

1. General Information

Title: Empowering MedicarePatients to Self-Manage Their Type 2 Diabetes Using Continuous Glucose Monitoring (CGM) – Investigational Device Pilot (SMA Investigational device)

Protocol Number: CGM_IRB_003

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2. Background Information

Diabetes is a disease which increases health risks for many other health conditions (Ramsey, 1999) and carries a large social and economic toll (Zhou, 2014; American Diabetes Association, 2013).

Strict glycemic control reduces risks for the development of microvascular and macrovascular complications in patients with diabetes. In the United Kingdom Prospective Diabetes Study (UKPDS), each 1% reduction in glycosylated hemoglobin (A1C) was associated with a 37% decrease in the risk for microvascular complications and a 21% decrease in risk for any end point or death related to diabetes (Stratton, 2000). In turn, improved blood glucose control can reduce the costs associated with the treatment and long-term complications of diabetes.

Given the serious consequences of poor glycemic control, tight glucose management has become today's standard of care. However, only half of patients with diabetes are achieving the level of control recommended by the American Diabetes Association (Lipska 2017). The reasons for poor control are numerous and complex (Skyler, 2000). They include lack of patient motivation, denial of disease, inability to afford test strips, discomfort from repeated finger sticks, and difficulties caused by co-morbid conditions.

Effective management of diabetes requires constant management of diet, physical activity and specialized glucose-lowering medications (Armstrong, 2017). The most effective diabetes management programs are delivered in-person (Polonsky, 2011; Cox, 2013; LeFevre, 2014; Ratner, 2005), and involve self-monitoring of glucose levels along with personalized health feedback to enhance patient motivation and promote positive behavior change (Polonsky, 2015; Cox, 2016). Increasingly, new diabetes management programs are being designed and evaluated that seek to deploy these best practices using web and mobile-based technology (Ralston, 2009; McMillan, 2017; Simenerio, 2010; Quinn, 2011; Philis-Tsimikas, 2014).

While hemoglobin A1C measurements are widely used by clinicians to evaluate management of type 2 diabetes (T2D), a growing body of evidence suggests that post-prandial plasma glucose (PPG) (Temelkova-Kurktschiev, 2000) and glucose variability (GV) (Takao, 2011) are risk factors for complications of T2D, independent of fasting plasma glucose (FPG) or A1C levels. Further, poorly controlled nocturnal glucose (NG) is common in individuals with T2D, and is associated with obstructive sleep apnea (Priou, 2015). PPG, GV, and NG therefore provide additional target metrics for management of glucose in individuals with T2D. In a practical sense, however, these metrics are difficult if not impossible for patients to monitor by measuring their blood glucose.

Real-time Continuous Glucose Monitoring (RT-CGM) for Type 2 Diabetes Patients

In developing an effective mobile diabetes management program RT-CGM has emerged as an effective educational tool for patients with diabetes to achieve tight glycemic control. Previous studies have found that T2D patients are better able to control their glucose levels using RT-CGM compared to blood glucose meter readings (Yoo, 2008; Cox, 2016) and that this effect is sustained even after discontinuation of RT-CGM use (Vigersky, 2012). By observing their plasma glucose levels in the context of daily life, patients can see how their levels (including important indices such as post prandial glucose (PPG), glucose variability (GV), and nighttime glucose (NG)) are affected by diet, exercise, medications, stress, and other personal factors. In addition, the ability of Dexcom's RT-CGM system allows for sharing

of data with a patient's health coach, thus enabling the effective delivery of a mobile diabetes management program.

Recognizing the value of CGM for T2D patients, we have developed a novel, integrated lifestyle modification program for those with T2D that leverages the real-time nature of CGM technology to provide a personalized educational experience for patients in their daily life to better manage their glucose levels.

3. Study Purpose

The purpose of this study is to evaluate an integrated, CGM-based lifestyle modification program for glucose management in patients with T2D. The study's primary aim is to collect implementation process measures regarding participant recruitment, program delivery, and device use. The secondary aim is to evaluate the impact of the program on the glucose management of people with T2D.

This pilot study will employ an investigational CGM system which has not been approved by the FDA. The system is a variant of the Dexcom G6 CGM system which received an investigational device exemption (IDE) from the FDA in 2016. In 2017 this investigational CGM system was designated by Chesapeake IRB as a Non-Significant Risk device for our research protocol Pro00021722.

4. Program Goal and Objectives

This program integrates CGM and state-of-the-art diabetes management education. It builds on previous and ongoing CGM-based program development work at Savvysherpa (see Appendix A for results of a preceding quality improvement initiative).

The goal of the program is to ensure that patients with T2D receive the tools, information, and support needed to use CGM effectively, and as a result become better at managing their glucose levels. The program is designed to overcome current barriers to CGM utilization.

The program will achieve its goal by helping patients

1. Access CGM technology
2. Use their CGM systems¹
3. Understand in real time how their behaviors impact their glucose levels
4. Improve glycemic control through sustainable behavior change

5. Program Description

All program participants will receive a smartphone-connected CGM system. This system will allow participants to view their glucose levels in real time and observe how their behaviors impact their glucose levels. Participants will also be assigned a personal coach who will provide support via phone to help patients problem solve, reflect on observations, learn and practice skills, and form healthy habits.

One major contributor to complication risk among patients with type 2 diabetes is medication non-adherence (Polonsky and Henry, 2016). CGM can help make the importance of medication adherence

¹ In the context of this study, a CGM system is defined as a CGM sensor, applicator, transmitter, and mobile app that is accessed through a smartphone.

more salient for patients by allowing them to directly observe the effects of medication on their glucose levels. Similarly, a recent review (Chacko, 2016) and meta-analysis (Savvysherpa internal analysis) suggests that appropriately-timed post-prandial activity can significantly reduce the rise in plasma glucose following a meal. Patients wearing CGM systems will have the ability to see exactly when and how their glucose levels are affected by variations in duration, frequency, and intensity of physical activity after a meal. Through coaching, patients can be guided and supported in making these observations and drawing connections to their daily lives.

Coaches will focus on four key aspects of T2D management:

- i. Medication optimization
Using CGM, patients will be able to see the impact of medication adherence on their glucose levels.
- ii. Impact of diet on glucose
Through CGM and coaching, the program will help participants understand the relationship between PPG levels and the types and amounts of food eaten.
- iii. Strategic physical activity to reduce PPG spikes
The program will encourage participants to track their post-meal activity via a wearable activity tracker. By observing their activity tracker data in tandem with their CGM data, patients will learn how they can use physical activity to help manage their glucose levels.
- iv. Nighttime glucose management
Use of CGM will make it possible for participants to observe their NG levels. Coaches will help participants identify strategies to manage nighttime glucose.

6. Methods and Procedures

The proposed program represents a new, comprehensive education approach to T2D self-management that is centered around the patient experience. The program will take place outside of the clinic setting. This will allow participants to observe their glucose 24-7 under a wide range of conditions.

Distinctive features of the program include:

- Program access for all eligible patients
- A ready-to-use smartphone that provides an enhanced data display and allows for greater patient interaction with data and educational resources that will be preloaded on the smartphones
- Pre-pairing of CGM system devices to minimize set-up required by patient
- Enhanced assistance with CGM device set-up and application
- An activity-tracking system that allows patients to observe the relationship between physical activity and glucose levels
- Individualized coaching to help patients understand their CGM data and make appropriate behavior changes
- Data-sharing with program staff

Compared to current clinical practice for T2D CGM use, the program offers numerous advantages (see figure 1).

