRB and FDA within ten (10) working days of the original SAE notification.

If determined that the UADE presents an unreasonable risk to participants, the investigators will terminate all investigations or parts of investigations presenting that risk as soon as possible, but not later than 5 working days after such determination is made and not later than 15 working days after first notice of the original SAE. A terminated study will not be resumed without IRB and FDA approval.

Medical Device Reporting (MDR) Events

A device issue, whether related to a complaint or not, is an allegation from the participant or study personnel regarding an indication of the failure of a device to meet user expectations for quality or performance specifications. Device issues will be recorded onto appropriate CRFs by site personnel. For purposes of this protocol, the CGM, Inpen, and Clipsulin devices are currently marketed. Therefore, the investigator will follow the required reporting regulations if an MDR reportable event occurs, according to standard operating procedures and FDA guidelines. (US MDR Reporting; Code of Federal Regulations Title 21 Part 803)

MDR reportable events are events that manufacturers become aware of that reasonably suggest one of their marketed devices may have caused or contributed to a death or serious injury, or has malfunctioned and the malfunction of the device would likely cause or contribute to a death or serious injury if the malfunction were to recur (21 CFR 803.3).

Disease related events

Hypo- and hyperglycemia will not be considered AEs unless subject has positive ketones of 1.2 mM or displays symptoms of hypoglycemia such as: loss of consciousness, slurred speech, hospitalization or EMS services called. One of the investigators will write up a description of the adverse event/unanticipated problem. All reportable new information (RNI) will be reported to the IRB within five calendar days after the PI learns of the event. RNI is any information that might meet the regulatory definition of an unanticipated problem involving risks to subjects or others or serious or continuing noncompliance that might impact the criteria for IRB approval.

The report will be submitted to the IRB by the principal investigator or study coordinator. A summary of all UP's and adverse events, including those that do not meet the requirement for RNI, will be submitted with the continuing review. The FDA will be notified of any unanticipated adverse event related to the use of the study device. Notification will be made within 10 days after the Principal Investigator becomes aware of the event. Any SAE, including death, due to any cause (related or unrelated to devices), that may occur during a clinical study will be reported immediately (within 1 working day of learning of the event).

Confidentiality Procedures:

To protect confidentiality, standard institutional practices will be followed as described in the OHSU Information Security and Research Data Resource Guide (http://ozone.ohsu.edu/cc/sec/isg/res_sec.pdf) to maintain the confidentiality and security of data collected in this study. Study staff will be trained regarding these procedures. See IRB protocol 19858 for a complete description of the confidentiality and security of the study data collected during this study to be stored in the OregonAPC repository.

Data for this project will be stored in OCTRI's installation of REDCap, a highly secure and robust web-based research data collection and management system. Features of REDCap that protect participants' privacy and data security include:

- Physical Security: OCTRI's REDCap software is housed on servers located in ITG's Advanced Computing Center providing locked physical security.
- Electronic Security: The REDCap servers are housed behind both the OHSU firewall and a second ACC firewall. All transmissions of data from the application are encrypted over HTTPS with the industry standard TLS 1.1 protocol (AES 256-bit encryption).
- Controlled User Access: REDCap is employs a robust multi-level security system that enables researchers to easily implement "minimum necessary" data access for their research staff, including specification of data fields that are identifiers. This feature includes “single click” ability to provide completely deidentified (removing all identified data fields and shifting dates) for analysis or other purposes. User activities are logged to enable auditing of all data access. Access is integrated with OHSU's network such that users who are also OHSU employees are authenticated against their OHSU network credentials.
- Data Integrity: REDCap is jointly managed in accordance with OHSU Information Security Directives by ACC staff and members of OCTRI's Biomedical Informatics Program, ensuring fidelity of database configuration and back-ups. User activities are logged to enable auditing of all data changes.

Paper files will be stored in locked filing cabinets in restricted access offices at OHSU. After the study, source documents will be maintained at the participating clinical center (or offsite record storage facilities) 2 years after a marketing application is approved for our group's decision support device or discontinuance of pursuit of marketing approval.

