PROTOCOL TITLE: Development of a context-aware glucose prediction algorithm in patients with type 1 diabetes

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PI: Jessica Castle MD

CO1450 **PROTOCOL TITLE: Development of a context-aware glucose prediction algorithm in patients with type 1 diabetes**

STUDY SITE: Oregon Health Science University
3181 SW Sam Jackson Park Rd
Portland, OR 97639

FUNDING:	NIH
PRINCIPAL INVESTIGATORS:	Jessica R. Castle MD; Peter Jacobs PhD
CO-INVESTIGATORS:	Joseph El Youssef MBBS Leah Wilson MD

Background:
T1D is characterized by the autoimmune destruction of β cells. These patients rely on the administration of insulin, putting them at significant risk of hypoglycemia and excessive hyperglycemia. Repeated exposures to hypoglycemia can result in hypoglycemia unawareness [1, 2]. These patients have a 20x increased likelihood of experiencing severe hypoglycemia compared with those patients without it [3]. Better approaches to helping people avoid hypoglycemia are critical to improve glycemic control and reduce complications. Continuous glucose monitoring (CGM) has been shown to help T1D patients improve time in range and avoid hypoglycemia [4, 5]. Automated Insulin Delivery (AID) systems have now become an important standard-of-care for people with T1D and have demonstrated a reduction, but not elimination, of hypoglycemia during long-term studies [6-10]. AID systems have not been shown to be effective at eliminating exercise-induced hypoglycemia, even when incorporating additional physical activity sensors such as heart rate and accelerometry sensors [11-16].

One limitation of current AID systems is that they have no knowledge about the context or environment that a person is currently experiencing. Contextual patterns can potentially improve the performance of an AID by recognizing environments or patterns of living that are related to changes in glucose. The team at OHSU is developing a context-aware glucose prediction algorithm that will capture context data from the patient both indoors and outdoors. This context data will be provided to the algorithm to allow for detecting contextual patterns that might relate to hypo- or hyperglycemia. The goal of this study will be the creation of a data set that will include contextual patterns along with glucose, insulin and physiological data. Participants will complete meals and exercise at specific times. The purpose of the prescribed meals and exercise sessions is to generate ground truth patterns that will be used in the design of the context-aware glucose prediction algorithm.

Primary Objective

- To assess the accuracy of the context-aware glucose prediction by comparing glucose prediction values against the Dexcom G6 CGM values using mean absolute relative error (MARE)
- To assess the accuracy of the context-aware glucose prediction by comparing glucose prediction values against the Dexcom G6 CGM values using mean relative error (MRE).

Study Hypothesis:

- The study hypothesis is that context pattern data will improve the accuracy of the prediction of hypoglycemia and hyperglycemia in the context-aware glucose prediction algorithm.

Primary Endpoints:

- Comparison of the accuracy of hypoglycemia prediction comparing glucose prediction values against the Dexcom G6 CGM values using mean absolute relative error (MARE).
- Comparison of the accuracy of hypoglycemia prediction comparing glucose prediction values against the Dexcom G6 CGM values using mean relative error (MRE).

Study Type

This is a single center randomized prospective study measuring the accuracy of the context-aware glucose prediction against the Dexcom G6 CGM values.

Study Population

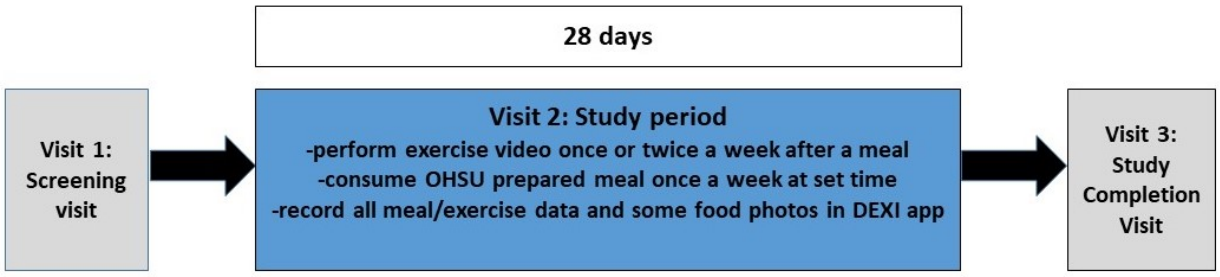
Study population will be adults with type 1 diabetes, ages 18 – 65 years of age. Older subjects are excluded due to higher risk of unrecognized coronary artery disease. Younger subjects are excluded as it is appropriate to assess safety and efficacy first in the adult population. Thirty subjects will be recruited to participate in studies.

Protocol Summary:

Subjects will be on study for 28 days. Sensor glucose, activity, exercise, insulin, indoor and outdoor contextual patterns and meal data will be collected during this time. Subjects will wear the Dexcom G6 CGM system and a FitBit Ionic (or similar FitBit), Polar, Garmin or Apple Watch physical activity monitor for the entire 28 days. Physical activity monitors will send data to the iPancreas mobile app created by OHSU. iPancreas will be supplied to participants on a separate study-provided phone. Subjects will continue to use their own insulin pump. Subjects will be asked to also wear a MotioWear indoor/outdoor context-aware tracking tag and to install the MotioWear beacons within their home. Subjects will be randomized to complete either aerobic, high intensity interval training, or resistance exercise videos twice weekly at home during weeks 1 and 2 and once weekly during weeks 3 and 4. Subjects will also ingest a self-selected meal prior to these prescribed exercise sessions. Subjects will consume a high carbohydrate dinner once each week on the same day, at approximately the same time (but not on the exercise days).

Subjects will use the T1 DEXI mobile app created by OHSU to capture meal and exercise data along with photos of meals over the 28 day period. Subjects will take photos of their food the day of and the day after they complete the exercise video. While at home, subjects will check CBG before and after exercise, for symptoms of hypoglycemia, and for Dexcom G6 alarms for sensor <70 mg/dL and >250 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



Background on MotioWear System

Our group at OHSU has developed a unique context measurement system in collaboration with MotioSens (Portland OR) called MotioWear. MotioWear (Figure 2) is comprised of a wearable tag, beacons that are plugged in around a home, and a data hub that captures the movement

and context data and transmits it back to a remote monitoring server. The wearable tag includes several sensors important for movement and context awareness: (1) a time of flight (TOF) radio transceiver that ranges with the beacon positioned around the home to track location and inferred activity of daily living, (2) a 9-axis inertial measurement including accelerometer, magnetometer, and gyroscope, (3) a Bluetooth low energy (BTLE) wireless transceiver for device interconnectivity, and (4) a global positioning system (GPS) sensor for outdoor tracking. We have developed sophisticated tracking and inference algorithms for indoor / outdoor tracking of a person wearing the tag and inferring context based on movement patterns [17-21].

Indoor context using MotioWear: MotioWear learns the specific regions of interest within a home through a simple calibration routine that takes about 15-20 minutes. During this home calibration routine, the person carries the MotioWear tag in their pocket while using the MotioWear smart-phone app to identify regions of interest (e.g. bathroom, shower, toilet, kitchen, bed, refrigerator etc). The system matches the x,y,z locations detected by the MotioWear tag during the calibration routine with the ROIs indicated on the MotioWear smart-phone app. After the calibration routine is completed, the system can infer the person's location within these regions of interest within the home and infer activities.