| CGM Process Component | Current Clinical Practice Using CGM for T2D (infrequently employed) | Drawbacks to Current Practice | Proposed Program | Advantages of Proposed Program |
|-----------------------|---|--|---|---|
| Selection/Recruitment | Physician identifies individual patient candidates for CGM | <ul style="list-style-type: none"> Identification of suitable candidates is ad hoc within a physician visit. | Eligible patients are identified through their health plans and invited to participate in the CGM-based glucose monitoring program. | <ul style="list-style-type: none"> No visit required No time required of physician All qualified patients have an opportunity to use CGM |
| Consent/Prescription | Physician discusses CGM with patient during a patient visit. Physician prescribes CGM system for patient. | <ul style="list-style-type: none"> Requires physician's time at each encounter to explain CGM to patient. | <p>Patient is provided with information related to CGM and program consent, and has the ability to discuss any related questions and concerns with program staff. Patients with medical questions related to their participation are referred to their providers.</p> <p>Under IRB-approved research, no prescription will be needed for eligible patients to receive a CGM device.</p> | <ul style="list-style-type: none"> Increased information and support available to ensure informed consent. |
| Laboratory measure | Usual monitoring of A1C levels (recommended every 3 or 6 months). | <ul style="list-style-type: none"> A1C levels reflect overall trends, providing limited information to help patients understand impact of specific decisions and behaviors. | Usual monitoring of A1C levels (recommended every 3 or 6 months). | <ul style="list-style-type: none"> Patients will be able to observe how their A1C levels may change as a result of their participation in the program. Patients will also be able to observe additional and more immediate effects of lifestyle changes to supplement their A1C measures. |
| Devices | Commercially-available CGM systems | <ul style="list-style-type: none"> Commercial CGM systems can be challenging for patients to apply and use. | Patients will receive an investigational CGM system, including a smartphone with the investigational app. Patients will also receive an activity tracker to measure activity in conjunction with CGM. | <ul style="list-style-type: none"> The investigational CGM incorporates design changes to improve usability compared to commercially-available CGM systems. The activity tracker extends patient tools to understand the role of activity in glucose management. |
| Distribution | Patient sends prescription to a wholesaler, which then ships the CGM system to the patient. The system consists of a CGM sensor, a transmitter, and a receiver. | <ul style="list-style-type: none"> Requires that the patient take action to fill prescription | Program houses stock of CGM systems. System is provided to patient along with program materials. | <ul style="list-style-type: none"> After the consent form is signed, no action required by patient in order to receive device. |

| | | | | |
|-----------------------------------|--|---|---|--|
| CGM system set-up and application | Patient applies device in-home, using manufacturer's instruction book, video, and technical assistance by phone. | <ul style="list-style-type: none"> Technical hurdles of system set-up and device application are especially challenging for seniors. | Program sets up apps and links program devices on behalf of patient before patient receives the system. Resources and instruction will be available in written form, video, telephone, and/or in-person to help patients with device application and system usage. | <ul style="list-style-type: none"> Minimal system set-up required of patient Expanded, personalized resources are provided to help patient learn to apply device and use system. |
| CGM-based education | Patient learning is self-directed | <ul style="list-style-type: none"> Benefit of using CGM may be limited by patients' capacity to understand and interpret data, literacy, sense of self-efficacy, or other factors. | Patients receive provider-approved materials and guidance from a coach to help them 1) understand how to interpret CGM data and 2) observe and determine in real-time how diet, medication, exercise, and other lifestyle choices may help them better control their glucose levels. Coaches will be able to view patient glucose data in order to provide support tailored to individual patients' data and circumstances. | <ul style="list-style-type: none"> Increased likelihood that patients will benefit from using a CGM system. |
| Integration of CGM into practice | Patients visit their PCPs every 3 or 6 months. Physicians may access patient CGM data online, although this is often difficult given time constraints. | <ul style="list-style-type: none"> Physicians must proactively take action to view patient CGM data online Physician guidance typically limited to patient visits | Patients use CGM data to understand and integrate best practices in diabetes self-management. | <ul style="list-style-type: none"> Empowers patients to self-manage their diabetes Ensures consistent oversight of patient device usage Adjunctive to patients' normal medical care |

Figure 1. CGM for Type 2 Diabetes Patients: Current Practice and Proposed Program Features

Program process

The program will be implemented as described below. The stages of program enrollment are summarized in figure 2.

Recruitment

Study participants will be recruited from UnitedHealthcare members in the Las Vegas area who are enrolled in a Medicare Advantage plan (Senior Dimensions®). To be eligible for the program, patients must meet specific inclusion/exclusion criteria.²

All eligible patients will be invited to participate in a CGM-based educational program that will consist of 10 weeks of CGM system use and activity tracker use with coaching. After using the devices for 10

² Inclusion/exclusion criteria have been determined by Dr. Kevin Kapov and Dr. Linda Johnson, Co-Investigators and Senior Medical Directors at Southwest Medical Associates.

weeks, patients may be offered the opportunity to continue to wear the activity tracker and upload their data with the smartphone through August 31, 2018.

Patients will be recruited to the program through targeted invitations.

Targeted invitations will be made to patients determined to be eligible based on patient medical claims. These patients will receive a letter of invitation from the program on behalf of UnitedHealthcare, followed by a second reminder letter. Interested patients will be directed to call study staff or fill out the online form for more information, and will consequently be called by a program representative. After the first invitation letter has been sent, a program representative will call the patient to offer a verbal invitation.

Patients at Southwest Medical Associates (SMA) in Las Vegas who may be appropriate study candidates may be given a program brochure by SMA physicians, staff, and/or program staff. If interested these patients may visit the program website and fill in an online form requesting a call, or call the program representative themselves. Physicians and staff may also call and invite potential study candidates to obtain study materials and to learn about the study by attending a meeting with program staff at the clinic, contacting program staff by phone or by filling out an online form to request a call from a program representative.

When speaking with the program representative, if patients express an intention to participate in the program, patients will be invited to meet with program staff in person to learn more about the program, have the consent form reviewed with them, and get started in the program if they so choose. Patients will have the option to meet with staff via a home visit, at a class, or in-clinic.

For patients that prefer to start using the system on their own without in-person assistance, the program representative will seek to ascertain whether these patients have experience with smartphones and apps and feel confident enough to apply the CGM system by themselves. If at any time these patients require additional assistance with set-up, they will have access to their coach. During the set-up period, these patients can also call the program to request in-person assistance.

All patients interested in participating in the study will receive a consent packet that contains a cover letter from the program, a program brochure, a copy of the program eligibility criteria, two copies of the consent and authorization form (one to sign and return and one to keep), an information sheet on CGM, a Fitbit sizing guide and a program survey.

