PROTOCOL TITLE: A crossover study to assess the effect of an artificial intelligence (AI)-based bedtime *smart snack* intervention in preventing overnight low glucose in people with T1D on multiple daily injections.	
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STUDY SITE:	Oregon Health & Science University 3181 SW Sam Jackson Park Rd Portland, OR 97239
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PRINCIPAL INVESTIGATOR:	Clara Mosquera-Lopez PhD
CO-INVESTIGATORS:	*Clinical team:* Leah M. Wilson MD / Diana Aby-Daniel PA-C *Engineering team:* Peter G. Jacobs PhD
IRB:	25174

Background

Despite the growing adoption of continuous glucose monitoring (CGM) and advances in insulin therapies, overnight low glucose is still a common problem for people living with type 1 diabetes (T1D). Nocturnal hypoglycemia, which accounts for 55% of level-two hypoglycemia events (glucose < 54 mg/dL) in people with type 1 diabetes (T1D) and 75% of level-two hypoglycemia events in children with T1D,[16]–[18] is particularly dangerous because people are unlikely to recognize symptoms while sleeping and are also less likely to awaken in response to hypoglycemia alarms from continuous glucose monitors (CGMs).[1], [2] In addition to the serious short-term effects of nocturnal hypoglycemia episodes, untreated nocturnal hypoglycemia can further impair the physiological counter-regulatory system and contribute to hypoglycemia unawareness.[3]–[5] Hypoglycemia unawareness may eventually result in recurrent asymptomatic hypoglycemia[19] and in some cases the dead in bed syndrome due to prolonged exposure to extremely low blood glucose levels during sleep.[20]

Advanced insulin therapies such as continuous subcutaneous insulin infusion (CSII) with insulin pumps and closed-loop systems are now available for managing glucose. However, most people with type 1 diabetes continue to use multiple daily injections (MDI).[21], [22] A recent study showed that MDI users spent more time with sensor glucose <54 mg/dL and experience more hypoglycemia episodes overnight than pump or closed-loop users.[22] Therefore, there is a need for effective interventions that help people with T1D on MDI to prevent nocturnal hypoglycemia.

Our group at the Oregon Health & Science University (OHSU) developed and evaluated a smartphone-based decision support app called DailyDose that combines CGM data and insulin data to provide comprehensive decision support for people with T1D on MDI. DailyDose provides on-demand insulin dosing recommendations, suggestions for glucose management around exercise, and hypoglycemia and hyperglycemia alarms.[6], [7] These features will not be

used in this study. A new feature of DailyDose, which will be evaluated in this study, is a module for prevention of low glucose overnight that provides a personalized bedtime *smart snack* recommendation based on the minimum overnight glucose level predicted by an advanced artificial intelligence (AI)-based model.

Primary Objective

To evaluate the benefit of an AI-based *smart snack* intervention (AI prediction model + personalized bedtime snack) in helping people avoid overnight low glucose as measured by the probability of overnight hypoglycemia, versus CGM-based glucose management (control period).

Secondary Objectives

- To measure time from bedtime until first CGM measurement <70 mg/dL if CGM stays below 70 mg/dL for at least 10 minutes
- To evaluate the effect of an AI-based *smart snack* intervention versus CGM-based glucose management (during control period) on glucose control overnight (announced bedtime + 8 hours) and across the full 24-hour/day study duration, as measured by other glycemic outcomes including the following metrics:
    - % time < 54 mg/dL
    - % time < 70 mg/dL
    - % time 70-180 mg/dL
    - % time > 180 mg/dL
    - % time >250 mg/dL
    - Mean CGM
    - Number of bedtime snacks treatments
- To assess the accuracy of the AI model in predicting overnight low glucose as measured by sensitivity and specificity during the control arm of the study.

Study hypothesis

We hypothesize that a smartphone-based bedtime *smart snack* intervention informed by a low glucose prediction AI model will reduce the probability of overnight hypoglycemia by 50% in people with T1D on MDI therapy compared with traditional CGM-augmented MDI glucose management. The probability of overnight hypoglycemia will be measured as the proportion of nights with nocturnal hypoglycemia episodes during intervention and control periods.

Endpoints

Primary endpoint

Probability of overnight hypoglycemia. An episode of overnight hypoglycemia is counted if sensor glucose is <70 mg/dL for at least two measurements during an eight-hour period following announced bedtime.

Time frame: The level-one unit of analysis is a single night, and each participant will contribute 27 consecutive nights under each condition.

Secondary Endpoints

- Time to the first low-glucose event (<70 mg/dL). Time until first CGM measurement <70 mg/dL when CGM remains < 70 mg/dL for at least 10 minutes
- Percentage of time in clinically relevant glucose ranges:
    - % time < 54 mg/dL
    - % time < 70 mg/dL
    - % time 70-180 mg/dL
    - % time > 180 mg/dL
    - % time >250 mg/dL

  Time frames: overnight (announced bedtime + eight hours) and across the full 24-hour/day study duration
- Mean glucose in mg/dL

  Time frames: overnight (announced bedtime + eight hours) and across the full 24-hour/day study duration
- Accuracy of overnight low glucose prediction as measure by sensitivity and specificity as measured during the control arm of the study
- Change in weight from start to end of intervention period, start to end of control period

Study Type

This is a single-center, open-label, crossover trial with two arms and two periods (2x2) and one-week washout period. The study is designed to evaluate the efficacy of an AI-based bedtime *smart snack* intervention in reducing nocturnal low glucose in people living with T1D on MDI therapy compared with traditional CGM-augmented MDI therapy as the control.