Appendix A: Physical Activity Readiness Questionnaire

Physical Activity Readiness Questionnaire (PAR-Q) and You

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly:

YES	NO		
☐	☐	1.	Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?
☐	☐	2.	Do you feel pain in your chest when you do physical activity?
☐	☐	3.	In the past month, have you had chest pain when you were not doing physical activity?
☐	☐	4.	Do you lose your balance because of dizziness or do you ever lose consciousness?
☐	☐	5.	Do you have a bone or joint problem that could be made worse by a change in your physical activity?
☐	☐	6.	Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?
☐	☐	7.	Do you know of any other reason why you should not do physical activity?

If you answered:

YES to one or more questions

Talk to your doctor by phone or in person BEFORE you start becoming much more physically active or BEFORE you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.

- You may be able to do any activity you want – as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

NO to all questions

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:

- Start becoming much more physically active – begin slowly and build up gradually. This is the safest and easiest way to go.
- Take part in a fitness appraisal – this is an excellent way to determine your basic fitness so that you can plan the best way for you to live actively.

Delay becoming much more active:

- If you are not feeling well because of a temporary illness such as a cold or a fever – wait until you feel better; or
- If you are or may be pregnant – talk to your doctor before you start becoming more active.

Please note: If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

Informed use of the PAR-Q: Reprinted from ACSM's Health/Fitness Facility Standards and Guidelines, 1997 by American College of Sports Medicine

Appendix B: Devices

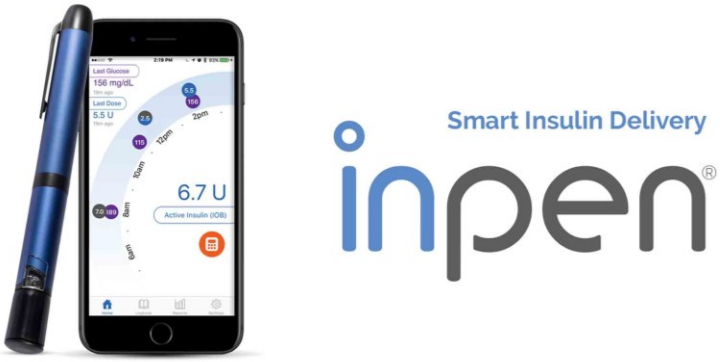
Apple Watch

Dexcom G6 Continuous Glucose Monitoring System which includes Sensor and Sensor Transmitter

iPhone Smart phone

Contour Next Blood Glucose Meter

InPen Smart Insulin Pen



Clipsulin Smart Insulin Pen

Appendix C: Hypoglycemia Awareness questionnaire:This survey item will be used to categorize awareness or having reduced awareness of hypoglycemia.

1. Check the category that best describes you: (check one only)

I always have symptoms when my blood sugar is low (A)
I sometimes have symptoms when my blood sugar is low (R)
I no longer have symptoms when my blood sugar is low (R)

2. Have you lost some of the symptoms that used to occur when your blood sugar was low?

Yes (R)
No (A)

3. In the past 6 months how often have you had moderate hypoglycemia episodes? (Episodes where you might feel confused, disoriented, or lethargic and were unable to treat yourself).

Never (A)
Once or twice (R)
Every other month (R)
Once a month (R)
More than once a month (R)

4. In the past year, how often have you had severe hypoglycemia episodes? (Episodes where you were unconscious or had a seizure and needed glucagon or intravenous glucose?)

Never (A)
1 time (R)
2 times (R)
3 times (R)
4 times (R)
5 times (R)
6 times (R)
7 times (R)
8 times (R)
9 times (R)

10 times (R)
11 times (R)
12 or more times (R)

5. How often in the last month have you had readings < 70 mg/dl with symptoms?

Never
1 to 3 times
1 time/week
2 to 3 times/week
4 to 5 times/week
Almost daily

6. How often in the last month have you had readings < 70 mgdl, without symptoms? R: 5<6, A: 6<5;

Never
1 to 3 times
1 time/week
2 to 3 times/week
4 to 5 times/week
Almost daily

7. How low does your blood sugar need to go before you feel symptoms?

60-69 mg/dl (A)
50-59 mg/dl (A)
40-49 mg/dl (R)
< 40 mg/dl (R)

8. To what extent can you tell by your symptoms that your blood sugar is low?
Never (R)
Rarely (R)
Sometimes (R)
Often (A)