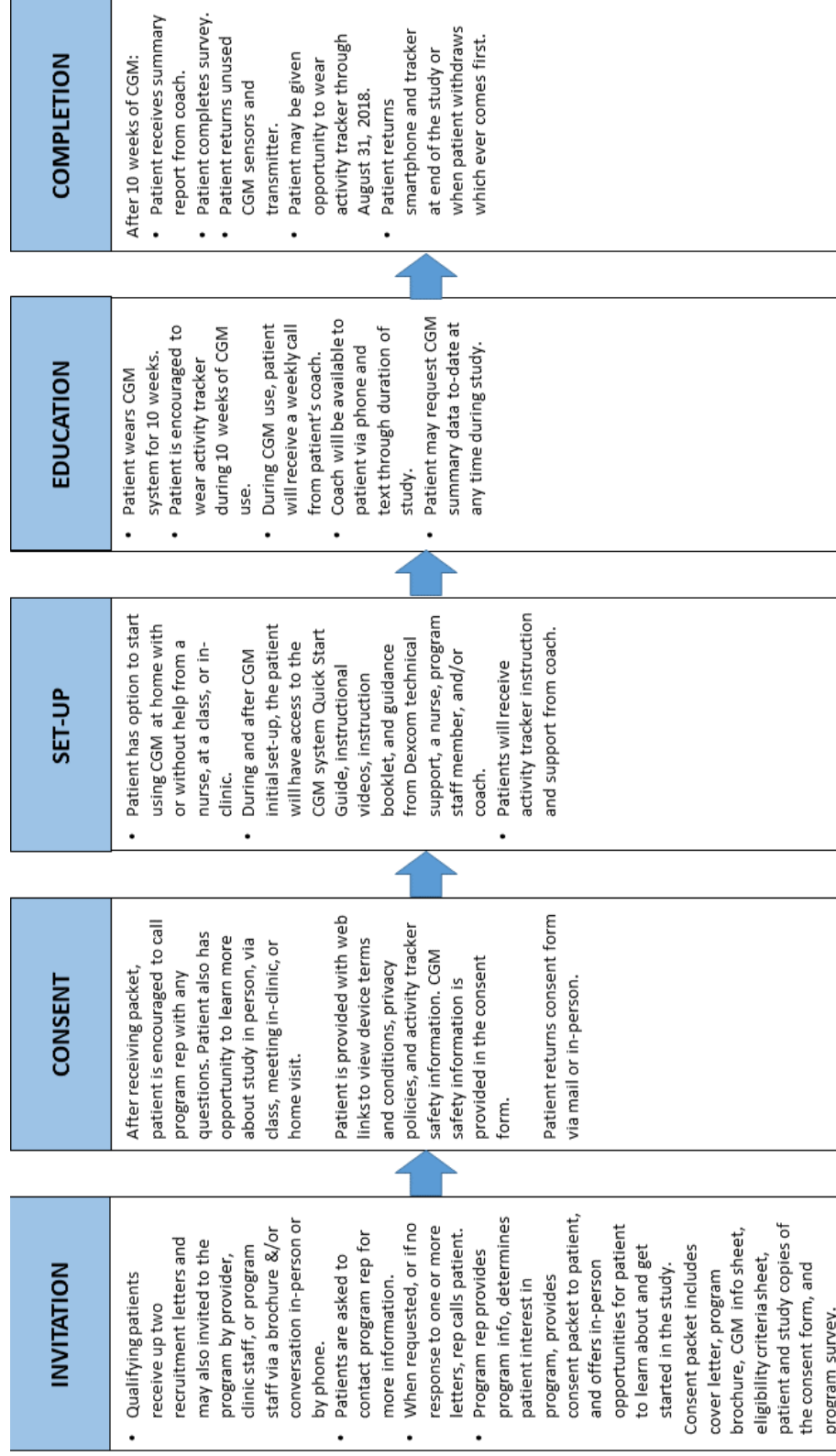


Figure 2. Type 2 diabetes CGM education program enrollment

Consent

Because the claims data used to assess patient eligibility will lag by two months (and thus may not capture very recent events or diagnoses) patients will be asked in the consent form to review the eligibility criteria and confirm that they meet it before signing the form.

To assure informed consent, prospective patients who receive study materials in the mail will be given at least two days to review the consent form and the opportunity to talk with a program representative who has been trained in human subjects research. Patients who attend an educational class, receive a home visit, or come to the clinic to learn about the study will be given ample time to read the consent form, the opportunity to take the consent form home (if applicable), and as much time as needed to talk with a program representative about the study. Patients with any medical concerns that they feel may affect their participation will be referred to their providers.

Patients will also be provided with a manufacturer resource phone number should they have any technical support questions related to the CGM system. Patients can call their coach or request in-person assistance on how to apply and setup the CGM system. The consent form itself will contain safety information related to study devices. Patients will also receive web links to the CGM system and activity tracker terms and conditions and privacy policies that they may view prior to providing consent. We will ask patients to review and agree to these terms prior to receiving their devices so that patient accounts can be created for the smartphone apps, thus reducing the set-up burden for the participant. Once participants receive their devices, this link will also be accessible on the smartphones for reference.

Patients will be able to provide consent either by signing a paper copy and returning it in the mail or in person (e.g. at a class, during a home visit, or at an in-clinic meeting). Patients will not receive devices prior to completing the informed consent.

Program Length

Participating patients will be asked to use a CGM system and an activity tracker for 10 weeks. After the 10 weeks, patients may be offered the opportunity to continue to use their smartphones and activity trackers as long as they continue to sync the tracker at least every three weeks through August 31, 2018.

Inventory and distribution

Dexcom will ship the investigational CGM systems to Savvysherpa, Inc. (Sponsor). Activity trackers will be obtained from Fitbit. All inventory will be accounted for and distributed according to good manufacturing practices. All devices will be stored in a secured environment with access limited to authorized personnel. After receiving a patient's signed and dated consent form, the CGM system and related program devices and materials will be provided to the patient.

Normally as per FDA regulations, a receiver that displays the patient's glucose data must be provided to the patient when an individual CGM prescription is filled. In this program, a smartphone, instead of a receiver, will be loaded with needed software applications and assigned to a patient. Use of a smartphone instead of a receiver will also help reduce the CGM system cost which may further help improve affordability and T2D patient access to this technology going forward.

The sensor and transmitter of the CGM system, the smartphone and the activity tracker each have unique identification numbers that will be assigned to an individual patient. This information will be

combined and stored with the assigned patient's name, device username, study identification number, etc. This information will also be securely sent to Dexcom for newly consented participants, allowing Dexcom to provide any needed technical support.

The Dexcom, Glucose Guide, and Fitbit app accounts will be set up on behalf of each patient in the study. The patient's first and last name along with a unique assigned username and password will be used to create accounts in all apps. The username and password will be printed on literature that only the patient receives. Patients' usernames and passwords will be stored on Savvysherpa's secure servers.

System set-up and application

All participants will receive a smartphone pre-loaded with apps associated with elements of the study program. These apps include the Dexcom CGM system app, the Fitbit app, and the Glucose Guide app created for this program to support patient coaching and research (e.g. texting, CGM secondary display). In addition, the Dexcom transmitter will be paired to the Dexcom app for each patient. Each of these steps by staff--app pre-loading, pre-registration and device pairing--will reduce the patient burden and allow program participants to begin the program by focusing on the fundamentals of using their devices.

Patients who choose to start using their CGM systems at home on their own will be asked to first review the instructional materials and videos. Patients who receive their devices in person will be provided with information and instruction at that time.

Program resources and instructions will be accessible to patients in written form, in person, via telephone, and via video to help them with device application and system usage.

CGM-based education and coaching

This part of the study will be implemented by coaches who have undergone diabetes management training that incorporates device information, educational content, and techniques based on behavioral discussion and patient self-learning/empowerment. Coaches will also be equipped to help patients use activity data in conjunction with their CGM use. Coaches will receive training regarding human research subjects to insure the ethical treatment and safety of all participants. All training will be reinforced during contact with study staff.

The information contained in the Standard of Care document has been approved by the study's Medical Directors (co-investigators) as providing fundamental diabetes self-management information to patients with T2D. In the Standard of Care document, patients are instructed that this information does not replace individual guidance given to patients from their providers.

Each participant will be assigned a coach who will provide education and support by phone and secure text messaging. During weeks when patients are using the CGM system, they will be scheduled to receive a weekly phone call from their coach. Otherwise, patients can reach out to their coach by leaving a voicemail for the coach. Coaches will return calls within two business days. Education will be centered around the four educational objectives (food intake and PPG, walking to reduce PPG, medication adherence, and nighttime glucose monitoring) and reinforcement of messages in the patient standard of care document. The coach will provide education on how to optimally use the RT-CGM system for self-discovery, focusing on effective times to look at the RT-CGM and behaviors that are likely to impact the CGM (outlined above). Coaches will assist participants in setting personalized goals and act as a

sounding board for participants to discuss their self-discoveries. Coaches will review with patients the Rule of 15 to deal hypoglycemic episodes.

Integration with patient care

Throughout the program, patients will be instructed to follow their normal care plan as directed by their physicians and as consistent with ADA 2017 standard-of-care guidelines. This includes taking medications as prescribed; engaging in physical activity—especially walking after meals; eating a diet that optimizes glucose control through food choice and timing; responding to hypoglycemia symptoms with a fingerstick and consuming a pre-determined amount of glucose; and monitoring emotional wellness. By providing a continuous graph of each participant's glucose, the CGM system illustrates how the above-described glucose management behaviors impact the participant's glucose.

Should patients in the course of the program experience any health problems associated with the use of their CGM devices, they will be directed to contact the study doctor's clinical research coordinator. The coordinator will assess the severity and relatedness of the event and arrange for appropriate care. Should patients mention a potential study-related health concern to their coach, the coach will actively work to assure the patient speaks with the study doctor, either through a warm transfer or callback.

Program devices

Dexcom CGM System

Patients in this study will employ an investigational-use only (IUO) CGM system manufactured by Dexcom, Inc. (San Diego, CA). The devices in this system (a sensor with auto-applicator, a transmitter, and a mobile application) represent a variation of the Dexcom G6 CGM system which received approval by the FDA under an investigational device exemption (IDE) on April 28, 2016. In 2017, Chesapeake IRB designated the device as a Non-Significant Risk device for our research protocol Pro00021722. The ways in which these study devices vary from the G6 system and the commercial G5 system are described here as well as in the attached Investigator's Brochure.

The investigational system represents several improvements over the commercially-available Dexcom CGM systems. The investigational applicator is designed to improve ease of use and reduce the risk of user error compared to Dexcom's G5 commercial device by simplifying the application process. While the commercial device requires the user to perform multiple actions to deploy the sensor-delivery needle, retract the needle, and release the applicator from the transmitter holder, the investigational applicator performs all of these steps with just one action by the user.