Study population

The study population will be adults with type 1 diabetes, aged 18 or older. Younger participants are excluded as it is appropriate to assess efficacy of proposed intervention first in the adult population. Twenty participants will be recruited to participate in this study.

Power analysis

A sample of 20 participants observed for 27 nights in each condition (total number of nights = 20*27*2 = 1,080) provides >90% power to detect a relative risk (RR) of 0.5 for nights in the intervention period compared to the control period, or >80% power to detect RR≤0.6. This was calculated assuming the risk of 0.09 for overnight hypoglycemia in the intervention period vs 0.18 in the control period (or 0.15 for RR=0.6), and an intra-cluster correlation coefficient (ICC) of 0.25. The effect is equivalent to a 50% relative reduction in the likelihood of nocturnal hypoglycemia.

Statistical power for this sample size was calculated by simulating 1,000 datasets with the assumptions above, fitting the mixed effects model, and determining the proportion of those datasets where the p value for the Wald test of the coefficient of the treatment effect was <0.05.

Control and intervention proportions were set after reviewing other crossover trials of similar interventions in similar populations.[22], [23] The ICC was determined by drawing samples of

20 individuals/27 nights per person per arm from a combined dataset of nights from the T1D Exercise study T1-Dexi dataset (T1-Dexi is the largest known dataset of physical activity in T1D, a joint effort by The Leona M. and Harry B. Helmsley Charitable Trust, Jaeb Center for Health Research, and the T1-Dexi study group) and a dataset provided to our group at OHSU by Glooko Inc (Mountain View, CA, USA), then calculating the ICC in an unconditional model. An ICC of 0.25 is just below the mean for ICCs calculated over 500 resamples ($ICC_{MEAN} = 0.27$). In the resampled source data, 85% of participants experienced hypoglycemia on at least one of the 27 sampled nights.

Protocol summary

Participants will be randomized to either first use CGM only to manage glucose for four weeks (control arm, usual care) followed by four weeks of DailyDose App + bedtime *smart snack* intervention (intervention arm), or vice-versa. There will be a one- to four week washout period between arms. See Figure 1 for a diagram of the study flow.

During the control arm, participants will wear CGM and will manage their glucose as usual (current care). Participants will be asked to wear a smart watch overnight to collect sleep metrics, weigh themselves weekly in the morning before eating, and answer a one-item sleep quality scale survey weekly. We will collect CGM measurements during the control arm for evaluation of effect of intervention and assessment of the accuracy of low glucose prediction.

During the *smart snack* intervention arm, participants will use the DailyDose app when they are getting ready for bed. An AI-based model in DailyDose will predict the likelihood of overnight low glucose at bedtime every night and will recommend a personalized snack to help avoid nocturnal hypoglycemia. The nutritional content of the snack (carbohydrate, protein, fat, etc.) will be dependent on the predicted overnight minimum glucose and the predicted time of the minimum overnight glucose level. During this arm, participants will also be asked to wear a smart watch overnight, weigh themselves weekly, and answer a one-item sleep quality scale survey weekly.

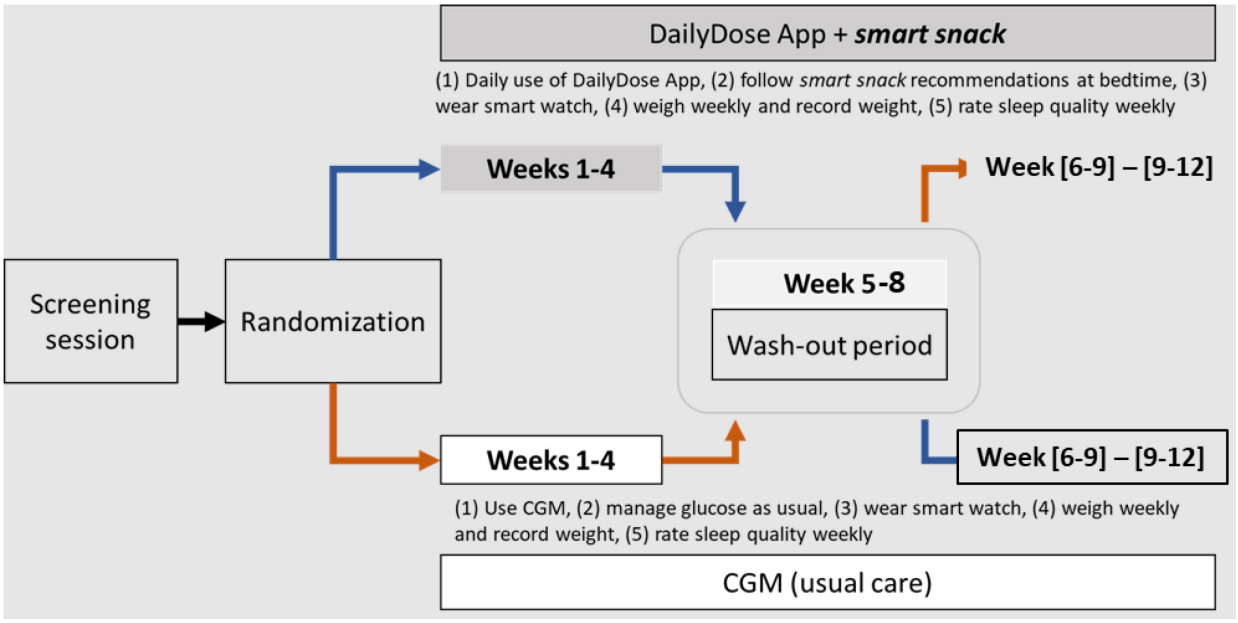


Figure 1. Study flow diagram

Subject criteria

Inclusion criteria

- Diagnosis of type 1 diabetes mellitus for at least 1 year
- Male or female participants 18 years of age or older
- Using multiple daily injections
- HbA1c <10% at screening
- Current use of a continuous glucose monitoring system with at least two episodes of overnight hypoglycemia (defined as sensed glucose <70 mg/dL for at least 10 minutes between the hours of 10 PM and 6 AM) within 30 days prior to screening
- Individuals with history of severe hypoglycemia requiring third party assistance must have a companion in the same dwelling as the study participant who will be linked to the participant's Dexcom app during the control arm of the study, and who is trained in the administration of glucagon.
- Willingness to follow all study procedures
- Willingness to sign informed consent and HIPAA documents