Outdoor context using MotioWear: MotioWear uses GPS to get outdoor context. Latitude and longitude collected by the MotioWear tag are overlaid on Google Maps (Figure 2); geographic information systems techniques are used to relate location to regions of interest including restaurants, parks, gyms, hospitals, etc.

While MotioWear is a sophisticated tool that we plan to use within this study to quantify context, a context-aware AID could potentially use contextual information gathered from a variety of other ubiquitous wearable and beacon-based technologies that are now becoming commercially available, including such in-home monitoring technologies developed by Google (Echo), Apple (iBeacon) and Amazon (Alexa). The purpose of our work with MotioWear is to demonstrate the benefit of context such that in the future, AID systems can make use of context regardless of how this context information is gathered; it is our intentent that CA-AID systems will be hardware agnostic, and not dependent on one platform such as MotioWear.

Subject Criteria

Inclusion Criteria:

1. Diagnosis of type 1 diabetes mellitus for at least 1 year.
2. Male or female subjects 18 to 65 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. Current use of an insulin pump for at least 3 months.
5. Able and willing to count

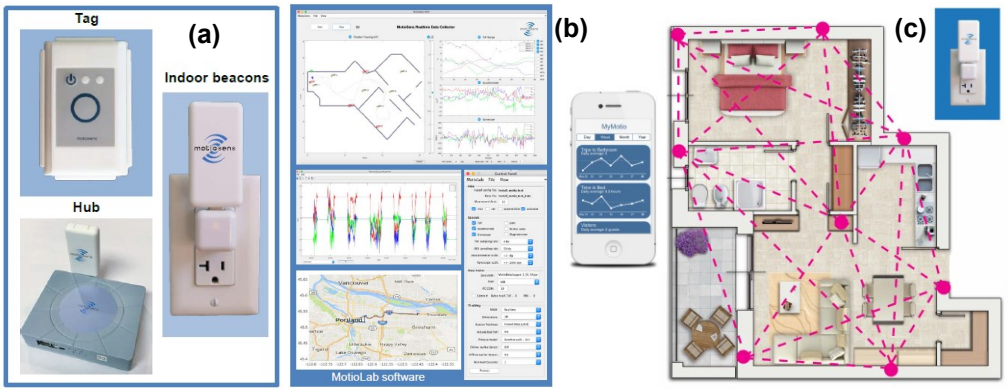


Figure 2: (a) MotioWear tag based indoor/outdoor tracking and context awareness system. (b) MotioLab software that can be used to do real-time tracking indoors and outdoors. (c) Beacons are placed around the home, creating a wireless mesh that the wearable communicates with. A smart-phone app identifies key regions of interest.

carbohydrates during study period as determined by the investigator after reviewing participant's insulin pump download.

6. A1C <10.5% at the time of screening.
7. Has a smart phone.
8. Willingness to follow all study procedures, including attending all clinic visits.
9. 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 2^{nd} or 3^{rd} 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. Hematocrit of less than 36% for men, less than 32% for women.
6. History of severe hypoglycemia during the past 12 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.
7. Adrenal insufficiency.
8. Any active infection.
9. Known or suspected abuse of alcohol, narcotics, or illicit drugs.
10. Seizure disorder.
11. Active foot ulceration.
12. Peripheral arterial disease.
13. Major surgical operation within 30 days prior to screening.
14. Use of an investigational drug within 30 days prior to screening.
15. Chronic usage of any immunosuppressive medication (such as cyclosporine, azathioprine, sirolimus, or tacrolimus).
16. Bleeding disorder or platelet count below 50,000.
17. Current administration of oral or parenteral corticosteroids.
18. 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).
19. Beta blockers or non-dihydropyridine calcium channel blockers.

20. Current use of any medication intended to lower glucose other than insulin (ex. use of liraglutide).
21. A positive response to any of the questions from the Physical Activity Readiness Questionnaire 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).
22. Any chest discomfort with physical activity, including pain or pressure, or other types of discomfort.
23. 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. Handouts may also be made available to faculty at Providence, Tuality, Kaiser and Legacy to pass along to patients/participants who show interest in the study. Records from OHSU Schnitzer Diabetes Clinic patients 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 involving Drs. Castle or El Youssef, 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 75 subjects may be screened in this study. Goal enrollment is 30 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)
Screening will take place within 12 weeks prior to Visit 2. All screening visits 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. 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. If subjects have had any of the aforementioned labs performed within the 3 months prior to the screening visit and we can access the results, a venous blood sample will not be taken for that test. An EKG will be completed. A study investigator will assess inclusion/exclusion criteria and review the subject's medical record for clarification as needed. The participant's insulin pump will be downloaded to determine if they are counting carbohydrates for meals. A three-digit subject ID number will be assigned to the subject. One research staff member and a study investigator will on site for this visit.
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.

This visit will take approximately 1.5 hours.

Study Start-up Visit (Visit 2):
Subjects will be on study for 28 days. Sensor glucose, activity, exercise, insulin, indoor and ouotdoor contextual patterns and meal data will be collected during this time. Subjects will wear the Dexcom G6 CGM system along with the Dexcom G6 smart phone application. Subjects will wear a FitBit Ionic (or similar FitBit), Polar, Garmin or Apple Watch physical activity monitor. Subjects will continue to use their own insulin pump. Subjects will be given a MotioWear indoor/outdoor context-aware tracking tag to wear and be shown how to install the MotioWear beacons within their home. Subjects may be asked to plug the MotioWear beacon into their router to improve data uploads. In this visit, they will be asked to complete a lifestyle questionnaire asking about their current exercise habits and blood glucose management. Subjects will be instructed on the use of the T1 DEXI mobile app created by OHSU to capture meal and exercise data along with photos of meals. Subjects will be instructed to take photos of their food the day of and the day after they complete the exercise video. Study staff may contact subjects by phone, text, or email for clarification if the meal photo is difficult to interpret. While at home, subjects will check CBG before and after exercise, for symptoms of hypoglycemia, and

for Dexcom G6 alarms for sensor <70 mg/dL and >250 mg/dL. Subjects will be provided with a Contour Next blood glucose meter for testing capillary blood glucose.

Subjects will be randomized to complete either aerobic, high intensity interval training, or resistance exercise videos twice weekly at home during weeks 1 and 2 and once weekly during weeks 3 and 4. Subjects will be instructed to complete the exercise for the video sessions in the same location in their home on the same day at approximately the same time. The exercise videos are approximately 30 minutes long. A list of exercises to be performed is provided in Appendix E. Subjects will also ingest a self-selected meal prior to these prescribed exercise sessions. Instructions for the exercise will be provided via video links. Subjects will be instructed to check a CBG before initiating exercise to ensure safety. Subjects will be instructed to consume a snack if glucose is <120 mg/dL and delay exercise until glucose is >80 mg/dL. Also, if glucose is >250 mg/dL, subjects will be instructed to calculate if a correction dose is needed and delay exercise until glucose is <250 mg/dL. Subjects will enter information about exercise into the T1 DEXI app. Subjects will receive reminders via phone or text to complete their exercise and to monitor adherence to protocol. Participants may also receive reminders to enter activity information through the T1DEXI app. Subjects will also be instructed to check a CBG after exercise and consume a snack if needed.