Appendix D: Confidence in Diabetes Self-Care Scale

I believe I can…	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Plan my meals and snacks according to dietary guidelines.	1	2	3	4	5
check my blood glucose at least two times a day.	1	2	3	4	5
Perform the prescribed number of daily insulin injections.	1	2	3	4	5
Adjust my insulin for exercise, traveling, or celebrations.	1	2	3	4	5
Adjust my insulin when I am sick.	1	2	3	4	5
Detect high levels of blood glucose in time to correct.	1	2	3	4	5
Detect low levels of blood gluose in time to correct.	1	2	3	4	5
Treat a high blood glucose correctly.	1	2	3	4	5
Treat a low blood glucose correctly.	1	2	3	4	5
Keep daily records of my blood glucose.	1	2	3	4	5
Decide when it's necessary to contact my doctor or diabetes educator.	1	2	3	4	5
Ask my doctor questions about my treatment plan.	1	2	3	4	5
Keep my blood glucose in the normal range when under stress.	1	2	3	4	5
Check my feet for sores or blisters every day.	1	2	3	4	5
Ask my friends or relatives for help with my diabetes.	1	2	3	4	5
Inform colleagues/others of my diabetes, if needed.	1	2	3	4	5
Keep my medical appointments.	1	2	3	4	5
Exercise two to three times weekly.	1	2	3	4	5
Figure out what foods to eat when dining out.	1	2	3	4	5
Read and hear about diabetes complications without getting discourgaged.	1	2	3	4	5

Appendix E: Diabetes Distress Scale

Directions: Living with diabetes can sometimes be tough. There may be many problems and hassles concerning diabetes and they can vary greatly in severity. Problems may range from minor hassles to major life difficulties. Listed below are 17 potential problem areas that people with diabetes experience. Consider the degree to which each of the 17 items may have distressed or bothered you DURING THE PAST MONTH and circle the appropriate number.

Please note that we are asking you to indicate the degree to which each item may be bothering you in your life, NOT whether the item is merely true for you. If you feel that a particular item is not a bother or a problem for you, you would circle "1". If it is very bothersome to you, you might circle a "6".

I am……	Not a problem	A slight problem	A moderate problem	Somewhat serious problem	A serious problem	A very serious problem
1. Feeling that diabetes is taking up too much of my mental and physical energy every day.	1	2	3	4	5	6
2. Feeling that my doctor doesn't know enough about diabetes and diabetes care.	1	2	3	4	5	6
3. Feeling angry, scared and/or depressed when I think about living with diabetes.	1	2	3	4	5	6
4. Feeling that my doctor doesn't give me clear enough directions on how to manage my diabetes.	1	2	3	4	5	6
5. Feeling that I am not testing my blood sugars frequently enough.	1	2	3	4	5	6
6. Feeling that I am often failing with my diabetes regimen.	1	2	3	4	5	6
7. Feeling that friends or family are not supportive enough of my self care efforts (e.g. planning activities that conflict with my schedule, encouraging me to eat the "wrong foods").	1	2	3	4	5	6

8. Feeling that diabetes controls my life.	1	2	3	4	5	6
9. Feeling that my doctor doesn't take my concerns seriously enough.	1	2	3	4	5	6
10. Not feeling confident in my day-to-day ability to manage diabetes.	1	2	3	4	5	6
11. Feeling that I will end up with serious long-term complications, no matter what I do.	1	2	3	4	5	6
12. Feeling that I am not sticking closely enough to a good meal plan.	1	2	3	4	5	6
13. Feeling that friends or family don't appreciate how difficult living with diabetes can be.	1	2	3	4	5	6
14. Feeling overwhelmed by the demands of living with diabetes.	1	2	3	4	5	6
15. Feeling that I don't have a doctor who I can see regularly about my diabetes.	1	2	3	4	5	6
16. Not feeling motivated to keep up my diabetes self-management.	1	2	3	4	5	6
17. Feeling that friends or family don't give me the emotional support that I would like.	1	2	3	4	5	6

Appendix F: Hypoglycemia Fear Survey

Participants will be instructed to circle one of the numbers to the right that best describes the last 8 weeks.

HFS-II (Adults)
© University of Virginia 1998

I. Behavior: Below is a list of things people with diabetes sometimes do in order to avoid low blood sugar and its consequences. Circle one of the numbers to the right that best describes what you have done during the last 6 months in your daily routine to AVOID low blood sugar and its consequences. (**Please do not skip any!**).