Exclusion criteria

- Individual 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
- Any active infection
- Known or suspected abuse of alcohol, narcotics, or illicit drugs (except marijuana use)
- Seizure disorder
- Use of non-insulin glucose lowering medications
- Use of steroids
- Stage-three or more advanced chronic kidney disease
- Cirrhosis
- Hypo- or hyper- thyroidism that is not medically optimized and on a stable regimen define as Thyroid-stimulating hormone (TSH) outside of the normal reference range based on screening labs
- Adrenal insufficiency
- 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).
- Any clinically significant disease or disorder which in the opinion of the Investigator may jeopardize the participant's safety or compliance with the protocol
- Individual working night shifts

Subject recruiting

Participants 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 newsletter or from the OHSU Subject Recruitment website. Handouts may also be made available to faculty at Tuality, Providence, Kaiser Permanent, 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 participants. Participants will also be recruited from a list of participants who participated in past OHSU studies who have agreed to be contacted regarding future studies (OHSU diabetes research registry and/or www.clinicaltrials.gov). Participants will be contacted using the approved telephone screening script and email template. Non-English-speaking participants 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.

This study will use Epic MyChart® to recruit potential participants. Researchers will send MRNs of potential participants that look eligible for the study to the EPIC research team. EPIC research will load the potential participants into the research recruitment in-basket. Researchers will then run the program and all MyChart® recruitment messages will send to potential participants asking them to participate. There is no risk of duplicate invitations as it is based on MyChart® accounts combined with Epic records and no duplication is possible.

Up to 40 participants may be screened in this study. Goal enrollment is 20 participants. Up to 3 participants will be replaced if needed, with a total enrollment of up to 23 participants.

Withdrawal Criteria

A participant may withdraw at will at any time or at the discretion of the investigator. A participant must be withdrawn if the following applies:

- Protocol deviation having influence on efficacy or safety as judged by the Investigator
- Substantial and repeated non-compliance with trial procedures
- Pregnancy
- Intention of becoming pregnant

Study procedures

Screening session

Screening will take place within 12 weeks prior to the start of the first arm of the study. Screening visits will take place at OHSU's Biomedical Engineering Point of Care (BME POC) Laboratory, the Harold Schnitzer Diabetes Health Center, or virtually using WebEx. This visit will take approximately 1.5 hours.

The participant 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. Prior to any screening procedures, study staff will explain the study, give the participant ample time to ask

questions and consider participation, and ensure that the participant voices their understanding of the informed consent and study requirements. To minimize the possibility of coercion and to ensure that participant is signing the appropriate version of the consent, an informed consent checklist will be used by study staff. For virtual screening visits, participants will be consented over WebEx and study staff will witness them signing consent. Participants will sign two consent forms. After the participant has signed the consent, a copy of the consent/authorization form will be given or sent to OHSU staff by the participant. For virtual visits, participants will keep one copy of the signed consent form and ship one to OHSU overnight. The original will be kept for the source document.

Study personnel will review medical history and medications. A physical exam performed within the last year will be reviewed by investigator via chart review. Height and weight measures will be obtained both in clinic and using a home scale for in-person visits. For virtual visits, height and weight will be self-reported to staff; weight will be measured using a home scale or taken from clinic note within the past year. Blood pressure and heart rate will be obtained from chart review by study staff or from at-home monitoring unit (if participant is in possession of one).

Individuals of child-bearing potential will take a urine pregnancy test (UPT), 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) and thyroid-stimulating hormone (TSH). Blood draw labs and urine pregnancy testing will be completed within 1 week of screening at an OHSU outpatient phlebotomy lab. If a participant had any of these labs drawn with in the last 6 months and results are available for review within Epic or CareEverywhere for the study investigator to review, then those labs do not need to be drawn at this point.

A study investigator will assess inclusion/exclusion criteria and may review the participant's medical record for clarification as needed. The participant's glucose sensor data will be downloaded at the time of the screening visit or accessed online to confirm that the participant has experienced nocturnal hypoglycemia (i.e., two events) in the 30 days prior to the screening visit. A three-digit participant ID number will be assigned to the participant. Participants will complete hypoglycemia awareness, diabetes distress scale, hypoglcemia fear survey, and sleep quality questionnaires that will serve as a baseline to compare against results obtained at the end of the intervention period.

Randomization

Participants will be randomized to start with the control or *smart snack* condition in 1:1 ratio using blocks of size 4 to 6 to ensure balance over the entire sample. Blinding of participants and study staff is not feasible; some analyses may be conducted under blinding.

Participants will be given a study Apple iPhone, and if not already using for personal use, a Dexcom G6 transmitter and sensor to use during the study, as well as an Apple Watch that will be paired with the study iPhone, and a study scale. All study devices, including a urine pregnancy test if applicable will be given to the participant during this visit or delivered via courier.