Subjects will consume a high carbohydrate dinner prepared by OHSU Bionutrition once each week on the same day at approximately the same time (but not on the exercise study video days). The meals can potentially be picked up all at once and frozen until use.

Subjects will be able to contact study staff for any issues with the devices. Study staff will follow-up with subjects every 7 days. Subjects may receive text messages from study staff with study reminders/instructions or clarification of meal photos. This visit should take approximately 1.5 hours, depending on subject experience. Participants will be asked to download his/her pump weekly or biweekly during the 28 days on study. This will allow for frequent data capture in case of a battery change or loss of power to the pump which can erase insulin data.

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/meals delivered to the participant via a courier and study staff virtually connecting with participants for training on the devices and study procedures while they are at home.

The study staff and participants will be screened for COVID-19 symptoms within the prior 14 days and day of the Start-up visit per “OHSU COVID-19 Clinical Research Risk Assessment Screening and Mitigation” protocol as follows:

- Fever or chills
- Cough
- Shortness of breath or difficulty breathing
- Fatigue
- Muscle or body aches
- Headache
- New loss of taste or smell
- Sore throat

- Congestion or runny nose
- Diarrhea

The study staff member(s) will go into the participant's home for installation of the tracking devices, maintaining appropriate social distancing. No more than two staff members will be assigned to installation. Due to the lengthy installation process, two staff members performing set up will help minimize time spent in the participant's home (with 2 staff - approximately 2 hours). The staff in the home will wear masks, eye shields and gloves during the installation. All participants and family members present during the installation will wear masks.

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:

- Responses from the "Lifestyle Questionnaire"
- Glucose sensor data (Dexcom G6)
- Insulin data from the subject's insulin pump.
- Physical activity data will be collected with the OHSU iPancreas app on a study provided phone and recorded through a FitBit Ionic, Polar, Garmin or Apple Watch. iPancreas will send physical activity data to the iPancreas server. This fitness data will include the following:
    - Heart rate
    - Step count
    - Metabolic expenditure
    - Sleep
    - Activity types (e.g. running, jogging, etc).
- Self-report food and exercise data logged by the participant

To collect the data, each participant in the study will use their own phone and a study provided phone to collect data.

- A Dexcom commercial app will collect data from the Dexcom G6 glucose sensor on the subject's phone or on a provided study phone.
- The activity watch commercial app will collect sleep data from the watch on the provided study phone.
- A custom app developed by OHSU called T1-Dexi will also be installed on the subject's phone or on a provided study phone. The T1-Dexi app has undergone a security review by OHSU IT and the results of this can be provided upon request.
- A custom app developed by OHSU called iPancreas will be installed on a provided study phone. The iPancreas app has undergone a security review by OHSU IT and the results of this can be provided upon request.

The T1-Dexi app will serve as the 'data aggregator' on the phone and will perform the following functions:

- T1-Dexi app will collect self-report meals and exercise data from the participants both as text / categorical selections and also as food photographs collected from the camera on the phone.
- Data is collected by the T1-Dexi app and this non-medical, deidentified data is pushed to the OHSU-version of the Amazon Web Services (AWS) Cloud instance. The following data is pushed to the Dexi AWS server:

    a. Photographs of the user's food as taken on their smart phone camera
    b. Food types and amounts as acquired by the T1-Dexi app
    c. Exercise types and amounts as acquired by the T1-Dexi app
    d. Insulin pen data acquired through Apple Health Kit
- Physical Activity Data is collected by the iPancreas app and this non-medical, deidentified data is pushed to the OHSU-version of the Amazon Web Services (AWS) Cloud instance. The following data is pushed to the iPancreas AWS server:
    a. Heart rate
    b. Accelerometry
    c. METs
- The data stored within AWS is de-identified and does not contain any information from the 18 HIPAA designations of personally identifiable information.

Day 28 Study Completion visit:
At this visit, the devices will be turned in and the subject's insulin pump will be downloaded. A study investigator will be available for consult if needed regarding insulin management. 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. If the study coordinator notes any significant redness or swelling, the study investigator will be contacted. 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 150 mg/dl. This visit will take approximately 1 hour.

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 with instructions on how to uninstall the tracking devices. Participants will connect with a study coordinator virtually to complete the visit.

If a study visit is stopped prematurely the subject will be asked if they can repeat the study visit that was terminated early with additional compensation provided. Repeating the study visit will be optional. If the study period is paused for a period of time, such as if the patient begins taking a medication that impacts glucose like steroids, the participant may be asked if they can repeat that part of the study period with additional compensation provided.

Cleaning and Disinfecting
All devices will be cleaned and disinfected between subjects. The Dexcom G6 transmitters, MotioWear devices and physical activity monitor 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 SANI-CLOTH AF3 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
The hypothesis of this study is that we will be able to identify contextual patterns in the movement data that will relate to glycemic outcomes. We will use machine learning techniques

including k-means clustering and Gaussian mixture models to group contextual patterns and then relate these groups of patterns with glycemic outcomes including the following:

- Time in hypoglyemia (<70 mg/dL)
- Time in hyperglycemia (>180 mg/dL)
- Time in a target range (70-180 mg/dL)
- Mean glucose
- Glucose variability (standard deviation and coefficient of variance).

We will evaluate if the clusters of contextual patterns are related to differences in glycemic outcome measures using generalized estimating equations, which takes into account correlated data and repeated measures. Data will be analyzed using an intention-to-treat analysis and missing sensed glucose values will be interpolated for up to 20 min segments.

Confidentiality and Protection of Human Subjects
RISKS and BENEFITS
Risks: The risks of the protocol procedures are considered minor. Subjects will be managing their own blood glucose as they normally would.
Risks from exercise include falls, sprains, bruises, very low risk of bone fractures and head trauma. The likelihood of significant harm is quite low.
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 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 $500 for completion of all study visits. If subjects withdraw early from the study, compensation will be given as follows: $125 per 7 study days in the study. If the subject completes a partial week, the subject will also receive $125 for the partial week. There is no compensation for the screening visit. 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 Entity:
This investigation will be monitored by the principal investigators, Jessica Castle, MD and Peter Jacobs, PhD. Drs. Jacobs and Castle have no commercial interest in any of the companies which manufacture any of the devices used in this study.

Data Collection:
Subject privacy will be protected by using a three-digit identifying number to code study documents. Study staff will record data required by the protocol onto the Case Report Forms (CRF). Case report forms (CRF) for this study will be entered into REDCAP, a clinical research electronic data application designed to support traditional case report form data capture for research studies housed at Oregon Health Science University and administered by the Oregon Clinical and Translation Research Institute (OCTRI). Investigators and research coordinator 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. Original, completed

CRF's will be kept with the PI in a designated repository. All data from CRF's will subsequently be entered into the authorized electronic REDCAP database.