To avoid low blood sugar and how it affects me, I ...	Never	Rarely	Sometimes	Often	Almost Always
1. Ate large snacks.	0	1	2	3	4
2. Tried to keep my blood sugar above 150.	0	1	2	3	4
3. Reduced my insulin when my blood sugar was low.	0	1	2	3	4
4. Measured my blood sugar six or more times a day.	0	1	2	3	4
5. Made sure I had someone with me when I go out.	0	1	2	3	4
6. Limited my out of town travel.	0	1	2	3	4
7. Limited my driving (car, truck or bicycle).	0	1	2	3	4
8. Avoided visiting friends.	0	1	2	3	4
9. Stayed at home more than I liked.	0	1	2	3	4
10. Limited my exercise/physical activity.	0	1	2	3	4
11. Made sure there were other people around.	0	1	2	3	4
12. Avoided sex.	0	1	2	3	4
13. Kept my blood sugar higher than usual in social situations.	0	1	2	3	4
14. Kept my blood sugar higher than usual when doing important tasks.	0	1	2	3	4
15. Had people check on me several times during the day or night.	0	1	2	3	4

II. Worry: Below is a list of concerns people with diabetes sometimes have about low blood sugar. Please read each item carefully (do not skip any). Circle one of the numbers to the right that best describes how often in the last 6 months you WORRIED about each item because of low blood sugar.

Because my blood sugar could go low, I worried about...	Never	Rarely	Sometimes	Often	Almost Always
16. Not recognizing/realizing I was having low blood sugar.	0	1	2	3	4
17. Not having food, fruit, or juice available.	0	1	2	3	4
18. Passing out in public.	0	1	2	3	4
19. Embarrassing myself or my friends in a social situation.	0	1	2	3	4
20. Having a hypoglycemic episode while alone.	0	1	2	3	4
21. Appearing stupid or drunk.	0	1	2	3	4
22. Losing control.	0	1	2	3	4
23. No one being around to help me during a hypoglycemic episode.	0	1	2	3	4
24. Having a hypoglycemic episode while driving.	0	1	2	3	4
25. Making a mistake or having an accident.	0	1	2	3	4
26. Getting a bad evaluation or being criticized.	0	1	2	3	4
27. Difficulty thinking clearly when responsible for others	0	1	2	3	4
28. Feeling lightheaded or dizzy.	0	1	2	3	4
29. Accidently injuring myself or others.	0	1	2	3	4
30. Permanent injury or damage to my health or body.	0	1	2	3	4
31. Low blood sugar interfering with important things I was doing.	0	1	2	3	4
32. Becoming hypoglycemic during sleep.	0	1	2	3	4
33. Getting emotionally upset and difficult to deal with.	0	1	2	3	4

Appendix G: Hypoglycemia Confidence Scale

	Not confident at all	A little confident	Moderately confident	Very confident
How confident are you that you can stay safe from serious problems with hypoglycemia when you are exercising?	1	2	3	4
How confident are you that you can stay safe from serious problems with hypoglycemia when you are sleeping?	1	2	3	4
How confident are you that you can stay safe from serious problems with hypoglycemia when you are driving?	1	2	3	4
How confident are you that you can stay safe from serious problems with hypoglycemia when you are in social situations?	1	2	3	4
How confident are you that you can stay safe from serious problems with hypoglycemia when you are alone?	1	2	3	4
In general, how confident are you that you can: avoid serious problems due to hypoglycemia?	1	2	3	4
In general, how confident are you that you can: catch and respond to hypoglycemia before your blood sugars get too low?	1	2	3	4
In general, how confident are you that you can: continue to do the things you really want to do in your life, despite the risks of hypoglycemia?	1	2	3	4
What is your best guess about how confident your spouse or partner feels about your ability to avoid serious problems due to hypoglycemia?	1	2	3	4

