Real-Time Continuous Glucose Monitoring to Aid Weight Loss in Prediabetes

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STUDY OVERVIEW

Study Title
Real-Time Continuous Glucose Monitoring to Aid Weight Loss in Prediabetes

Abbreviations
Real-Time Continuous Glucose Monitoring (RT-CGM)

Study Aims and Outcome Measures
RT-CGM has revolutionized the treatment of patients on intensive insulin therapy and its utility can also be harnessed to help individuals with prediabetes make healthful lifestyle changes. Successful weight loss requires adherence to lower calories, regular exercise, and self-monitoring. This proposal will test the hypothesis that RT-CGM will facilitate all of these components for successful weight loss by functioning as a continuous self-monitor and guiding healthful food choices and physical activity.

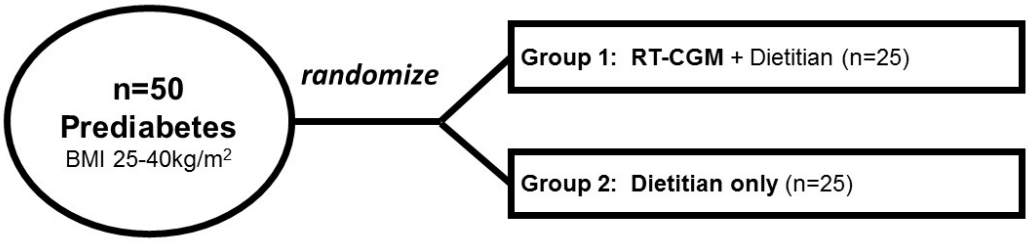
AIM #1: Compare weight loss.
Intermittent RT-CGM use will augment dietitian-guided weight loss in individuals with prediabetes.

AIM #2: Compare physical activity.
Intermittent RT-CGM use will increase physical activity compared with dietitian support only.

Other measures will include glucose indices (fasting glucose, A1c).

Study Population
We aim to enroll 50 participants who are overweight/obese with prediabetes. Please see **APPENDIX A** for more detailed inclusion/exclusion criteria.

Design
This will be a randomized, parallel-group, pilot study of intermittent RT-CGM with dietitian support versus dietitian support only.



Duration
We anticipate that the entire study will take 24 months through data analysis. Each eligible candidate who voluntarily consents to participate in the study will be active on the study for a total of 4 months.

KEY STUDY PERSONNEL

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Co-Principal Investigator
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Study Dietitian
Leah Groppo

Study Coordinator
Pending

FUNDING SOURCES

Stanford Diabetes Research Center Pilot and Feasibility Grants Program

Study Protocol

1. BACKGROUND

The heart of diabetes prevention is lifestyle changes and weight reduction. The pivotal Diabetes Prevention Program (DPP) study clearly demonstrated that weight loss of 7% and moderate physical activity reduced the incidence of type 2 diabetes (DM2) in individuals with prediabetes.[1] In addition, lifestyle changes were superior to early initiation of metformin, a glucose-lowering medication. While benefits of lifestyle changes are undeniable, successful interventions are lacking to help individuals with prediabetes make and sustain lifestyle changes leading to significant weight loss. Currently, DPP-modelled "real-life" interventions show an average weight loss of 4% and show drop-out rates as high as 50%.[2]

The goal of this proposal is to test the hypothesis that **real-time continuous glucose monitoring (RT-CGM) will facilitate weight loss in overweight/obese individuals with prediabetes**. Although controversy exists regarding optimal diets and interventions for weight loss, there is consensus that the following components are generally needed to lose weight:[3] 1) reduction in energy intake, 2) participation in physical activity and 3) incorporation of self-monitoring (e.g., food tracking). We hypothesize that RT-CGM will help the user achieve all of these components and lose weight. Unlike other health trackers which relies on user input, RT-CGM provides continuous monitoring and instantaneous feedback on glucose levels which reflect user food choices and physical activity. A small sensor is inserted below the skin and into the interstitial fluid. The sensor measures glucose from 40 to 400mg/dL every 5 minutes and transmits the data wirelessly to a display such as a smart phone (Fig. 1). Eating generally increases and exercise decreases glucose concentrations. As individuals with prediabetes have some degree of insulin secretory dysfunction and hyperglycemia, certain food choices (high in carbohydrate content, added sugars, and calories) may increase glucose more than other healthful choices. Thus, RT-CGM can monitor when eating is occurring and also can provide feedback on the effect of food choices to adversely increase glucose. Furthermore, it can also reflect the beneficial effects of exercise to lower glucose. Thus, coupled with education, we hypothesize that RT-CGM can be used as a self-monitoring device to motivate healthful food choices and physical activity that maintain lower glucose and aid weight loss.