Recording of Data:
Investigators and staff will record data collected during the clinical trial on the CRF's. Case report forms (CRF) for this study will be entered into REDCAP, a clinical research electronic data repository housed at Oregon Health Science University and administered by the Oregon Clinical and Translation Research Institute (OCTRI). The REDCAP CRFs will include:

1. Screening form
2. Startup visit
3. Study Completion visit
4. Adverse Event form
5. Serious Adverse Event form
6. Concomitant Medications
7. Lifestyle questionnaires

The Principal Investigators may authorize other personnel to make entries in the CRF.

The de-identified data collected during this study will be used for analysis of the primary and secondary endpoints listed in this protocol. This data will also be stored in the OregonAPC repository according to IRB protocol 19858. During screening, participants may sign the consent form to store their study data in the data repository. The data to be collected includes: 1) glucose sensor data, 2) blood glucose data, 3) insulin data, 4) physical activity data, and 5) food and exercise data. All data, except for blood glucose and insulin, is aggregated by the DEXI app. The blood glucose data is collected through downloading the Contour Next BG meters and exporting data as an excel file. The insulin data is collected by downloading the subject's insulin pump. There are no biological specimens collected during this study.

Monitoring Procedures:
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 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.

Triggers for reporting unanticipated problems are seizure, hospitalization, death or any other occurrence considered serious by the PI. If ongoing monitoring of the closed-loop studies reveals studies repeatedly being terminated because of unresponsive hyperglycemia or repeated serious hypoglycemia (resulting in altered mental status, loss of consciousness, or seizure) believed not amenable to revisions in control system parameter tuning, 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. 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.

Any adverse event (AE) and/or unanticipated problem (UP) will be reported to the investigator monitor immediately by one of the investigators. Hypo- and hyperglycemia will not be considered AEs unless subject has positive ketones or displays symptoms of hypoglycemia such as: loss of consciousness, slurred speech, hospitalization or EMS services called. One of the investigators will always be on-call during the closed-loop studies and 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.

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. 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.

Appendix B: Devices

FitBit

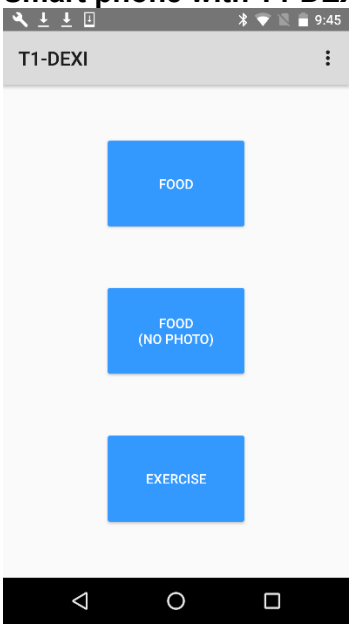
Garmin Watch

Polar Watch

Apple Watch

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

Smart phone with T1 DEXI app



Contour Next Blood Glucose Meter

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: Exercise Video Outlines

Aerobic Exercise Video Outline		
Segment	**Segment Time**	**Activities**
Warm-Up Intro (2 min)	**0:00 – 2:00**	**0:00: Welcome! Marching Reach Up** **0:30: Side to Side Kick Back Pull Back** **0:45: Side to Side Kick Back Butt Kick** **1:00: Side to Side Kick Back Butt Kick Reach out** **1:15: Grapevine** **1:30: Grapevine with Arm Circles**
Active Exercise **(30 min)**	**Each activity is performed for 30 seconds**	**1. Modified Jump rope** **2. Jumping jacks** **3. Side to Side Knee Raise (alternate left/right crunch)** **4. Side Steps (active recovery)** **5. Modified Jump rope** **6. Jumping Jacks** **7. Side to Side Knee Raise (alternate left/right crunch)** **8. Side Steps (active recovery)** **9. Arms Alternating A, T and Y with Heal Tap** **10. Left Jab Bounce (left foot forward)** **11. Side Steps (active recovery)** **12. Arms Alternating A, T and Y with Heal Tap** **13. Right Jab Bounce (right foot forward)** **14. Side Steps (active recovery)** **15. Right Leg Lunge Alternate Forward Back** **16. Left Leg Lunge Alternate Forward Back** **17. Jog in Place Hands Raised** **18. Side Steps (active recovery)** **19. Right Leg Lunge Alternate Forward Back** **20. Left Leg Lunge Alternate Forward Back** **21. Jog in Place Hands Raised** **22. Side Steps (active recovery)** **23. Squat to Upper Cut (right foot forward)** **24. Right Jab Bounce (right foot forward)** **25. Side Steps (active recovery)** **26. Squat to Upper Cut (left foot forward)**

		27. Left Jab Bounce (left foot forward) **28. Side Steps (active recovery)** **29. Horse Stance Overhead Reach Side Bend/ Standing Alternating Side Bend** **30. Side Jump with Squat Alternating Left Right** **31. Right Lateral lunge with Right Knee Drive Pull Up** **32. Left Lateral Lunge with Left Knee Drive Pull Up** **33. Side steps (active recovery)** **34. Horse Stance Overhead Reach Side Bend/ Standing Alternating Side Bend** **35. Side Jump with Squat Alternating Left Right** **36. Right Lateral lunge with Right Knee Drive Pull Up** **37. Left Lateral Lunge with Left Knee Drive Pull Up** **38. Side steps (active recovery)**

Intermittent High-Intensity Interval Exercise Video Outline		
Segment	**Segment Time**	**Activities**
Warm-Up Intro (2 min)	**0:00 – 2:00**	**0:00: Welcome!** **0:15: Jog with Front Japs** **0:30: Hip Circles Feet Apart** **0:45: Side to Side Reach Out** **1:00: Alternating Direction Arm Circles Feet Apart** **1:15: Side steps (active recovery)** **1:45: Intro for exercise**
Active Exercise (30 min)	**Each activity is performed for 40 seconds, followed by a 70 second cool down**	1. **High Knee Sprint with Heel Tap – 40 seconds high intensity** 2. **Side steps (active recovery)-10 seconds** 3. **Side Steps with Arm Pull Back-1 minute** 4. **Alternating Knee Lunges (knee touching ground) then Jump Up Arms Raised then Squat-high intensity-40 seconds** 5. **Side steps (active recovery)-10 seconds** 6. **Side Steps with Arm Pull Back-1 minute**