The investigational sensor has a lifetime of 10 days, as opposed to the 7-day lifetime of Dexcom's commercial G5 sensor. As a result, users will not need to change their sensors as often, further reducing risk for any difficulties or inconvenience associated with sensor application. The sensor has also been redesigned to reduce sensor error associated with the use of acetaminophen, thus improving the reliability of sensor readings.

Compared to the Dexcom G6 transmitter, the IUO transmitter has a lower design profile to improve everyday wearability.

The mobile (smartphone) app displays glucose information in real-time. To maintain the accuracy of these readings, the system must be calibrated periodically based on fingerstick readings from a blood glucose meter. After initial calibrations, the investigational app requires less frequent calibrations than

the commercial device. While the commercial system requires calibration every 12 hours, after the first day the investigational system requires calibration every 24 hours. This improvement is expected to further improve the usability and acceptance of the CGM system.

During CGM wear, a sterile disposable glucose sensor is applied on the abdomen and held in place with an adhesive. The wire-like sensor is not significantly thicker than the needles used in syringes for insulin injection. The needle insertion depth ranges from 0.35 – 0.55 inches.

Once in place, the sensor pod consists of a glucose oxidase-based electrochemical sensor placed subcutaneously to measure interstitial glucose concentrations over a 40-400 mg/dL range. The transmitter attached to the sensor pod will wirelessly send the sensor's glucose measurements via Bluetooth to a smartphone for display of trends and continuous glucose readings every 5 minutes. Readings will also be stored in the cloud. In using cloud storage, the smartphone also permits protected sharing of data with coaches and other authorized study staff. The smartphone also provides a more user-friendly interface, including larger text. Alerts, alarms, and reminders will be set to minimize disruption for the patient while still supporting proper use of the device and allowing for patient customization.

Participants will need to calibrate their CGM systems using a commercially available blood-glucose meter per manufacturer instructions.

As part of the system's instructions for use, users are informed of the following:

- The system does not replace blood glucose measurements.
- Blood glucose values may differ from sensor glucose readings and the value from the blood glucose meter should be used for treatment decisions.
- Symptoms of high and low glucose should not be ignored. If sensor readings do not fit with symptoms, blood glucose should be measured with a blood glucose meter.

Upon completion of 10 weeks of CGM and activity tracker use, patients will be asked to return their CGM transmitters and unused sensors. Patients may be offered the opportunity to continue to use their smartphones and activity trackers as long as they continue to sync the tracker at least every three weeks through August 31, 2018. During the study, patients can reach out to their coaches as desired by phone and secure text messaging. Likewise, coaches can reach out to patients by phone and secure text messaging. Automated text messages will also be sent to patients as part of the program. Patients will return their smartphones and activity trackers at the end of the program.

Blood-Glucose Meter

An over-the-counter blood-glucose meter will be used to approximate levels of glucose in the blood to calibrate the Dexcom CGM System. The battery-powered blood glucose meter will consist of an on/off switch, a display, and an opening for test strips. Patients are expected to already own their own blood glucose meters as part of their normal standard-of-care. Patients who do not have a glucose meter will be provided one to use and keep following the study.

Activity Tracker System

To help patients observe how physical activity impacts glucose levels, patients will be provided with a Fitbit Charge 2 wrist-worn activity tracker. This activity tracker will display in real-time the cumulative number of steps taken by the patient each day.³ The patient will also be able to view his/her step history via an app on the smartphone. The Fitbit activity tracker system consists of an activity tracker, a compatible charging cable, and an associated smartphone app that syncs step data to the Cloud.

Patients will be invited to wear the activity tracker from the start of the program.

Per protocol, patients will be asked to use their activity trackers for 10 weeks during the same period of CGM use. Afterwards, patients may be given the opportunity to use their activity trackers through August 31, 2018, if patients sync their tracker data at least once every three weeks. Patients will return the tracker and the smartphone at the end of the study.

Training of site staff

Registered nurses will provide in-person assistance to patients in the application and use of the CGM. These nurses, along with program representatives, and all study staff interacting with patients will also be trained to answer any questions patients may have related to providing informed consent, and will be trained by the Sponsor in their respective roles. All research staff (excluding clinic staff) who interact with patients will receive training on the ethical treatment and safety of human research subjects.

7. Selection and Withdrawal of Subjects

Study participants will be recruited from UnitedHealthcare members in the Las Vegas area who are enrolled in a Medicare Advantage plan (Senior Dimensions®). To be eligible for the program, patients must meet specific inclusion/exclusion criteria. All Medicare Advantage patients who meet this criteria will be invited to participate in the program regardless of their latest A1C test.

We intend to enroll 500 program participants (defined as those to whom program materials and devices have been delivered). When 500 participants have been enrolled, any patients that have been recruited but who have not yet been enrolled (including those who may have signed a consent form) will be asked if they would like to be notified of any other upcoming study opportunities for which they may be eligible.

Inclusion Criteria

To be included in the study, patients must:

- Be diagnosed with type 2 diabetes
- Be able to read, speak and understand English
- Have access to a telephone
- Have a Medicare Advantage plan through Senior Dimensions®

³ The Fitbit may also record and display distance walked, calories burned, active minutes, hourly activity, stationary time, heart rate, and sleep stages, duration, and consistency; and contain tools to help users meet their personal health and fitness goals.

Exclusion Criteria

Patients will not be eligible if any of the following criteria pertain to them:

- Pregnant
- Blind
- Deaf
- Receiving chemotherapy or radiation therapy to treat cancer (either now or within the last six months)
- Misusing any drugs (including alcohol, painkillers, hallucinogens, or others)
- Critically ill
- Diagnosed with or experiencing:
 - Kidney disease stages 4 and 5
 - End stage renal disease
 - Severe liver disease
 - Dementia
 - Schizophrenia
 - Bipolar disorder
 - Autism
 - An intellectual or learning disability
 - Arrhythmias other than atrial fibrillation
 - Congestive heart failure
- Has had a:
 - Myocardial infarction within the last 6 months
 - Stroke within the last 6 months
 - Stroke that resulted in significant disability (e.g., unable to write clearly or walk)

When a patient is referred to the program by the clinic and this patient is not eligible due to a diagnosis of congestive heart failure, one of the study's medical advisors will make a clinical judgement as to whether the severity of the patient's congestive heart failure warrants exclusion from the study.

Initial eligibility will be determined using medical and pharmacy claims data. Since these claims will not address all inclusion and exclusion conditions, patients will confirm their eligibility by reviewing the eligibility criteria provided in the consent packet and the consent form, and attesting to their eligibility by signing the consent form.

If during the study a patient's status changes such that s/he is no longer eligible to participate, the patient will be removed from the study and will be asked to return all devices (with the exception of used sensors, the used transmitter, and the glucometer if the patient received one).

Patient Participation

All program participants will participate at-will and have the freedom to terminate their participation at any time. Participants, including those who intend to withdraw from the program or those who have withdrawn will be able to access program coaches for assistance with any program-related questions or issues.

During the time that patients use the CGM system, coaches will schedule weekly calls with them. If patients demonstrate by their actions that they no longer want to participate in the study by no longer syncing their CGM or activity tracker data, outbound call or text messaging efforts will be made to reach the patient. If after three weeks there has been no data received and no communication with the patient, a voicemail will be left asking patients to reply within three days or they will be considered dropped from the study. No response to these voicemails will result in the shipment to these patients of a postage-paid box and a letter. The letter will inform patients that they are considered as non-participating and need to return the CGM devices, activity tracker, and smartphone.

During the course of the program, should any participant report medical issues that may affect that patient's ability to participate in the program, the patient will be directed to consult with his/her physician.

8. Treatment of Subjects

This program will provide dedicated resources to assure informed consent.

Patients will be instructed to continue to follow the advice of their physicians, including taking prescribed medications.

Patients will sign and date an IRB-approved consent form that indicates that if they are injured from applying or wearing the CGM system or activity tracker in the course of the program that they will receive treatment and that their insurance may be billed. Copays and costs related to injuries from applying or wearing the CGM devices and activity tracker which are not paid for by patient's insurance will be covered by Savvysherpa (Sponsor). Charges for medical care will be based on insurance contracted rates and not mastercharge sheet prices.