Fig 1. Glucose readings from RT-CGM displayed on a smart phone can be used to motivate food choices and physical

RT-CGM is an existing technology that is being underutilized. There has been little direct examination of RT-CGM as a behavior modification and weight loss tool in individuals with prediabetes. CGMs currently are indicated for patients treated with intensive insulin therapy such as those with type 1 diabetes.[4] Use of CGM in individuals with type 1 diabetes has been consistently shown to improve glucose control.[5,6] In limited studies in patients with DM2, use of CGM also has been successfully used to motivate behavioral change and weight loss.[7] The potential benefits of CGM also are suggested by studies of activity monitors in the general population.[8] Collectively, those individuals most adherent with tracking food, activity and weight show the greatest weight loss.[9] With this understanding, RT-CGM may function as the ultimate self-monitoring device as instantaneous glucose changes will reflect effects of food choices and physical activity.

The goal of this proposal is to assess whether **RT-CGM will augment dietitian-guided weight loss and influence food choices and physical activity in overweight/obese patients with prediabetes**. In essence, we will be evaluating whether CGM can function as the ideal self-monitoring device.

Study Rationale

Currently, over a third of adults qualify for the diagnosis of prediabetes,[10] and 5-10% of those with prediabetes progress to DM2 every year.[1,11] Lifestyle changes and weight loss significantly delay the progression to DM2.[1] However, weight loss remains challenging and newer tools are desperately needed to help overweight/obese individuals with prediabetes change lifestyle and lose weight.

RT-CGM has revolutionized the treatment of patients on intensive insulin therapy and its utility can also be harnessed to help individuals with prediabetes make healthful lifestyle changes. Successful weight loss requires adherence to lower calories, regular exercise, and self-monitoring.[3] **This proposal will test the hypothesis that RT-CGM will facilitate all of these components for successful weight loss by functioning as a continuous self-monitor and guiding healthful food choices and physical activity.**

Overweight/obese patients with prediabetes will be randomized to intermittent RT-CGM with dietitian support (n=25) versus dietitian support only (n=25). The CGM group will wear the RT-CGM for 10 days at baseline, months 1 and 2. The baseline RT-CGM will be the "learning phase" to teach effects of usual food intake and activity on glucose levels. The subsequent CGM trials will be used to enforce healthful eating and at least 150-min of moderate intensity exercise to maintain normal peak glucose less than 140 mg/dL ("enforcement phase").

2. STUDY AIMS

If any of the primary or secondary outcome measures are changed, study staff must update clinicaltrials.gov.

The primary objective will be to determine whether intermittent use of a RT-CGM will facilitate weight loss in individuals who are overweight/obese with prediabetes.

2.1. Primary Outcome Measure

AIM #1: Compare weight loss.

Intermittent RT-CGM use will augment dietitian-guided weight loss in individuals with prediabetes.

2.2. Secondary Outcome Measure

AIM #2: Compare physical activity.

Intermittent RT-CGM use will increase physical activity compared with dietitian support only.

Other measures will include glucose indices (fasting glucose, A1c).

3. STUDY DESIGN

3.1 Sample Size

We aim to have 50 total participants in this study.

3.2 Study Population

We aim to enroll 50 participants who are overweight/obese with prediabetes. Please see **APPENDIX A** for more detailed inclusion/exclusion criteria.

3.3 Study Location

Participants will be recruited from the San Francisco Bay Area. The research study office is located near the Stanford Hospital and Clinics at 300 Pasteur Drive, Stanford, CA 94305.

Blood draws will occur in the Boswell Clinic Laboratory at 300 Pasteur Drive, Level 1, A12, Stanford, CA 94305.

3.4 Study Duration

We anticipate that the entire study will take 24 months through data analysis.

Months 1-3
-Prepare IRB and study protocols

Months 4-14
-Recruit 5 individuals per month

Months 14-18
-Last group of participants completes protocol

Months 18-24
-Data cleaning
-Data analysis

3.5 Randomization

Eligible participants will be consented for the study and have baseline measurements before being randomized to either the RT-CGM versus dietitian only group. Participants will be randomized according to a computerized random number generator.

4. STUDY PROCEDURES

4.1 Study Design

This will be a randomized, parallel-group, pilot study of intermittent RT-CGM with dietitian support versus dietitian support only. We will randomize 50 individuals who are overweight/obese (BMI 25-40 kg/m^2) with prediabetes. A registered dietitian will meet with all volunteers monthly for 3 months and advise on a hypocaloric diet (500 kcal/day deficit) and physical activity (150 minutes per week). (See Fig 2).