		7. **High Plank Alternating Knee Reach – 40 seconds high intensity** 8. **Side steps (active recovery)-10 seconds** 9. **Side Steps with Arm Pull Back-1 minute** 10. **Advanced Plank (Bear Crawl) Alternating Forward Backward– 40 seconds high intensity** 11. **Side steps (active recovery)-10 seconds** 12. **Side Steps with Arm Pull Back-1 minute** 13. **Diagonal Plank Alternating Reach Out Opposite Arm Leg Back to Middle-40 seconds high intensity** 14. **Side steps (active recovery)-10 seconds** 15. **Side Steps with Arm Pull Back-1 minute** 16. **Skate-Hop Alternating Sides with Arm Lunge Forward Opposite Knee Kick Back-40 seconds high intensity** 17. **Side steps (active recovery)-10 seconds** 18. **Side Steps with Arm Pull Back-1 minute** 19. **Single Leg Crouch Down then Same Knee Forward-5 Left then 5 Right-Repeat-40 sec high intensity** 20. **Side steps (active recovery)-10 seconds** 21. **Side Steps with Arm Pull Back-1 minute** 22. **Burpee (Bent Waist Rapid Jog Arm Punches Down then Plank then Jump Up)– 40 seconds high intensity** 23. **Side steps (active recovery)-10 seconds** 24. **Side Steps with Arm Pull Back-1 minute** 25. **Lay on Back-Feet Up Knees Locked-Reach Forward to Toes-40 seconds high intensity** 26. **Side steps (active recovery)-10 seconds** 27. **Side Steps with Arm Pull Back-1 minute** 28. **Upper Body Swimmer (High Plank Alterating Arm Circle Forward)-40 seconds high intensity**

Resistance Exercise Video Outline		
Segment	**Segment Time**	**Activities**
Warm-Up Intro (2 min 20 sec)	**0:00 – 2:20**	**0:00: Alternating Heel Kick Forward Arm Swing**

		0:15: Arms on Hips Alternating Straight Leg Extend with Bend at Waist **0:30: Arms on Hips Alternating Straight Leg Extend with Bend at Waist Add Arm Sweep** **0:45: Alternating Leg Lunge Knee 90 Degrees Arm Sweep Up** **1:10: Crunch (Arms Behind Head Alternating Knee Touch to Elbow)** **1:30: Scarecrow (Knees Slightly Bent Torso Forward Arms Down then Up)** **2:00: Alternating Side Lunge Arms Up/Down** **2:20: Toe Touches with Spread Arms/Legs**
Active Exercise (28 min)	**Each activity is performed at a controlled pace in good form. Aiming for about 2 seconds to pull the weight the entire range, holding for 1 second, then controlling the return of the movement in about another 1 seconds.**	**Set 1: (approximately 8 min) Upper Body** **Resistance band bicep curl 3 x 8** **Resistance band side lateral shoulder raise 3 x 8** **Resistance band bent over row 3 x 8** **Resistance band bent over row arm forward then back 3 x 8** **Set 2: (approximately 10 min) Lower Body** **Resistance band squat 3 x 8** **Resistance band deadlift 3 x 8** **Resistance band reverse lunge 3 x 8** **Resistance band glut crunch with hip raise 3 x 8** **Set 3: (approximately 10 min) Total Body and Abs** **Resistance band side lunge to diagonal lateral raise 3 x 8/side** **Resistance band (standing) squat with arm raise 3 x 8/side** **Resistance band (on back) alternating opposite arm and leg extend straight 3 x 8** **Resistance band (on back) alternating opposite arm and leg extend bent 3 x 8** **Resistance band (standing) alternating right/left crunch 3 x 8**

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CLINICAL RESEARCH CONSENT AND AUTHORIZATION
SUMMARY OF KEY INFORMATION ABOUT THIS STUDY

TITLE: **Development of a context-aware glucose prediction algorithm in patients with type 1 diabetes**

PRINCIPAL INVESTIGATOR: Jessica Castle MD *(503) 494-7072*

You are being asked to join a research study. This consent form contains important information to help you decide if you want to join the study or not.

PURPOSE:
The purpose of the study is for the creation of a dataset that will be used for the development of a glucose prediction system for the management of diabetes. This dataset will include glucose sensor values, fingerstick glucose values, insulin data, food and rescue carbohydrate consumption, as well as information on the type, intensity and duration of exercise. It will also include context data, which is collected from a sensor tag on the user's body and sensors distributed in their living space. This data recognizes environments and patterns of living that are related to changes in glucose.

DURATION:
Your participation in the study will consist of 3 visits over approximately 8 weeks. Most visits will last 1.5-2 hours.

PROCEDURES:
If you decide to take part in this study, you will have a number of tests and procedures.

- After you qualify, you will begin the study with Visit 2, the start-up visit for the 28 day study. You will be asked to fill out a lifestyle questionnaire asking about your current exercise routine and blood glucose management. You will be given the Dexcom G6 CGM, a physical activity watch connected to a study phone, and a tracking tag to wear and a tracking beacon to install in your home for use during the next 28 days. You will install theG6 app on your personal phone.
- You will be shown how to use a smart phone app on your phone to enter all of your meal and exercise data along with meal photos.
- You will be asked to complete a 30-minute exercise video once or twice a week with a meal prior to exercise.
- You will be asked to pick up and then consume a prepared meal once each week on the same day at a set time at home.

- At the end of the 28 days, you will come in for a one-hour study completion visit where we will download your insulin pump.

RISKS: There are risks involved in participating in the study, some of which may be very serious. These may include, but are not limited to, more common risks such as high blood glucose, low blood glucose to less common risks such as falls/injuries while exercising, or allergic reaction from the insulin.

BENEFITS: You will not directly benefit from taking part in this research. This research may benefit future people with type 1 diabetes by helping to develop better management tools for diabetes.

ALTERNATIVES: You may choose not to participate in this study or participate in another study if one is available.

This is a voluntary research study. You do not have to join the study. Even if you decide to join now, you can change your mind later. Please ask the Investigator if you have any questions about the study or about this consent form.

END OF CONSENT SUMMARY

OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

IRB#: 20248

Clinical Research Consent and Authorization Form

TITLE: **Development of a context-aware glucose prediction algorithm in patients with type 1 diabetes**

PRINCIPAL INVESTIGATOR: Jessica Castle MD (503) 494-7072

WHO IS PAYING FOR THE STUDY?: National Institute of Health (NIH)

WHO IS PROVIDING SUPPORT FOR THE STUDY?: Dexcom

OHSU is being compensated by the funder to conduct this study. This is to pay for tests performed only for study purposes, and for the time involved on the part of the investigator(s) and study staff. You may freely discuss this with your physician and the investigator if you have concerns. Your study doctor and the research staff have no financial involvement with the funder and are not being paid directly by the funder for conducting this study. However, they may have travel expenses covered by the funder to attend study training meetings.

DO ANY OF THE RESEARCHERS HAVE A CONFLICT OF INTEREST WITH THIS STUDY?
OHSU and Drs. Jacob and Wan (co-investigators) and Jonathon Folsom have a financial interest in MotioSens, a company that is involved in this study. The nature of this financial interest and the design of the study have been reviewed by two committees at OHSU. They have put in place a plan to help ensure that this research study is not affected by the financial interest. If you would like more information, please contact the OHSU Research Integrity Office at (503) 494-7887.