Patients with medical concerns related to the study devices will be instructed to contact the study doctor and/or his staff for evaluation. Patients with any other health concerns will be encouraged to see their health providers, or if needed, seek emergency assistance as part of their normal standard of care.

Patients and study staff will be provided with the device manufacturers' technical assistance telephone numbers to report any device-related problems or concerns.

Patients will be provided with a program phone number to call and report other problems or concerns. Patients who need assistance with the application and use of the CGM system can call their coach or be scheduled for an educational class.

9. Assessment of Safety

While the proposed program is essentially educational in nature, every effort will be made to ensure that patients are using their devices properly. Should any concerns about patient safety arise, patients will be directed to see the study doctor or his staff, and if necessary, seek emergency medical assistance.

The Dexcom Continuous Glucose Monitoring System described in this protocol is considered by the Sponsor to be of non-significant risk as it does not meet the definition of a significant risk device per 21 CFR 812.3(m), in that CGM

- (1) Is not intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- (2) Is not purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- (3) Is not for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- (4) Otherwise does not present a potential for serious risk to the health, safety, or welfare of a subject.

Additionally, the system is being used in a manner not entailing significant risk, in that it is being used for educational purposes and as an adjunct to normal care.

The following information supports a non-significant risk determination for the device that will be used in this protocol:

- Chesapeake IRB has previously designated this CGM investigational device as a Non-Significant Risk device for our research protocol Pro00021722;
- FDA-approved Dexcom CGM Systems have been considered a non-significant risk device;
- The CGM devices used in this study are being used on-label in the intended population;
- The Medtronic-Minimed Guardian RT® CGMS, an FDA-approved device using similar technology, has been considered a non-significant risk device;
- The FreeStyle Navigator® CGMS, an FDA-approved device using similar technology, has been considered a non-significant risk device;
- The insertion needle thickness used in the device is not significantly thicker than the needles used in syringes for insulin injection and the potential needle insertion depth is less than 0.6 inches;
- None of the expected device-related adverse events as defined in the protocol and associated documents would be life-threatening or would result in any permanent impairment of a body function or permanent damage to a body structure;
- There are no expected electrical safety risks as the device has passed the electrical safety tests as per EN45502-1 and EN60601;
- If the subject feels any discomfort during the course of the study, he/she will be able to remove the device immediately (the device is not permanent);
- The device is being used to complement, not replace, self-monitoring of blood glucose meter information, and readings are not intended to be used alone to make diabetes self-management decisions. As with the currently approved device and per intended use of similar technologies, subjects in the study will be instructed not to use the device for diabetes therapy or management;

- Subjects will be instructed to monitor their blood glucose levels as per their usual practice.

Adverse events (AE) associated with the use of the device include pruritus (severe itchiness present 48 hours after removal), erythema (reddening of the skin present 48 hours after removal), and inflammation (swelling and pain, defined as 8 or greater on a 10 point scale 48 hours after removal) where the adhesive touches the skin; local infection at insertion site; and shooting pain located at the site of the sensor (defined as 8 or greater on a 10 point scale). Rarely, the sensor wire will fracture when the sensor is being inserted, worn, or removed. If a sensor breaks and no portion of it is visible above the skin, the participant will be instructed to not remove it and seek medical care from the study doctor and/or his staff.

No serious adverse events (SAE) or Unanticipated Problems (UP) are expected as a result of participation in this minimal risk study. However, AE, SAE and UP will be monitored in the following ways:

- Participants in the study will be instructed to call the study doctor's clinical research coordinator to report all AE, SAE and UP related to the use of the CGM devices. The study doctor and/or his staff will assess the severity of any health problems associated with the device, and if needed, see the patient at the study clinic to assure appropriate care.
- Study coaches will listen for any reports of AE or SAE or UP in the course of their communications with participants, and will connect reporting patients with the study doctor's clinical research coordinator so events can be assessed and documented and patients can receive care, if needed.
- Any reports of AE or SAE or UP received by Dexcom's Technical Support representatives will be documented and reported to the Sponsor. Coaches will then promptly notify the study doctor's clinical research coordinator of these reports so that the coordinator can then follow up with the patient to assess event severity and relatedness, and schedule the patient for care, if needed.

The Sponsor-Investigator will receive CGM-related AE and SAE and UP information from Dexcom through secure data transfers. AE and SAE and UP information from the study doctor will also be stored and transferred securely. Any other records pertaining to AE and SAE from patient conversations with program staff will be recorded and documented using call-management software and the patient's Case Report Form.

The Sponsor-Investigator will ensure proper reporting of AE and SAE and UP to Chesapeake IRB, the CGM manufacturer, the FDA, and any other regulatory bodies according to regulations and standard operating procedures. (See Appendix C for a chart illustrating the reporting process, and Appendix B for AE assessment guidance for coaches.)

Patients will be provided with a summary printout of their recorded CGM data at the end of their participation with CGM. Patients can request a summary printout anytime during the trial. Patients can share their CGM data with their providers.

The Standard of Care guidelines associated with the program direct patients to seek medical care when needed. Guidance exists within the guidelines to seek medical advice when glucose values are extremely high over long periods of time, fluctuate rapidly from high levels to low levels and vice versa, or a

pattern of low glucose values is present. Coaches will remind patients of these guidelines but will not give medical advice. Coaches can send summary CGM data to patients upon patient request.

Because the CGM data is an adjunct to patients' diabetes care, the investigator and research staff will NOT constantly monitor patients' realtime CGM data nor will research staff and coaches contact patients' medical providers on behalf of patients when low or high CGM values are observed. Patients will be responsible for using the blood glucose meter to manage their diabetes and to seek medical attention when needed.

Episodes of hyperglycemia or hypoglycemia that require patients to seek medical attention will be considered an AE or SAE depending upon the situation.

10. Data Collection and Statistical Analysis

This study is a formative evaluation to assess the implementation of a program that uses state-of-the-art tools and techniques (e.g. streamlined patient set-up, multi-channel education through coaching, and high-quality, patient-friendly devices) to engage patients in an educational program for CGM-based diabetes management. To do this, we will collect data to measure the degree to which each of the three program elements has been effective.

As an evaluation study, the study is not hypothesis-driven, and involves no statistical analysis plan for hypothesis-testing. Further, as participation will be based on self-selection with no group assignment; there is no sample size calculation. Rather, this study is exploratory in nature.

In this study we anticipate enrolling 500 patients with T2D. Since our primary aim is to perform a formative evaluation of a new program, we plan to collect measures relevant to enrollment and device distribution processes, telephone and secure text messaging with study participants, and any challenges encountered (by both study participants and administrators) in the implementation of the program. We view these measures as benchmarks that will inform future program iterations and quality improvement efforts. We will also investigate whether the program may be more effective for certain subgroups; for example, whether observed differences in program adoption, persistence, behavior change, or changes in diabetes management markers (e.g., estimated glucose values and hemoglobin A1C measurements), vary according to such factors as age, familiarity with technology, educational attainment, or disease progression.

Data Collection

Since our program achieves its efficacy through education, self-discovery, and the behavior change that results from that education, we will collect data about our ability to connect with and engage participants in the program. Specifically, we will collect data on recruitment efforts (e.g., recruitment rate; patient preferences in setting up their devices (i.e., via self-start, home visit, or in-class); information related to study enrollment (e.g., method and date of enrollment, pre-program survey); and program engagement metrics (e.g., device calibrations, use of companion mobile application, CGM component completion rates). By enrolling in the study, participants consent to the acquisition, review, and analysis of data from their medical records. We will also collect the following data, which will allow us to both evaluate the program as delivered, and to help us tailor future versions of the program to better serve the participants that we enroll:

- Reasons for declining to participate, as given to program personnel at different contact points
- Recordings of coaching calls and introductory training sessions
- Observations from coaches about the most effective calling procedures, behavioral strategies, talking points, and online facilitation techniques
- Time dedicated to device preparation, and to each aspect of the introductory training session
- Total letters sent, and the number returned due to bad addresses
- Recruitment strategies to which each potential participant was exposed
- Total coaching calls attempted and completed per participant, and the durations of those calls
- Suggestions made during coaching calls and during the exit interview about how to improve the program
- Demographic information such as age, education, and social support
- Survey results to assess familiarity with technology such as computers and smartphones, knowledge about nutrition and self-care, and self-efficacy in disease management.