Control arm (4 weeks)

There will be a visit at the start of the control arm that will be held virtually using WebEx. This visit can be held in clinic. The purpose of this visit is to have the participants learn how to use study devices and the Dexcom app. Using the Webex platform, study staff can connect virtually

with participants for training on the devices and study procedures while they are at home. Participants will be trained in how to use the Dexcom G6 CGM system for those not already using the Dexcom G6 system including insertion, sensor change, and calibration. For participants who are current users of Dexcom G6 CGM system, the insertion, change, and calibration of the Dexcom G6 CGM device will not be discussed during this meeting. Participants will be trained in how to pair the Dexcom G6 transmitter to the Dexcom app on a provided study smart phone, to start and stop a new sensor session, and how to enter calibrations. The CGM alerts will be set at 70 mg/dL and 250 mg/dL. For participants with history of severe hypoglycemia requiring third party assistance, low glucose alerts will be conservatively set to 85 mg/dL. Participants can modify these settings. Participants will be instructed to manage their glucose as they normally do. For those participants with history of severe hypoglycemia requiring third party assistance, a participant's companion (who lives in the same house and is trained in the administration of glucagon as per study inclusion criteria) will be linked to the participant's Dexcom app. The Apple Watch will be paired with the Apple iPhone by the study staff before giving them to participants. Participants will be trained in how to use the Apple Watch, which will be used during the study to collect sleep data. This visit will take approximately 0.5 - 1.5 hours, depending on the subject's experience.

At the beginning of the control period, participants will record their weight using a scale provided by the study staff. During the 4-week control period, participants will wear Dexcom G6 CGM and the study Apple Watch. The Apple Watch will be used to track sleep metrics; therefore, participants are asked to wear the smart watch overnight and charge it during the day.

The goal of this control period is to gather CGM glucose data to assess baseline time in overnight hypoglycemia (<70 mg/dL and <54 mg/dL) and other glucose control metrics (mean glucose, % time in range 70-180 mg/dL, % time below range, % time above range) and evaluate the accuracy of the overnight low glucose prediction algorithm.

Participants will weigh themselves weekly in the morning after urinating and before eating their first meal and to record their weight to track baseline weight changes. Participants will also answer a one-item sleep quality survey weekly. Participants will be contacted weekly by study staff to collect weight measurements and responses to the sleep quality question.

There will be a closeout visit at the end of this arm that will last 10-15 minutes. This visit can be held virtually. Availability of Dexcom CGM data will be confirmed by the study staff and the participant will be asked about adverse events and medication changes. Participants that will use their own Dexcom G6 will share their Dexcom Clarity data with the clinic at this visit.

DailyDose + *smart snack* intervention arm (4 weeks)

There will be a visit at the start of the intervention arm that will be held at OHSU's Biomedical Engineering Artificial Intelligence for Medical Systems (AIMS) Laboratory, the Harold Schnitzer Diabetes Health Center, or virtually using WebEx. A urine pregnancy test might be required for individuals of childbearing potential if the last pregnancy test was more than 7 days prior. This test must be negative before further participation is allowed. During this session, participants will go through the onboarding process with the DailyDose app. This process will occur with the study staff and involve:

- Training on using the Dexcom G6 CGM within the DailyDose app
- Setting up low and high blood glucose CGM-based alerts

- Setting up bedtime for running nocturnal low glucose prediction and receiving bedtime snack recommendation when applicable
- Review *smart snack* options that will be recommended by DailyDose and provided to participants during the intervention period (study protocol, Table 1) as well as present accessible snack alternatives (e.g., those already documented in the study protocol Table 2), in case participants has any allergies or food aversion related to DailyDose *smart snack* options. The study staff will also provide a card with bedtime snack options and replacements so that participants can easily find adequate alternatives to the snacks recommended by DailyDose (study protocol, Appendix F).
- Training on usage of the DailyDose app including how to setup alerts, predict likelihood of nocturnal low glucose, accept/decline *smart snack* recommendations, and use of the insights tab / settings / logbook features
- Training on usage of the Apple Watch

DailyDose has glucose alerts for safety. The Dexcom G6 CGM alerts in DailyDose will be set at 70 mg/dL and 250 mg/dL with user able to adjust. For participants with history of severe hypoglycemia requiring third party assistance, low glucose alerts will be conservatively set to 85 mg/dL. There is a very low glucose alert (glucose <55 mg/dL) that cannot be adjusted.

This visit will take approximately 2-3 hours, depending on the subject's experience.

Participants will go home and use the nocturnal low glucose alert feature of the DailyDose system for the next four weeks. Study staff may contact participants via text message or phone call at other times at the investigator's discretion. At the beginning of the intervention period, participants will record their weight using the scale provided by the study staff. Participants will wear Dexcom G6 CGM and the study Apple Watch. The Apple Watch will be used to track sleep metrics. Participants will use DailyDose and an AI-based prediction model to predict at bedtime the likelihood and time of the minimum overnight glucose. A *smart snack* recommendation will be given if there is a probability of overnight glucose drop below 70 mg/dL. The recommended bedtime treatment will have a carbohydrate content between 15 or 30 g depending on the predicted glucose drop, and a glycemic index defined by the estimated time of the predicted hypoglycemia event. If nocturnal hypoglycemia (glucose < 70 mg/dL) is predicted to occur 4 hours after bedtime, the recommended snack will have a balance of carbohydrate with higher amounts of protein or fat content. Several snack options will be provided to participants, so that there is more uniformity across participants (see Table 1). Participants will be instructed to manage their glucose as they normally do with the addition of these *smart snack* recommendations. Participants will have the ability to accept or decline *smart snack* recommendations.