Appendix H: Insulin Delivery Satisfaction Survey

My insulin delivery system…	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Helps me to feel more in control of my diabetes.	1	2	3	4	5
Works well when I need it.	1	2	3	4	5
Doesn't really benefit me much.	1	2	3	4	5
Helps me feel more positive about the future.	1	2	3	4	5
Helps me keep my blood glucose levels stable.	1	2	3	4	5
Helps me to have good blood glucose control.	1	2	3	4	5
Is too complicated.	1	2	3	4	5
Is too much of a hassle to use.	1	2	3	4	5
Has too many pieces and parts to manage.	1	2	3	4	5
Takes too much time to use.	1	2	3	4	5
Is too expensive.	1	2	3	4	5
Is often embarrassing to use when I am in public.	1	2	3	4	5
Makes it difficult to be as spontaneous as I'd like to be.	1	2	3	4	5
Is inconvenient to use when I am away from home.	1	2	3	4	5
Is a hassle to carry around.	1	2	3	4	5
Helps me to avoid missing or forgetting doses.	1	2	3	4	5
Helps me to be more spontaneous in my life.	1	2	3	4	5
Helps me feel less restricted by diabetes.	1	2	3	4	5

Appendix I: System Usability Scale

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
I think I would like to use this product frequently.	1	2	3	4	5
I found the product unnecessarily complex.	1	2	3	4	5
I thought the product was easy to use.	1	2	3	4	5
I think I would need the support of a technical person to be able to use this product.	1	2	3	4	5
I found the various functions in the product were well integrated.	1	2	3	4	5
I thought there was too much inconsistency in this product.	1	2	3	4	5
I imagine that most people would learn to use this product very quickly.	1	2	3	4	5
I found the product very awkward to use.	1	2	3	4	5
I felt very confident using the product.	1	2	3	4	5
I needed to learn a lot of things before I could get going with this product.	1	2	3	4	5

Appendix J: Global Physical Activity Questionnaire

Physical Activity

Next I am going to ask you about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be a physically active person.
Think first about the time you spend doing work. Think of work as the things that you have to do such as paid or unpaid work, study/training, household chores, harvesting food/crops, fishing or hunting for food, seeking employment. *[Insert other examples if needed]*. In answering the following questions 'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate, 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate.

Question	Response	Code
Work		
Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like *[carrying or lifting heavy loads, digging or construction work]* for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P 4*	P1
In a typical week, on how many days do you do vigorous-intensity activities as part of your work?	Number of days __	P2
How much time do you spend doing vigorous-intensity activities at work on a typical day?	Hours : minutes ___ : __ hrs mins	P3 (a-b)
Does your work involve moderate-intensity activity, that causes small increases in breathing or heart rate such as brisk walking *[or carrying light loads]* for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P 7*	P4
In a typical week, on how many days do you do moderate-intensity activities as part of your work?	Number of days __	P5
How much time do you spend doing moderate-intensity activities at work on a typical day?	Hours : minutes ___ : __ hrs mins	P6 (a-b)
Travel to and from places		
The next questions exclude the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example to work, for shopping, to market, to place of worship. *[Insert other examples if needed]*		
Do you walk or use a bicycle (pedal cycle) for at least 10 minutes continuously to get to and from places?	Yes 1 No 2 *If No, go to P 10*	P7
In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?	Number of days __	P8
How much time do you spend walking or bicycling for travel on a typical day?	Hours : minutes ___ : __ hrs mins	P9 (a-b)

Physical Activity, Continued		
Question	**Response**	**Code**
Recreational activities		
The next questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness and recreational activities (leisure), *[Insert relevant terms]*.		
Do you do any vigorous-intensity sports, fitness or recreational *(leisure)* activities that cause large increases in breathing or heart rate like *[running or football]* for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P 13*	P10
In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational *(leisure)* activities?	Number of days ⌊__⌋	P11
How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P12 (a-b)
Do you do any moderate-intensity sports, fitness or recreational *(leisure)* activities that cause a small increase in breathing or heart rate such as brisk walking, *[cycling, swimming, volleyball]* for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P16*	P13
In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational *(leisure)* activities?	Number of days ⌊__⌋	P14
How much time do you spend doing moderate-intensity sports, fitness or recreational *(leisure)* activities on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P15 (a-b)
Sedentary behaviour		
The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent sitting at a desk, sitting with friends, traveling in car, bus, train, reading, playing cards or watching television, but do not include time spent sleeping. *[INSERT EXAMPLES] (USE SHOWCARD)*		
How much time do you usually spend sitting or reclining on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P16 (a-b)

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