CO1450

WHY IS THIS STUDY BEING DONE?:
You have been invited to be in this research study because you have type 1 diabetes. The purpose of this study is to create a dataset that will be used in developing a glucose prediction model for an automated insulin delivery system. We will collect glucose sensor values, fingerstick glucose values, insulin data from your insulin pump, food and rescue carbohydrate data, and exercise data. We will also collect context data through sensors worn on your body and distributed in your home. Context means "what you are doing at a given time and where you are doing it". This data will help us recognize repeatable patterns in your life. An example of this might be consistent low blood sugars while you at the gym on Mondays and Wednesdays from 6-8am. With the data, we can determine how those patterns affected your glucose. We believe that an automated insulin delivery system can use context data to recognize environments and living patterns that negatively affect your glucose. With the data collected by this study, we hope to

design a system that can help predict low or high blood sugars based on known behavior patterns, adjust insulin accordingly and improve the time glucose is in the target range.

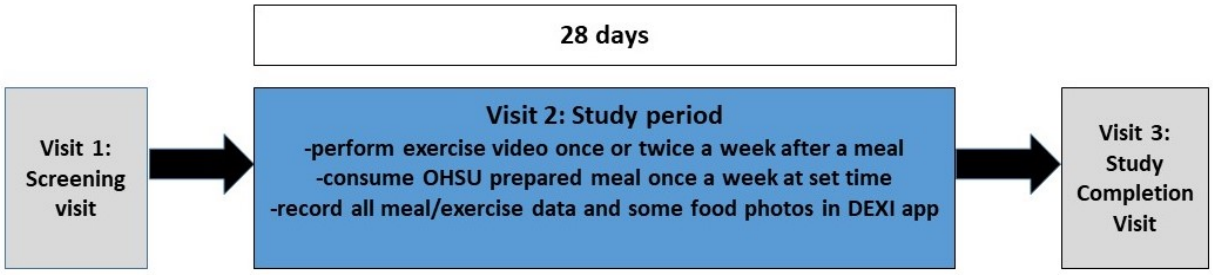
This study requires 3 visits to the clinic and will take approximately 8 weeks to complete.

The data we collect during your study will be kept in a data bank, also called a repository. This data will be stored indefinitely and may be used and disclosed in the future for research.

WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY?

Visit 1 is a screening visit. If you qualify, you will participate in the study for 28 days. During the study, you will manage your blood sugar as you normally would using your own insulin pump with the addition of using the Dexcom G6 sensor and the Dexcom G6 app. You will also wear a physical activity watch and a tracking tag on your body, as well as placing tracking beacons in your home. The physical activity watch data will be collected on the iPancreas app. We will provide a phone with this app on it. You will use a mobile app, DEXI, to track your physical activity and meal data while at home, including taking pictures of your food on certain days. You will install the DEXI study app and the Dexcom G6 app on your phone. You will also be given a study-provided phone that will collect your heart rate data from your physical activity monitor. You will complete an exercise video twice a week during weeks one and two and once a week during weeks 3 and 4 at home after eating a meal of your choice. For the exercise, you will have an equal chance of being assigned to aerobic (cardio), anaerobic (strength), or high intensity interval exercise video sessions. You will also pick up and consume a dinner prepared by OHSU Bionutrition once a week on the same day at a set time at home. See **Figure 1** below for a diagram of the study flow. Data collected from/about you in this study will be used to develop a glucose prediction model for an automated insulin delivery system.

Figure 1: Study Flow Design



You will be using the Dexcom G6 CGM system including a sensor and transmitter. The Dexcom G6 CGM system is an FDA approved device. We expect to study up to 30 subjects in this study at OHSU.

Clinic Visit #1: Screening Visit:
The screening visit will be completed at the OHSU Oregon Clinical and Translational Research Institute Clinic (OCTRI), the Biomedical Engineering Point of Care (BME POC) Laboratory or at the OHSU Harold Schnitzer Diabetes Health Center. After this consent form is signed, you will have blood drawn for tests. The blood test is to monitor diabetes control, liver and kidney function, electrolytes, and blood count. About one tablespoon of blood is needed for these tests. If you have had any of these tests completed in the last 3 months and we can access the results, we will not draw blood for that test. If the blood tests show that you have medical problems such as kidney disease, liver disease or anemia, it will not be possible to include you in the study.

You will also be asked questions about your medical history, and a brief physical exam will be performed. Your vitals will be taken (height, weight, pulse, blood pressure) along with a capillary blood glucose reading. If you are a woman who can become pregnant, you will need to take a urine pregnancy test. This test must be negative for you to participate in the study. You will also have an EKG done. As part of the screening procedures for this study, the investigator will review your medical records for information related to your eligibility in the study. For example, they may review your recent lab results and visit notes from your endocrinologist. We will download your insulin pump in order to determine how often you are counting carbohydrates for meals.

You will be asked to fill out 2 questionnaires. These questionnaires will be used by the investigators to accurately ascertain your:

- Physical activity readiness
- Hypoglycemia awareness

When the risk of Covid-19 is considered to be significant and OHSU is at reduced operations, only one staff member will be in the room with you at a time wearing a mask and maintaining social distancing and the only time staff will have to be within 6 feet is when the study investigator is completing the physical exam and when research staff is completing the EKG and drawing blood for screening labs. We will give you a mask to wear during the visit.
This visit will take about one and a half hours.

Clinic Visit #2: Start-up Visit for 28 day study
This visit will be completed at the OHSU Oregon Clinical and Translational Research Institute Clinic (OCTRI), the Biomedical Engineering Point of Care (BME POC) Laboratory or at the OHSU Harold Schnitzer Diabetes Health Center. This visit will last approximately 1.5 hours, depending on user experience.

You will continue to use your own insulin pump and manage your glucose as you normally would for the 28 days. You will be asked to answer questionnaires from the "Lifestyle Questionnaire," that ask about your exercise routine and your blood sugar control.You will insert a Dexcom G6 CGM according to the manufacturer's directions and connect to the Dexcom G6 app, setting the alerts at 70 and 250 mg/dl and changing out every 10 days. You will be given a physical activity watch connected to the iPancreas app on a study-provided phone. You will be given a tracking tag to wear and shown how to install tracking beacons in your home. You may be asked to plug the MotioWear beacon into your router to improve data uploads You will also be instructed on a mobile app, T1 DEXI. You will enter your physical activity and meal data into this app, including taking photos of all of your food on the day of and the day after exercise. You will install the study app, the commercial app for the activity watch, the app for the activity watch and the Dexcom G6 app on your personal phone. (If your phone is not compatible with the study apps, the provided study phone may be used.)

You will be asked to complete two at-home exercise sessions using a 30 minute exercise video during weeks 1 and 2 and one session during weeks 3 and 4 after a meal of your choice. You will be assigned to either aerobic (cardio), anaerobic (strength), or high intensity interval exercise video sessions. You will be instructed to consume a snack if your glucose is <120 mg/dL and delay exercise until your glucose is >80 mg/dL. Also if your glucose is >250 mg/dL, you will be instructed to calculate if a correction dose is needed and delay exercise until glucose is <250 mg/dL. You will be given a Contour Next blood glucose meter and strips. You will be instructed to check your glucose after exercise and to consume a snack if needed.