A secondary goal is to evaluate the effectiveness of the program as implemented in this study. On all patients we will collect interstitial glucose levels from the CGM device, activity and other available data from the activity tracking device, any changes in prescription medication use during the normal course of participants' medical care outside of the study, routine lab measures, any changes in mental health (specifically depression), and total costs of medical care before, during, and after the study. Patients will be asked to share information contained in their medical records and claims through December 31, 2027, even if patients stop early from participating in the study.

The following measurements will be collected from study participants:

| Data Elements from Participants | Source | Data Collection Time | | | |
|---------------------------------|--------------------------------|----------------------|------------------------|---------------------------|-------------------------------|
| | | Study Enrollment | During course of study | CGM Completion (10 weeks) | Post-Program through 12/31/27 |
| Age | Medical Record ¹ | X | | | |
| Time since diabetes diagnosis | Enrollment Survey ² | X | | | |
| Race/Ethnicity | Enrollment Survey ² | X | | | |
| Hemoglobin A1C | Medical Record | X | | X | X |
| Diabetes Distress Questionnaire | Enrollment Survey ² | X | | | |
| Cancer Indicator | Medical Record ¹ | X | | | |
| Heart Failure Indicator | Medical Record ¹ | X | | | |
| | | | | | |
| Diabetes medication indicator | Medical Record ¹ | X | | X | X |
| Metformin indicator | Medical Record ¹ | X | | X | X |
| Glipzide indicator | Medical Record ¹ | X | | X | X |
| Pioglitazone indicator | Medical Record ¹ | X | | X | X |
| Rosiglitazone indicator | Medical Record ¹ | X | | X | X |
| Sitagliptin indicator | Medical Record ¹ | X | | X | X |
| Linagliptin indicator | Medical Record ¹ | X | | X | X |
| Saxagliptin indicator | Medical Record ¹ | X | | X | X |
| Exenatide indicator | Medical Record ¹ | X | | X | X |
| Liraglutide indicator | Medical Record ¹ | X | | X | X |
| Glyburide indicator | Medical Record ¹ | X | | X | X |
| Basal insulin indicator | Medical Record ¹ | X | | X | X |
| Bolus insulin indicator | Medical Record ¹ | X | | X | X |
| Other prescription drug use | Medical Record ¹ | X | | X | X |
| Interstitial glucose levels | CGM device ³ | | X | X | |

| | | | | | |
|---|---------------------------------------|---|---|---|---|
| Contacts with program coaches | Coaching platform ⁴ | | X | X | X |
| Interactions with secure texting | Digital app ⁵ | | X | | X |
| Accelerometer data, including daily steps, distance walked, calories burned, active minutes, hourly activity, walking goal achievement, stationary time; heart rate; sleep stages, duration, and consistency; and any other metrics as available. | Activity tracking device ⁶ | | X | | X |
| Total cost of medical care during program | Medical Record ⁷ | | | | X |
| WHO-5 Well-Being Index (depression screen) | Pre/post study surveys | X | | | X |
| Exit Interview Questionnaire | Post-study survey ⁸ | | | | X |

¹These items will be abstracted from the patient's medical record or administrative claims by Savvysherpa research staff

²This survey will be mailed to participants or delivered over the phone by a coach or call agents.

³Dexcom will securely transfer CGM-based EGV measurements to Savvysherpa.

⁴"Coaching platform" refers to any interactions with human coaches via phone or secure text message.

⁵Savvysherpa will collect patients' use of text messaging.

⁶Savvysherpa will data from activity trackers via participants syncing their activity tracking devices.

⁷Savvysherpa researchers will identify this from participants' administrative medical claims.

⁸This survey will be mailed to participants or delivered over the phone by a coach or call agents.

Statistical Analysis

Formative evaluation

During and after the study, we will conduct a qualitative assessment to evaluate the implementation of the proposed diabetes self-management program. Qualitative information to be analyzed will include coaches notes, descriptions of requests for technical support, observations of home visits, and information provided through participant surveys. The purpose of this study is to generate insights that will inform a future, larger study evaluating the effectiveness of the program across a larger study population. While we will measure many of the same outcomes in that future study, the design and implementation will evolve based on the results of the current study. We intend to conduct multivariate analyses to evaluate program implementation performance in various subgroups; for example, we will evaluate enrollment rates, program completion rates, and other participation metrics against participant demographics and disease progression measures. This analysis will be carried out using intent-to-treat analysis principles.

Program effectiveness

While it is not the primary aim of this study, the data we collect will be used to evaluate the program's effectiveness in maintaining participants' glycemic control. We will evaluate changes in participants' A1C measurements over time, as well as summary statistics of interstitial glucose measurements obtained from CGM devices, similar to those examined by Lind et al. (Lind, 2017). Endpoints of interest to this analysis include but are not limited to average measured glucose levels over the course of the study, glucose variability, and frequency and nature of medical care utilization throughout the study timeframe. This analysis will provide insight into patients' ability to self-manage their glucose levels using the program, as well as help refine the program and inform the design of a future, larger study of its effectiveness.

All eligible participants will be included in the analysis.

11. Direct Access to Source Data/Documents

The Sponsor-Investigator, Dexcom, and the study doctor will permit any program-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), deemed necessary by the IRB, and will provide direct access to relevant source data/documents as may be required.

12. Risks

This is a minimal risk study. Program participants are being asked to wear a Fitbit activity tracker and a Dexcom CGM system.

Risks of the Activity Tracker Device

The Fitbit has a wrist band. Skin irritation from these devices is a remote possibility (there are very few reports in the online literature regarding this occurrence with similar devices). Study participants who experience skin irritation will be instructed to remove the activity tracker during sleep, and/or to alternate wearing it on the opposite wrist. There is also a slight risk that the privacy of the activity tracker data could be exposed if an unauthorized source hacks into the activity tracker's data system. Due to security and authorization that Savvysherpa has in place this risk is minimal.

Risks of CGM

When the wire-like sensor is deployed by the applicator, participants can expect a sensation similar to a needle insertion for a blood draw. Risks of CGM use include discomfort during sensor insertion, along with pain, inflammation, redness, swelling, minor bleeding and minor infection at the sensor insertion site. Participants might also experience these symptoms as a result of contact between the adhesive pad of the sensor and the skin. In rare cases, an infection can spread to other parts of the body.

Allergic reactions can develop in response to the sensor, the adhesive, and other parts of the CGM. If these symptoms occur, participants have the ability to remove the CGM at will and can anticipate that their symptoms will clear up within one week.

The sensor and/or applicator may fracture during use. If a sensor remains in the skin, there is minimal risk to the patient as long as a physician confirms there are no symptoms of infection or inflammation.

Patients will be advised that the investigational sensor, transmitter, and smartphone must be removed before Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, or diathermy treatment. The device is MR Unsafe. Participants should not bring any portion of the device into the MRI environment. The Dexcom IUO CGM System has not been tested during MRI or CT scans or with diathermy treatment. The magnetic fields and heat could damage the device, causing it to stop displaying glucose readings, display inaccurate glucose readings, or prevent alerts.

Patients will also be advised of CGM system warnings that may affect the proper operation of the device and/or the patient's safety. These warnings will be described in the informed consent and authorization form, and in the informational materials provided to patients when they receive their systems.

Patients will be provided with a phone number for Dexcom's Technical Support. Staff for this line will be well-qualified to address any potential questions and risks associated with the investigational device. Significant or serious health risks with CGM are not anticipated.

The same precautions have been taken to code and/or encrypt the investigational system's electronic data as have been taken with the commercial Dexcom devices. Regardless, throughout the program, patients will be advised not to rely on the device to make any treatment decisions, and to measure their blood glucose in order to confirm any symptoms of hypoglycemia.

Risks of Glucose Meter

Finger-stick blood samples will be taken during this study. This may cause some discomfort, pain, bruising, and/or soreness afterwards. Rarely, an infection may occur. Routine finger-stick sampling for use with a blood glucose meter is already standard-of-care for T2D patients.

Risks of Medical Record Review and Data Collection

This project involves extracting Protected Health Information (PHI) from patients' medical records. PHI will also be extracted from Dexcom patient databases. Activity tracker data will be synced via https from the trackers to the secure servers of Fitbit. Data collected from the activity trackers will then be sent via https to Savvysherpa's secure servers. Personally Identifiable Information (PII) will be collected from health providers, Dexcom, and/or Fitbit, as well as through survey responses, coach-patient texts, call recordings, online program engagement, and/or in-person group participation at educational classes. The combined dataset will be de-identified by removing personal identifiers from each system and replacing them with a unique study identifier.