Table 2 shows nutritional content of the options for recommended snacks.

***Smart snack* options**	**Low glucose predicted 0-4 hours after bedtime**	**Low glucose predicted 4-8 hours after bedtime**

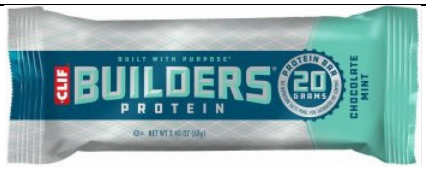
Small		
		
Large	 x 2	 x 2
	 x 2	

Table 1. Smart snack options and recommended amounts based on overnight low glucose predictions. The *CLIF BUILDERS* protein bars are gluten free. The *Oats 'n Honey* bars might contain trace amounts of gluten.

Snack option	Quantity	Measure	Wgt (g)	Cals (kcal)	Prot (g)	Carb (g)	Fat (g)	TotFib (g)	Sugar (g)
SLOW ABSORPTION									
Granola bar, crunchy, oats and honey	1	Each	21	95	1.5	**14.5**	3.5	1	5.5
Protein bar, chocolate peanut butter, Builders	1	Each	68	290	20	**29**	11	--	17
Protein bar, chewy, peanut almond & dark chocolate	1	Each	40	200	10	**15**	12	--	6
Protein bar, chocolate, Builders	1	Each	68	280	20	**31**	9	--	17

Protein bar, vanilla almond, Builders	1	Each	68	290	20	**29**	11	--	16
QUICK ABSORPTION									
Juice drink, cranberry cocktail	4	Ounce-weight	113.4	53.83	0	**13.46**	0	0	13.46
Juice, orange	4	Ounce-weight	113.4	54.65	0	**12.75**	0	0	11.29

Table 2. Smart snack options with macro nutrient analysis.

Participants will weigh themselves weekly in the morning after urinating and before eating their first meal and to record their weight to track baseline weight changes. Participants will also answer a one-item sleep quality survey weekly. Participants will be contacted weekly by study staff to collect weight measurements and responses to the sleep quality question.

At the end of the intervention period, participants will complete hypoglycemia awareness, diabetes distress scale, hypoglycemia fear survey, and sleep quality questionnaires to compare results with the questionnaires completed during the screening session.

There will be a closeout visit at the end of this arm that will last about 30 minutes. This visit can be held virtually. Availability of Dexcom CGM data will be confirmed by the study staff and the participant will be asked about adverse events and medication changes.

Washout period (1 - 4 weeks)

There will be a one- to four week washout period between the control and intervention arms (or between intervention and control arms depending on randomization sequence). The use of the DailyDose app will be discontinued during this period for those participants who were randomized to start using DailyDose. Participants will use their own sensors during the washout period and will manage their glucose as they normally do. Participants are not required to weigh themselves, complete questionnaires, or wear the Apple Watch during this week. No visits are scheduled during the washout period.

Study Completion session

This visit will be completed within 2 weeks of completion of all study procedures. Participants will participate in a 1:1 online meeting with study staff. In this session, study staff will share with participants the factors that contributed to higher predicted probability of nocturnal low glucose during the study (e.g., if a certain type of exercise was to be the biggest contributor to nocturnal hypoglycemia risk). Participants will complete a short survey to evaluate usability aspects of the DailyDose overnight low glucose prevention module using a structured script. This meeting will take about 1 hour and will be recorded after receiving participant's authorization. Participants can also receive information about their risk factors for overnight low glucose and complete the closing survey over the phone in a call with study staff.

Participants will be given shipping boxes for sending all study devices back including the Apple iPhone, Apple Watch, Dexcom G6 transmitter and scale, as well as paper forms with weight records and survey responses. After this session all study devices will be turned in. If the 4-week DailyDose + smart snack intervention period or the control period are paused for a period of time

due to technical problems, the participant may be asked if they can complete additional time in study with the goal to collect at least 2 weeks worth of data in at least one of the arms of the study, such that the participant can be included in the statistical analysis. Additional compensation will be provided for additional time in study. Problems that would qualify for extending the study time are 1) insufficient study supplies requiring the participant to go off of DailyDose + smart snack intervention or to discontinue the control arm for a period of time (such as running out of CGM supplies or bedtime snacks), 2) issues with the smartphone such that DailyDose cannot be used/accessed (such as a due to a damaged phone or problems with the internet connection that prevent data from being uploaded to the remote monitoring system), 3) issues with the CGM system or the capture of the CGM data during the control period or during the intervention period such that DailyDose cannot generate bedtime recommendations due to insufficient CGM data, or 4) scheduling issues such that the participant is unable to complete the control or the DailyDose + smart snack intervention period continuosly. Participants can complete up to 4 additional weeks to make up time the study was paused for technical reasons. Repeating the study time will be optional.The study team will track when participants extend their study time and the reason and this will be included in the annual report to the FDA.