You will be asked to pick up and consume a high carbohydrate dinner prepared by OHSU Bionutrition once each week at home on the same day at the same approximate time of day (but not on the exercise days). The meals can be picked up all at once and frozen until use. You will be asked to download your pump weekly or biweekly during the 28 days on study. This will allow for frequent data capture in case of a battery change or loss of power to the pump which can erase insulin data.

When the risk of Covid-19 is considered to be significant and OHSU is at reduced operations, the start-up visit can be completed by video with the study devices and meals being delivered to you by a courier. You will need to install a software program called Webex on your personal device for the video visit. Webex is a secure virtual software platform approved for use with OHSU patients. Study staff are available to assist with the install. To make installation quicker, no more than two research staff members may need to go into your home for installation of the tracking devices while maintaining appropriate social distancing. The staff members will wear masks, face shields and gloves during the installation. All participants and family members present during the installation will wear masks. Members of your household and our study staff will be screened for COVID-19 symptoms within the prior 14 days and day of the installation.

If you experience difficulties with the devices, study staff will be available for assistance by phone or email. Study staff will follow-up with you every 7 days. You may be contacted at additional times by phone, email or text by study staff. For example, staff may contact you to clarify the content of your food photos or to remind you to complete your exercise or pick up your meal.

Clinic Visit #3: Study Completion Visit
At this visit, study staff will remove the Dexcom sensor and you will turn in all devices. Study staff will download your insulin pump. A study investigator will be available for consult if needed regarding insulin management. The sensor will be taken out earlier if the sensor is not working correctly or the investigator decides it should be removed. It will also be taken out if you ask for it to be removed. We will inspect the skin where the sensor was placed and will take a photo of the area if it is red or swollen. Your face will not be included in the photograph. There is little risk of identification unless you have an identifying tattoo or mark on your stomach. If the study coordinator notes any significant redness or swelling, the study investigator will be contacted. If you have a red area around the place where the sensor was, the study investigator may ask you to return to the clinic to make sure you do not have an infection. This visit will take approximately 1 hour.

There is the option to complete this visit by video using Webex. You will be given shipping boxes for sending all devices back at the end of the study. You will be given a checklist of equipment to return with instructions on how to uninstall the tracking devices. You will connect with a study coordinator virtually to complete the visit.

If the study period is paused for a period of time, such as if you begin taking a medication that impacts glucose like steroids, you may be asked if you can repeat that part of the study period with additional compensation provided.

During the screening visit, you will have blood drawn for tests. Your blood will be destroyed after the OHSU lab finishes running the tests listed in table below. The following data will be collected during this study and stored in a repository: 1) Dexcom G6 sensor data, 2) blood glucose data from a study Contour Next BG meter, 3) insulin data from your pump, 4) physical activity data, 5) food and exercise data that you entered into the DailyDose app, and 6) context data from the tag worn on your body and the beacon from your home. In the future, this data may

be used for other research studies at OHSU. The data will be labeled as described in the **WHO WILL SEE MY PERSONAL INFORMATION?** section.

If you have any questions regarding this study now or in the future, contact the principal investigators Jessica Castle, MD at (503) 494-7072 or Peter Jacobs PhD at (503) 494-3870 or you can contact the study coordinator Debbie Branigan at 503-418-9070.

Clinic Visit Schedule

Visit Number	1	3	4
Procedures	Sign consent, obtain medical history and vitals	28 day study start-up visit	Study completion visit
Lab Tests	Blood Panel*, EKG, pregnancy test (if applicable)	Pregnancy test (if applicable)	
Physical Exam	History and Physical Exam		Exam of skin
Time	1 ½ hours	1 ½ hours	60 minutes

*****The Blood Panel includes HgbA1C, liver tests (ALT, AST, albumin), kidney tests (creatinine), and electrolytes (Na, K, Ca) and a complete blood count to rule out anemia.

WILL I RECEIVE RESULTS FROM THE TESTING IN THIS STUDY?

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

We will run routine labs at your screening visit to monitor diabetes control, liver and kidney function, electrolytes, and blood count to determine if you are eligible for the study. We do not plan to share your test results with you or your primary care provider. However, if we discover information that is important for your health care, either in this study or in the future, we will contact you and ask if you want to know the results. If you choose to receive the results, you may need to have the test repeated in a non-research laboratory. You may learn information about your health that is upsetting or that impacts your health. You will be able to ask the investigator about any of the study results.

WHAT RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?:

Risk of Low and High Blood Sugar

Exercise can cause the blood sugar to drop. Symptoms of low blood sugar can include sweating, weakness, shaking and not feeling well. The Dexcom app will have high and low glucose alerts that you can adjust. There is a very low glucose alert that cannot be adjusted. Symptoms of high blood sugar includes increased thirst, tiredness, blurred vision and irritability. It is unlikely that you will experience severe low or high blood sugar because of the use of the Dexcom G6 sensor with alarms set.

Blood Draw Risks

We will draw blood from your arm at the screening visit. You may feel some pain when your blood is drawn. There is a small chance the needle will cause bleeding, a bruise, an infection, or fainting.

Exercise
You will be completing exercise. You may feel tired and may have low or high blood sugar. Rarely, exercise may cause a heart attack, irregular heart rate or death. You will an EKG performed at screening.

Dexcom Sensor
The Dexcom sensor may produce pain when it is inserted into the skin, similar to a pump site insertion or insulin injection. Rarely, a skin infection can occur at the site of insertion of the sensor. Itchiness, redness, bleeding and bruising at the insertion site may occur. An allergy to the tape that holds the sensor to the skin is possible. The risk of skin problems could be greater if you use a sensor for longer than it is supposed to be used. There is a chance that the sensor or needle may break under your skin. This is not expected to occur, but if it does, you should speak with your study doctor about what to do.

Finger Stick Blood Glucose Measurements
During the study blood glucose measurements need to be made with a finger stick. The finger stick may cause pain or bruising.

Pregnancy Risks for Women
If you are nursing an infant or you are pregnant now, you cannot be in the study. This study may involve risks to an embryo, fetus, or nursing infant that are currently unknown. If you are sexually active and could become pregnant, you and your male partner(s) must use birth control that works well or you must not have sex. The investigator will talk to you about the types of birth control that are acceptable. You will have to do this the whole time you are in this study. If you become pregnant during the research study, please tell the investigator and your doctor immediately.

Lifestyle Questionnaire
There is a slight risk of a breach of confidentiality with your questionnaire responses. However, the plan listed in the section "WHO WILL SEE MY PERSONAL INFORMATION?" makes it unlikely that the breach would occur.

Other Side Effects
One risk to taking part in this study is that the study may not be effective in helping to treat your disease. This means you may spend time in the study that may not provide you with any health-related benefits. You may have some side effects we do not expect.

Risks from Storage of Data in Repository
There is a slight risk of a breach of confidentiality from keeping your data in a repository. However, the plan listed in the section "WHO WILL SEE MY PERSONAL INFORMATION?" makes it unlikely that a breach would occur.

Risks from Using Provided Study Phone
You will be provided with a phone with security controls in place. These controls include password access so only you can access the phone. However, if you lose the phone - or it is stolen - data could be accessed by other individuals not authorized by you to view your

information. In using the study phone, you accept the risk, however slight, that your information could be compromised.