The combined data set will be stored in Savvysherpa's HITRUST-certified secure server environment that can only be accessed by authorized personnel via a physically secured room. Any links between personal identifiers from the source systems and study identifier will be deleted ten years after study completion. Recordings of educational classes, coaching sessions, and coach-patient texts will also be deleted ten years after study completion. PII associated with these recordings may be visible to program staff and Dexcom in the course of quality improvement efforts and the development of training, but the identities and privacy of participants will otherwise be maintained.

There is a risk that the information could be inadvertently disclosed to another entity although the risk is very small given the data security measures in place.

Risks of Unsecured Communication

Participants will be contacted via phone and secure text messaging. Phone communication will not be secured putting the participants at risk of having PII inadvertently disclosed. Secure text messaging is subject to hacking.

13. Benefits

Participants in the study may develop a greater personal understanding of how their lifestyle habits (e.g. physical activity, diet) affect their glucose levels (e.g. average glucose, PPG, GV, and NG). What they learn will help them understand better how to self-manage their glucose and be healthier. Information gained from this program will be used to further refine the program so that it can benefit more people.

14. Compensation

During the study, participants will use a free Fitbit Charge 2 activity tracker and a Dexcom CGM system for 10 weeks. Study participants will also have access to their personal CGM data (up to 24 hours) via the Dexcom CGM system app while using the CGM system and in a summary report after they have finished

using the system. During the 10 weeks of CGM use, participants will receive free over-the-phone and secure text messaging communication with coaches related to CGM and diabetes self-management.

To compensate participants for the time it will take to get set-up and use their devices (e.g. receive a home visit/attend a class/attend an in-clinic meeting, or seek other assistance; study and understand program materials; maintain device function via calibrations and charging, return study devices, etc.), patients will be compensated up to a total of \$250 according to the following schedule:

| Study task | Compensation |
|--|---------------------------------|
| Wearing a Dexcom® CGM sensor for the first 10 days and wearing Fitbit Charge 2™ for 7 out of those 10 days | \$190 |
| Wearing a CGM sensor for each additional 10 days and wearing Fitbit Charge 2 for 7 out of those 10 days | \$10 (total not to exceed \$60) |

Patients need not wear their 10-day sensors continuously, nor will they need to wear the same sensor for 10 days in order to qualify. Compensation will be provided in the form of a gift card after the participant has completed the program, or upon withdrawal from the study, whichever comes first.

Participants may be invited to continue to wear and upload data from their activity trackers (defined as syncing at least every three weeks through August 31, 2018). Patients will return the smartphone and activity tracker to the Sponsor at the end of the study.

Patients who received a glucometer (\$40) may keep it.

Study participants will also continue to have access to their personal physical activity dashboard after the study ends.

15. Quality Control and Quality Assurance

All study staff interacting with patients will receive training in the fundamentals of the ethical treatment and safety of human subjects. The Principle Investigator will be responsible for assuring that program staff receive this training and that the entire research team adheres to the protocol. The Principle Investigator will also ensure that the principles of Good Clinical Practice are being followed.

In addition, the research team participating in this study represent individuals whose qualifications and experience have equipped them to collect and analyze confidential patient data. The study's medical advisors (Co-Investigators) will meet with the Principle Investigator to review progress and offer any direction that may be needed with regard to patient safety. The HITRUST-certified environment in which data will be stored will provide a high level of protection for all data collected (see below).

16. Ethics

The proposed program will involve patients with a medical condition. The program recruitment strategies assure that prospective patients have access to a staff member with whom they can discuss and ask questions about the program before signing an informed consent form and then while participating in the program. Patients who receive study materials in the mail will have a minimum of two days to review study materials and ask questions of research staff before signing and dating the informed consent form. Patients who meet with study staff (e.g. at a home visit, educational class, or in-

clinic meeting) will be given ample time to read the consent form and as much time as needed to talk with a program representative about the study. There is no limit to the number of times patients may speak with program staff before making a decision about whether to participate.

As some participants may not want their condition to be known to others, they will have the option and resources to start using the CGM system without having to attend a class. The program will serve as an adjunct to normal medical care.

Patients will have the freedom to use the CGM system and activity tracker at times of their choosing. They will be participating at-will, may withdraw from the study any time, and will face no adverse consequences from the program or their providers if they withdraw from the study or choose not to participate at all.

We want this study to be minimal risk. As such not all patients with T2D will be eligible. The inclusion/exclusion criteria preclude certain patient populations with T2D that would benefit from participating in the study. However, resource constraints and the management of risk do not allow for all patients with T2D to participate at this time.

17. Data Handling and Record Keeping

Data will be collected by these entities:

- Savvysherpa will collect medical record data and claims cost data from participants' medical records.
- Dexcom will collect interstitial glucose data and data related to device use (such as calibration timestamps) from participants in the CGM program.
- Savvysherpa will collect program data from the participants directly and from the program. Program data will include survey responses, call recordings, coach-patient secure texts, and/or in-person group participation at educational classes.
- Fitbit will collect data from activity trackers.

Dexcom, Fitbit, and provider data will be shared with Savvysherpa. Savvysherpa will have access to versions of the data that include personally identifiable information (PII) and protected health information (PHI) from all of these entities.

PHI will be extracted from the following sources and brought into Savvysherpa's study infrastructure—a HITRUST-certified secure server environment.

- Savvysherpa will work with providers to assure secure data transfer of medical record and claims cost data.
- Claim records and medical records stored in a physically secured room will be accessed by an authorized party, extracted from the room using documented procedures, and loaded into the study infrastructure.
- Dexcom CGM patient readings will be sent from Dexcom secure servers over a secure, encrypted connection to the secure, encrypted study cloud infrastructure.
- Data from the activity trackers will be synced via Bluetooth to the client's application. From the application, the data will be sent via https to the client's secure servers. From the client's secure servers, the data will be sent to Savvysherpa via https.

- Authorized program advisors will communicate with patients via phone call, and also by secure text messaging to smartphones issued to each patient. Messages will be delivered to an app utilizing patient's credentials over an encrypted connection to the messaging server. Data, notes, and recordings related to these transactions will be stored within the study infrastructure.

Within the study infrastructure, communication between servers and data stored on servers will be encrypted and accessed via login by authorized personnel for the purpose of assisting and advising patients in the program, and for conducting related analysis and program optimization.

The combined dataset will be de-identified by removing personal identifiers from each system and replacing them with a unique study identifier. A list connecting personal identifiers and the unique identifier will be maintained and stored by Savvysherpa in a separate password-protected database. Any links between personal identifiers from the source systems and study identifier will be deleted 10 years after the completion of the study. Recordings of coaching sessions and group participation activity will also be deleted 10 years after the completion of the study.

Over the course of the program Savvysherpa will have the PII necessary to allow for patient contact as outlined in the protocol. This will be described in the informed consent document.

18. Financing and Insurance

The Sponsor of the study is Savvysherpa, Inc. Some or all funding for this program will be provided by Savvysherpa and/or its affiliates.

19. Publication Policy

The investigators intend to publish on the proposed implementation activities or results.

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21. Supplementary Materials (uploaded)

The Investigator's Brochure for Dexcom's investigational CGM system will be uploaded as part of our argument that this is a Non-Significant Risk device.

22. Appendix A



Piloting the Dexcom CGM System with Medicare Type 2 Patients: Phase 1

September 2016

Executive Summary

As part of a health system's diabetes quality improvement initiative, we created an educational program for Medicare patients with type 2 diabetes incorporating the Dexcom G5 continuous glucose monitoring (CGM) system and activity trackers. In this initial two-week pilot program, we wanted to learn about patients' recruitment rates, compliance with device tasks, and general responses to the CGM system and program model.

Recruitment

- We called 60 patients to invite them to the program, reaching 39 (65%) of patients by phone.
- 16 (27%) accepted the phone invitation.
- 11 (18%) participated by attending the in-service and applying their first CGM sensor.

Compliance

- In week one, 10 out of 11 participants independently calibrated their first CGM sensor after the sensor's two-hour warm-up period.
- In week two, 8 out of 11 participants independently applied and calibrated their second CGM sensor after the sensor's two-hour warm-up period.