Table 3: Schedule of Events

[1] DailyDose abbreviated Dd

[2] Randomization order abbreviations Control first (CG) Intervention first (IG)

[3] (CG) only

[4] (IG) only

		1st 4 weeks					2nd 4 weeks					
Description of visit procedures	**Screening**	**Dd[1] (IG)[2] or Control (CG)[2] initiation visit**	**Phone check-in**	**Phone check-in**	**Phone check-in**	**Dd[1] (IG)[2] or Control (CG)[2] close out visit**	**Dd[1] (CG)[2] or Control (IG)[2] initiation visit**	**Phone check-in**	**Phone check-in**	**Phone check-in**	**Dd[1] (CG)[2] or Control (IG)[2] close out visit**	**Study Completion Visit**
Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Visit Window		**1-84 days**	**7 days**	**7 days**	**7 days**	**7 days**	**7 days**	**7 days**	**7 days**	**7 days**	**7 days**	**14 days**
Visit Activities and Data Collection												
Consent participant, signing consent form and HIPAA	X											
Assess subject eligibility to participate in study	X											
Measure height	X											
Measure weight	X	X	X	X	X	X	X	X	X	X	X	
Measure BP and pulse	X											
Physical exam performed by investigator	X											

Collect demographic and other baseline characteristics	X											
UPT if applicable and not done in last 7 days (Point of care)	X	X					X					
Collect blood sample for HbA1c, CBC, CMP, TSH testing	X											
Collect information about medical history	X											
Collect information about concomitant medications	X	X	X	X	X	X	X	X	X	X	X	
Download participant's glucose sensor	X											
Complete 3 surveys	X					X[4]					X[3]	
Randomization		X										
Collect data on Adverse Events		X	X	X	X	X	X	X	X	X	X	
Train participants on the study procedures to do at home		X					X					
Train participants on use of Dexcom G6 CGM system with G6 and Clarity apps		X[3]					X[4]					
Train participants on use of Apple Watch		X										
Collect sleep quality survey response			X	X	X	X		X	X	X	X	

Training on using DailyDose including setting up Dexcom G6 with alerts and snack recommendations		X[4]					X[3]					
Schedule upcoming visits		X					X					
Confirm availability of Dexcom G6 CGM data in Clarity						X[3]					X[4]	
Complete usability survey												X
Collect study devices												X

Stopping rule criteria

The study will be stopped if any of the following occur after the start of the study:

- The participant requests that the treatment be stopped
- Participant pregnancy
- One episode of diabetic ketoacidosis as defined as symptoms such as polyuria, polydipsia, nausea, or vomiting, serum ketones >1.5 mmol/L or moderate/large urine ketones, either arterial blood pH<7.3 or venous pH<7.24 or serum bicarbonate <15, and treatment provided in a health care facility.
- One episode of severe hypoglycemia defined as a hypoglycemic event resulting in altered consciousness requiring another person to actively administer carbohydrate, glucagon, or other resuscitative actions.

Cleaning and Disinfecting

All devices will be cleaned and disinfected between participants. The Apple iPhone andApple Watchwill be cleaned by study staff. Technicians who are disinfecting units will wash hands thoroughly and wear gloves. All items will undergo intermediate-level disinfection using Oxivir Tb Germicidal disposable wipes. The disinfectant will be applied and allowed to air dry. After disinfection, when the units are completely dry, they will be placed in a sealed bag labeled with subject information.

Data Collection

We will be collecting de-identified physiologic data from people with T1D. The following data will be collected from participants in this study:

- Glucose sensor data (Dexcom G6 system)
- Self-report *bedtime snack* and exercise data logged by the participant on DailyDose
- Self-report weight logged by participant
- Sleep data from Apple Watch
- Responses to surveys

To collect the data, each participant in the study will be given an Apple iPhone and an Apple Watch. The iPhone will have the Dexcom G6 app and the DailyDose app installed. These apps will collect CGM data and log related to physical activity, bedtime snacks, and overnight low glucose predictions. The data from the Apple Watch will be exported from Apple Health or Apple iTunes as .cda or .xml files.

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

- Collect self-report bedtime snacks and exercise data from the participants
- Aggregate all the data collected from the glucose sensor and self-logged snacks and exercise data
- to be stored as de-identified data within the iCloud storage area of the phone

DailyDose Guidance Remote Monitoring (GRM) Cloud Server

All the data collected will be streamed over the Internet (using secure sockets encryption) to an OHSU secure instance of an AWS cloud storage server every five minutes. Authentication between the phone and the AWS server is done using self-expiring JSON Web Tokens (JWT). Data transmitted between the phone and the AWS server is encrypted using HTTPS/SSL. The code managing authentication and data transfer is Python version 3.7.0. Data acquired from the app is displayed via a physician web portal. The physician web portal user interface is written in Javascript version 1.8.5. There is no personally identifiable data stored with the data sent to the AWS server. The server shall be capable of receiving the following types of data from DailyDose (1) overnight low glucose predictions and smart snack recommendation data, (2) CGM data, (3) alerts, (4) settings. All types of data shall be indexed by subject ID and by date/time. Each data packet shall be accompanied by an authenticated JWT token. The AWS server has undergone a security review by OHSU IPS.

Confidentiality and Protection of Human Subjects

Access to data/specimens is restricted to study personnel. Access to data requires OHSU ID/password authentication. 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. The data stored within the GRM Cloud Server and Dexcom Clarity is de-identified and does not contain any information from the 18 HIPAA designations of personally identifiable information. OHSU ITG has granted an Exception approval for using and storing data on the GRM. Data stored on the GRM will be deleted once the study is complete.

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

The three-digit identifying subject number will also be used to code paper study documents. Study staff will record data required by the protocol onto the Case Report Forms (CRF) during the study. The CRFs and all surveys will be collected on paper. Data for this project will be stored on the GRM, developed and maintained by our group, that has undergone a security review. Investigators and research coordinators will verify that the procedures are conducted according to the approved protocol. All paper source documents will be kept in a locked cabinet for a minimum of five years. The CRFs will include:

- Screening form
- Control arm start-up visit
- Control arm completion visit
- Intervention arm start-up visit
- Intervention arm completion visit
- Surveys

- Study completion visit
- Physician CGM Review Form
- Phone/Email Update Form
- Adverse Event form
- Serious Adverse Event form
- Concomitant Medications

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

To protect confidentiality, standard institutional practices will be followed to maintain the confidentiality and security of data collected in this study. Study staff will be trained with regard to these policies.