WHAT ARE MY CHOICES IF I DECIDE NOT TO TAKE PART IN THIS STUDY?

You may choose not to be in this study. If you do not take part in this study, the alternative is to continue your current diabetes treatment and care. You could chose to use the Dexcom G6 CGM system for management of your diabetes without being in the study. We encourage you to discuss your options with your study doctor, your general primary care physician, or another health care professional.

WHO WILL SEE MY PERSONAL INFORMATION?

We will take steps to keep your personal information confidential, but we cannot guarantee total privacy. To protect your privacy, you will be assigned a 3-digit number to identify your study data. The key associating the 3-digit number and your personal identifying information will be restricted to the study staff. It will also be encrypted and kept secure on a restricted OHSU drive in a limited access folder. The study phone you will use will be registered to this 3-digit number. All of the data stored on the phone will be associated with this ID. The data that will be stored includes:

- Exercise, sleep and activity data from the exercise Watch
- glucose sensor data from the Dexcom G6 CGM
- insulin from your insulin pump
- the food and exercise data you log in the study app (this app has undergone a security review by the OHSU Information Technology department)
- the context data collected from the wearable tags and beacon in your home

We will create and collect health information about you as described in the WHY IS THIS STUDY BEING DONE? and the WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY? sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study and store in a repository.

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The funder of this study, National Institute of Health (NIH), and Dexcom Inc., and the funder's representatives
- The Food and Drug Administration
- The Office for Human Research Protections, a federal agency that oversees research involving humans

Those listed above may also be permitted to review and copy your records, including your medical records.

Your name, date of birth and social security number may be provided to the study funder (or an organization acting on their behalf) so the funder can meet Medicare reporting requirements

Data from this study may be shared with other investigators for future research studies. All identifying information about you aside from some dates will be removed from the data before it is released to any other investigators.

To protect your privacy, you will be assigned a 3-digit number to identify your study data. There will be a key linking your 3 digit subject ID to your personal health information. The study phone you will use will be registered to this 3-digit number. All of the data stored on the phone will be associated with this ID. The key is encrypted with a password and stored in a secure OHSU cloud database. The lead coordinator, Deborah Branigan, and research coordinators listed on this IRB protocol will have access to this encrypted key but outside researchers will not.

By participating in this study, you are giving permission for your data to be stored indefinitely in a repository in order to be used in future research studies. Generally, a research repository collects, stores and distributes data for use in future research projects. Storing and gathering lots of data together can help to conduct future research and avoid re-collecting data over and over again. The purpose of this data repository will be to combine all of the study data from the OregonAPC group into one set for future engineering development of diabetes technologies.

The data stored on the phone is uploaded into a secure OHSU approved cloud database repository along with your blood glucose data from the meter and pump. Data access will be reviewed and tracked to ensure that data is only released to authorized individuals. The data will remain in the cloud database until the PI for the repository, Dr. Jessica Castle, decides to discontinue the repository. The termination will include the destruction of the data in a secure way. If you withdraw your consent from this project, your data will be destroyed.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

When we send specimens or information outside of OHSU, they may no longer be protected under federal or Oregon law. In this case, your specimens or information could be used or re-released without your permission.

We may continue to use and disclose your information as described above indefinitely.

Some of the information collected and created in this study may be placed in your OHSU medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

WILL ANY OF MY INFORMATION OR SAMPLES FROM THIS STUDY BE USED FOR ANY COMMERCIAL PROFIT?

Any data obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study.

Further, you will have no responsibility or liability for any use that may be made of your samples or information.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?
There will be no cost to you or your insurance company to participate in this study.

You will receive $500 for completion of all study visits. If you withdraw early from the study, compensation will be $125 per 7 days on study. There is no compensation for the screening visit. If you complete a partial week, you will also receive $125 for the partial week. We will request your social security number in order to process any payments for participation.

You will receive additional compensation for completion of study procedures at home. You will get $2 when you complete and enter a required exercise or meal session on the correct time/date. You can receive a maximum of $6/week in incentives. We will text you once a week to notify you of your progress.

You may receive payment via a debit card. There may be fees (for example, if the card is inactive for more than six months), which will be deducted from the balance on your card. Details on how to use the card and any fees are included in the separate card member agreement and FAQ sheet given to you with the debit card.

Payment received as compensation for participation in research is considered taxable income for a research subject. If payments are more than $600 in any one calendar year, OHSU is required to report this information to the Internal Revenue Service (IRS). Research subject payments exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the research subject and a copy will be sent to the IRS.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?:
If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact Dr. Jessica Castle by phone at (503) 494-7072 or page her at (503) 494-8311 or Peter Jacobs by phone at (503) 494-3870.
If you are injured or harmed by the study device or study procedures, you will be treated. OHSU and the funders do not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.

If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

WHERE CAN I GET MORE INFORMATION?
If you have any questions, concerns, or complaints regarding this study now or in the future, contact Jessica Castle at (503) 494-7072, Peter Jacobs at (503) 494-3870 or Deborah Branigan at (503) 418-9070.

This research has been approved and is overseen by an Institutional Review Board ("IRB"), a committee that protects the rights and welfare of research participants. You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

WHAT ARE MY RESPONSIBILITIES IN THIS STUDY?

There are important instructions for you to follow during the study. We will ask you to use the DEXI app for entering your meal, rescue carbohydrate, exercise data and food photos. We will also ask you to wear your physical activity monitor to collect data using the iPancreas app. We will ask you to respond to the glucose sensor alarms and insert a new G6 sensor every 10 days. We will ask you to wear a tracking tag and place beacons for tracking in your home. We will ask you to exercise two times per week 90 minutes after a meal and to pick up and eat a prepared meal once a week at home during the 28 days.

DO I HAVE TO TAKE PART IN THIS STUDY?

Your participation in this study is voluntary. You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study.

Your health care provider may be one of the investigators of this research study and, as an investigator, is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

The participation of OHSU students or employees in OHSU research is completely voluntary and you are free to choose not to serve as a research participant in this protocol for any reason. If you do elect to participate in this study, you may withdraw from the study at any time without affecting your relationship with OHSU, the investigator, the investigator's department, or your grade in any course.

IF I DECIDE TO TAKE PART IN THIS STUDY, CAN I STOP LATER?

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. If you choose not to join any or all parts of this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Jessica Castle, MD

Oregon Health and Science University
3181 SW Sam Jackson Park Rd.
MC: OP 05-DC
Portland, Oregon 97239
castleje@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

If you choose to withdraw from the study, you will be asked to bring in all of the study devices and have the Dexcom sensor removed.

If in the future you decide you no longer want to participate in this research, we will destroy all your information. However, if your samples are already being used in an ongoing research project and if their withdrawal jeopardizes the success of the entire project, we may ask to continue to use them until the project is completed.

You may be removed from the study if the investigator stops the study, you become pregnant, you develop serious side effects, or you do not follow study instructions.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

SIGNATURES:

State: Your signature below indicates that you have read this entire form and that you agree to be in this study.

We will give you a copy of this signed form.

Participant Printed Name	Participant Signature	Date
Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date