General responses

- Participants joined the program primarily because of their physicians' recommendations.
- Participants either 1) quickly understood the potential for using CGM to identify behaviors that impact their glucose, or 2) did not demonstrate an understanding of this relationship and would need more support to do so.
- Many participants struggled with the small-motor skills needed to apply the CGM sensor and transmitter and to press buttons on the receiver and activity tracker.
- Roughly half of participants were interested in using the CGM system again to manage their diabetes.

Conclusions

Based on these findings, we conclude that:

- A portion of this population will wear a CGM device and can, with training, remove and apply CGM sensors by themselves.
- With support for their individual needs, this population can benefit from using CGM to understand and manage diabetes.
- Participants need more time and coaching to use CGM devices confidently and to understand their data.
- Sharing patients' data with program staff would allow the program to design and provide relevant support for those patients.

Recommendations

To continue to develop this program, we recommend:

- Phase 2: Implement and observe other methods of delivering devices, educating patients, and obtaining patients' CGM data.
- Phase 3: Based on findings from phases 1 and 2, design and test this program on a larger scale with the goal of improving patients' A1c levels.

Observational Report

23. Appendix B

Adverse Events Severity and Relatedness Questions

May 2017

When patients share a complaint, program coaches will identify the complaint in the Anticipated Complaints Guidebook. Based on the complaint type, coaches will then ask questions to determine:

1. Severity of the complaint (e.g., Mild, Moderate, or Severe), and
2. Relatedness of the complaint to the use of program devices (e.g., Not Related, Probably Not Related, Possibly Related, and Probably Related)

Coaches will document answers in the templates provided, including the Adverse Event document.

If the complaint falls in any of the severity categories highlighted in **red**, the coach will make a “warm transfer” to the study doctor and/or his staff so that the patient can be scheduled for an ancillary appointment.

If the complaint is an emergency, patients will be instructed to call 911.

If a patient has a complaint that is not listed in the Anticipated Complaints Guidebook, the coach can “warm transfer” the patient to the study clinic for guidance. The coach will document as much as possible in Adverse Event document. Follow up with the clinic will determine severity and relatedness.

Coaches will contact the PI when situations arise that are not covered in the Anticipated Complaints Guidebook.

Skin Redness or Rash – Severity Category

1. On a scale of 1 to 10, where 1 is very little, and 10 is severe, how would you rate the redness of your skin or rash?
 - If 1-5, do not record as AE, **unless itchiness and/or pain are moderate**
 - If 6-7, Mild AE
 - If 8-9, Moderate AE
 - If 10, Severe AE
2. Are you experiencing **pain or itchiness** where your skin is red or where you have a rash?
 - If no, stop.
 - If yes, on a scale of 1 to 10 where 1 is very little, and 10 is severe, how would you rate the **itchiness**?
 - If 1-5, do not record as AE
 - If 6-7, Mild AE
 - If 8-9, Moderate AE
 - If 10, Severe AE

- If yes, on a scale of 1 to 10 where 1 is very little, and 10 is severe, how would you rate the **pain**?
 - If 1-2, do not record as AE
 - If 3-5, Mild AE
 - If 6-8, Moderate AE
 - If 9-10, Severe AE

Skin Redness or Rash – Relatedness Category

1. Where is the location of the redness or rash?
 - If in the same location as the sensor on your skin, then Probably Related
 - If in a location where a sensor was within 2 days, then Possibly Related
 - If in a location where a sensor was 2+ days in the past, then Probably Not Related
 - If in a location where a sensor was never placed, then Not Related

Skin Itchiness – Severity Category

1. On a scale of 1 to 10, where 1 is very little, and 10 is severe, how would you rate your skin itchiness?
 - If 1-5, do not record as AE
 - If 6-7, Mild AE
 - If 8-9, Moderate AE
 - If 10, Severe AE

Skin Itchiness – Relatedness Category

1. Where is the location of the itchiness?
 - If in the same location as the sensor on your skin, then Probably Related
 - If in a location where a sensor was within 2 days, then Possibly Related
 - If in a location where a sensor was 2+ days in the past, then Probably Not Related
 - If in a location where a sensor was never placed, then Not Related

Insertion Site Pain or Discomfort – Severity Category

1. On a scale of 1 to 10, where 1 is very little, and 10 is severe, how much does your pain or discomfort affect your ability to do your daily activities?
 - If 1-2, do not record as AE
 - If 3-5, Mild AE
 - If 6-8, Moderate AE
 - If 9-10, Severe AE

Insertion Site Pain or Discomfort – Relatedness Category

1. Where is the location of the pain or discomfort?
 - If in the same location as the sensor on your skin, then Probably Related
 - If in a location where a sensor was within 2 days, then Possibly Related
 - If in a location where a sensor was 2+ days in the past, then Probably Not Related
 - If in a location where a sensor was never placed, then Not Related

Insertion Site Swelling – Severity Category

1. On a scale of 1 to 10, where 1 is very little, and 10 is severe, how would you rate the amount of swelling?
 - If 1-5, do not record as AE
 - If 6-7, Mild AE
 - If 8-9, Moderate AE
 - If 10, Severe AE

Insertion Site Swelling – Relatedness Category

1. Where is the location of the swelling?
 - If in the same location as the sensor on your skin, then Probably Related
 - If in a location where a sensor was within 2 days, then Possibly Related
 - If in a location where a sensor was 2+ days in the past, then Probably Not Related
 - If in a location where a sensor was never placed, then Not Related

Insertion Site Bruising – Severity Category

1. On a scale of 1 to 10, where 1 is very little, and 10 is severe, how much bruising do you have?
 - If 1-5, do not record as AE, **unless the bruise is getting bigger, see question 2**
 - If 6-7, Mild AE
 - If 8-9, Moderate AE
 - If 10, Severe AE
2. Is the bruise or bump getting bigger?
 - If no, stop
 - If yes, Moderate AE
 - If yes and bruise is significantly getting bigger, Severe AE

Insertion Site Bruising – Relatedness Category

1. Where is the location of the pain or discomfort?
 - If in the same location as the sensor on your skin, then Probably Related
 - If in a location where a sensor was within 2 days, then Possibly Related
 - If in a location where a sensor was 2+ days in the past, then Probably Not Related
 - If in a location where a sensor was never placed, then Not Related

Insertion Site Bleeding – Severity Category

1. Has the bleeding stopped?
 - If no, then: “Is the spot of blood greater than the size of a nickel?”
 - If no, then stop.
 - If yes, then Severe AE
 - If yes, then: “Is the spot of blood greater than the size of a nickel?”
 - If no, then stop.
 - If yes, then Severe AE

Insertion Site Bleeding – Relatedness Category

1. Where is the location of the bleeding?
 - If in the same location as the sensor, then Probably Related
 - If in a location where a sensor was within 2 days, then Possibly Related
 - If in a location where a sensor was 2+ days in the past, then Probably Not Related
 - If in a location where a sensor was never placed, then Not Related

Insertion Site Infection – Severity Category

1. Do you notice signs of infection that include inflammation, drainage, pus discharge and pain?
 - a. If no, then stop
 - b. If yes, on a scale of 1 to 10, where 1 is very little and 10 is severe, how much inflammation, drainage, pus discharge and pain do you have?
 - If 1 – 8, Moderate AE
 - If 9 – 10, Severe AE

Insertion Site Infection– Relatedness Category

1. Where is the location of the infection?
 - If in the same location as the sensor on your skin, then Probably Related
 - If in a location where a sensor was within 2 days, then Possibly Related
 - If in a location where a sensor was 2+ days in the past, then Probably Not Related
 - If in a location where a sensor was never placed, then Not Related

Detached/Broken Sensor Wire – Severity Category

1. Do you see the sensor wire sticking out of your skin?
 - If no, then stop
 - If yes, then ask: On a scale of 1 to 10, where 1 is very little, and 10 is severe, how would you rate your pain or discomfort
 - If 1 – 7, then Mild AE
 - If 8 – 9, then Moderate AE
 - If 10, then Severe AE

Detached/Broken Sensor Wire – Relatedness Category

1. Where is the location of the broken sensor wire?
 - If in the same location as the sensor, then Probably Related (no other logical choice)

24. Appendix C

Clinical Oversight & Adverse Event Reporting