Paper files will be stored in locked filing cabinets in restricted access offices at site. 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. Electronic data will be stored on encrypted computers, laptops, and study smartphones. Electronic data is stored in OneDrive. DailyDose data will be housed in a custom cloud database on an OHSU secure server called the GRM. Access to data/specimens is restricted to study personnel. Access to data requires ID/password authentication.

Risk and Benefits

Risks: The risks of the protocol procedures are considered minor. Daily management of glucose for people with type 1 diabetes brings a risk of hyperglycemia and hypoglycemia, but users are unlikely to experience severe low or high blood sugar because there are low and high glucose alerts available with the DailyDose app. Other risks are those associated with CGM use, but not directly related to this study. The following events have been identified as possible anticipated device-related adverse events of the FDA-approved Dexcom G6 sensor insertion and wear:

- Excessive pain or discomfort from either system deployment or during wear period (8 or greater on a 10-point Likert scale)
- Excessive bleeding, defined as requires removal of the device to stop bleeding
- Hematoma, defined as induration at the sensor insertion location (ecchymosis is a known consequence of needle skin puncture or pressure from sensor pod and will not be captured as an adverse events)
- Edema from sensor and/or adhesive tape that is significant and non-resolving within 48 hours of sensor pod removal

- Erythema from sensor and/or adhesive tape that is significant and non-resolving within 48 hours of sensor pod removal
- Local infection, defined as presence of pus at either sensor wire or sensor pod site
- Sensor or introducer needle fracture during insertion/wear/removal. For this reason, the study investigator will inspect each removed sensor for the possibility of breakage or fracture. Any evidence of sensor breakage will be recorded and reported to FDA and the sensor company.

There is a risk that the participant may consume a smart snack at night in response to the nocturnal low glucose alert and become hyperglycemic overnight. The DailyDose app will alert the participant if their glucose becomes too high using the high glucose alerts within the app. Participants will be instructed to manage high glucose levels as they usually do.

Benefits: The subject may not directly benefit from being in this study; however, their participation may help to advance decision support tools for preventing dangerously low glucose levels overnight.

Costs

Participants will receive $400 for completion of the study. If participants withdraw early from the study, compensation will be given as follows: $40 per week for the control or DailyDose + *smart snack* periods. There is no compensation for the screening visit. If a participant completes additional time on study to make up for time the study was paused due to technical issues, participants will receive an additional $40 per week.

Monitoring Procedures

This investigation will be monitored by Leah M. Wilson, MD and Joseph El Youssef, MD. Dr. Wilson and Dr. El Youssef have no commercial interest in any of the companies which manufacture any of the devices used in this study. This protocol is written in accordance with the principles established by the 18th World Medical Assembly General Assembly (Helsinki, 1964) and amendments and clarifications adopted by the 29th (Tokyo, 1975), 35th (Venice, 1983), 41st (Hong Kong, 1989), 48th (Somerset West, South Africa, 1996), 52nd (Edinburgh, 2000), 53rd (Washington, 2002), 55th (Tokyo, 2004), 59th (Seoul, 2008), and 64th (Brazil, 2013) General Assemblies. The investigator will ensure that the study described in this protocol is conducted in full conformance with those principles, the protocol, current FDA regulations, ICH Good Clinical Practices (GCP) guidelines, Good Laboratory Practices (GLP) guidelines, local ethical and regulatory requirements, including the Federal Food, Drug and Cosmetic Act, U.S. applicable Code of Federal Regulations (title 21), any IEC requirements relative to clinical studies.

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

Unanticipated problems, including study, disease or device-related problems, will be detected by reviewing descriptions of known or foreseeable adverse events and risks in the IRB-approved research protocol and the current IRB approved consent form, any underlying disease or

conditions of the subject experiencing the adverse event, a careful assessment of whether the adverse event is related or possibly related to the subject's participation in the study or if root cause or associations is with study devices.

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

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

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

- Date of event
- Severity
- Outcome
- Resolution of event

Unanticipated Adverse Device Effect (UADE)

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

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

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

Medical Device Reporting (MDR) Events

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

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

Adverse event reporting

Hypo- and hyperglycemia will not be considered AEs unless the subject has positive ketones of 1.2 mM or displays symptoms of hypoglycemia such as: loss of consciousness, slurred speech, hospitalization, or EMS services called. Disease related events that are chronic in nature and occur as part of the progression of the diabetes disease state (i.e., diagnoses of retinopathy, nephropathy, and neuropathy) will not be captured as AEs in this study.

One of the investigators will write up a description of the adverse event/unanticipated problem. All reportable new information (RNI) will be reported to the IRB within five calendar days after the PI learns of the event. RNI is any information that might meet the regulatory definition of an unanticipated problem involving risks to participants 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 UPs and adverse events, including those that do not meet the requirement for RNI, will be submitted with the continuing review. The FDA will be notified of any unanticipated adverse event related to the use of the study device. Notification will be made within 10 days after the Principal Investigator becomes aware of the event. Any SAE, including death, due to any cause (related or unrelated to devices), that may occur during a clinical study will be reported immediately (within 1 working day of learning of the event).

Statistical analysis methods

The differences between the control and intervention arms will be evaluated using a multilevel mixed effects model with nights (or 24-hour/day study duration) as the level 1 units of analysis and study participants as level 2. The outcome Y_{ij} for the ith night for the jth participant is given by the following equation:

$$Y_{ij} = \beta_0 + \beta_1 Tx_{ij} + \beta_2 Sequence_j + \beta_3 Period_{ij} + b_{0j} + \epsilon_{ij}$$

- $Tx_{ij} = 0$ for the control condition or $Tx_{ij} = 1$ for the *smart snack* intervention,
- Sequence = AB or BA at the participant level, and
- Period =1 or 2

- The term b_{0j} represents a random intercept for participant to reflect the correlation between repeated measurements; a random slope for the treatment effect may also be considered.

A significant Wald test for the coefficient of the treatment variable, β1, would provide evidence that the intervention differed significantly from the control condition.

A significant Wald test for the coefficient of the sequence variable, β2, would indicate that there was a carryover effect.

A p value less than 0.05 will be considered statistically significant.

Covariate adjustment: Sequence and period will be included in statistical models as described above but are not expected to be statistically significant.

Compliance analysis: We will model the overnight hypoglycemia endpoint with recommendation accepted/rejected as a predictor in the intervention period to test if accepting recommendations is associated with lower risk of nocturnal hypoglycemia.

Adjustment for multiplicity: No adjustments will be made for multiplicity for the pre-specified primary and secondary outcomes.

Hypothesis testing framework: All comparisons will be made as tests of equivalence.

Interim analyses: Interim analysis might be performed to define if more participants are included in the study if a participant does not experience any overnight hypoglycemia episode during the control arm.

Timing of final analysis: Final analysis will be completed after data collection and processing is complete.

Missing data

Participants who contribute at least 14 nights plus 24 hours following bedtime in at least one of the study conditions will be included in the analysis. Missing sensed glucose values will be interpolated for up to 30 min segments. Longer periods of missing data will be omitted. If missing data represent >10% of observation time (which will be truncated if a participant leaves the study early), we will examine distributions of other variables in the dataset to see if they differ between those with high/low levels of missingness. We will consider methods to reduce bias in the estimate of treatment effect such as including covariates in the main outcomes model.

Appendix A: Devices

Apple Watch

Apple iPhone

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

Scale

Appendix B: 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 mg/dL, 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 C: Diabetes Distress Scale

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

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

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

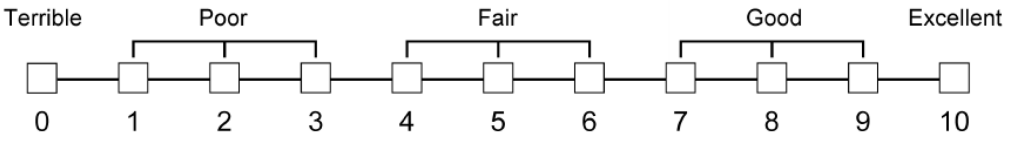
me to eat the "wrong foods").						
8. Feeling that diabetes controls my life.	1	2	3	4	5	6
9. Feeling that my doctor doesn't take my concerns seriously enough.	1	2	3	4	5	6
10. Not feeling confident in my day-to-day ability to manage diabetes.	1	2	3	4	5	6
11. Feeling that I will end up with serious long-term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

Appendix D: Sleep quality Scale[24]

INSTRUCTIONS:

- *The following question refers to your overall sleep quality for the **majority** of nights in the **past 7 days ONLY**.*
- *Please think about the quality of your sleep **overall**, such as how many hours of sleep you got, how easily you fell asleep, how often you woke up during the night (except to go to the bathroom), how often you woke up earlier than you had to in the morning, and how refreshing your sleep was.*

1. During the **past 7 days**, how would you rate your sleep quality overall?
*(Please mark only **1** box)*



Appendix E: Study completion interview script

Questions:

1. What did you call the app?
2. General understanding of app
    a. If you were telling someone else about the app, how would you describe it?
    b. What do you think is the best feature of the app?
    c. What were the positives and negatives of the app?
3. Expectations of the app
    a. What were your expectations of the system before you started the trial?
    b. Do you think predicting nighttime lows and providing snack recommendations would help you with diabetes management?
    c. Did anything surprise you about the app?
4. Usability of the app
    a. Which of the issues below was the biggest problem during the study?
        i. The App was confusing to use
            - What were the difficult parts of using the app? Why?
        ii. The app was visually unappealing
        iii. The app crashed
        iv. The app was missing features I consider important
            - What were those features
    b. Rate the following aspects of the app (scale 1 to 5, 5 is best possible score)
        i. Stability
        ii. Navigation
        iii. Functionality
        iv. Look and feel
5. Trusting the App
    a. How easy was it to trust the predictions and recommendations of the app to avoid nighttime low glucose?
    b. Would you use the app right now to help you avoid nighttime low glucose?
    c. Would you use the app outside of the study if you could?
6. Barriers to Use
    a. What might stop you from wanting to use this system in the future if it was available?

Appendix F: Hypoglycemia fear survey

HFS-II (Adults)

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

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

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

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

Appendix G: Bedtime snacks alternatives

DailyDose recommended snack	**Alternative 1** (Gluten free)	**Alternative 2** (Contains dairy but is gluten, nut, and shellfish free)	**Alternative 3** (Contains wheat and soy; no nuts, dairy, or shellfish)	**Aternative 4** (No gluten, dairy, shellfish, or nuts)
1 bar from package  1 bar 	1 bar 			
2 bars from package 	1 bar 	Low fat fruit yogurt 6 oz   	Graham crackers 2 sheets 	
1 bar 				

				Fruit snacks 0.9 oz 

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