4.2 Recruitment

Preliminary recruitment strategies will include:

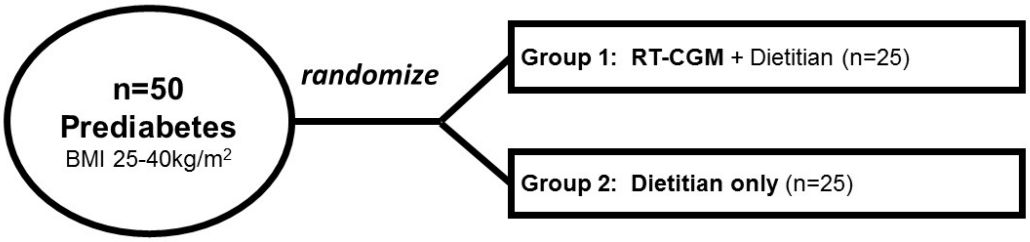
- Recruitment through the Endocrinology Clinic.
- Targeted mass mailings from existing study participants lists (individuals who expressed interest in participating in future studies) and other email lists, currently over 10,000 emails.

Pace of recruitment will be monitored throughout the study. Since the recruitment timeline can be difficult to predict, if the pace is significantly slower than anticipated, the Primary Investigators may decide to alter the budget, timeline, and/or elements of study design (e.g., alter enrollment target, increase budget, reduce elements of data generation) accordingly.

4.3 Intervention

Participants will be randomized 1:1 to either the CGM group with dietitian support or Dietitian-only group (See Fig 2). At baseline, patients in the CGM group will wear a Dexcom RT-CGM for 10 days and be advised to keep a food and activity log for 7 days (This will be the “learning phase”). They will then meet with a registered dietitian to review CGM and food/activity log and be advised on a 500 kcal deficit diet and 150 min/week physical-activity goal. They will also be advised to target postprandial glucose less than 140 mg/dL. They again will wear CGM for 10 days followed by dietitian consultation at months 1 and 2 (“enforcement phase”).

Volunteers randomized to Dietitian-only group will meet with a dietitian at baseline, months 1 and 2. They will also be advised to keep a food and activity log for 7 days prior to meeting with the dietitian. They also will be advised on a 500 kcal deficit diet and 150 min/week physical-activity goal.



Months	0	1	2	3
RT-CGM (in Group 1 only)	$X^{learning}$	$X^{enforcement}$	$X^{enforcement}$	
Dietitian	X	X	X	
Fasting glucose/A1c	X			X
Weight	XX	X	X	X
Physical Activity Review	X	X	X	X
Food Log Review	X	X	X	

Fig 2. Protocol Overview

5. STATISTICAL CONSIDERATION

5.1 Statistical Basis for Sample Size

The primary endpoint will be amount of weight lost in RT-CGM vs Dietitian-only group. Based on a previous weight-loss study of overweight/obese individuals with prediabetes,[16] with 50 participants, we anticipate detecting a within group difference in weight of 1.8 kg and between group difference of 8kg with 80% power and type 1 error of 0.05. Drop out of 20% will results in effect sizes of 2 and 9kg, respectively.

5.2 Statistical Plan

In progress.

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APPENDIX

A. Inclusion/exclusion criteria

Inclusion Criteria	
	Comments
Age	≥ 18 years
Overweight/obese	BMI 25-40 kg/m^2, or ≥23 if Asian
Prediabetes	fasting glucose of 100-125 mg/dL and/or A1c 5.7-6.4%

Exclusion Criteria	
Age	<18 years
BMI	>40 kg/m^2
Medications	Taking medications known to affect glucose (e.g., anti-hyperglycemic) or weight (e.g., weight-loss medicaitons)
Physical limitation	Cannot ambulate
Planning pregnancy	Women pregnant currently or planning to become pregnant during the course of the study and/or breastfeeding

Anti-hyperglycemic medications	
	Metformin
	Other
Weight-loss medications	
	phentermine
	Saxenda (liraglutide)
	Contrave (naltrexone/bupropion)
	Belviq (lorcaserin)
	Qsymia (phentermine/topiramate)
	Xenical (orlistat)

B. Questionnaire

The following questionnaire will be conducted at baseline and at the end-of-study:

- IPAQ (International Physical Activity Questionnaire) – to assess physical activity in last 7 days at 6 time points.

CL, C., & AL, M. (2003). International physical activity questionnaire: 12-country reliability and validity. *Medicine & Science in Sports & Exercise, 35*(8), 1381-1395.

C. Outcome Measurement Methods

Anthropometrics.

Glucose indices (fasting glucose, HbA1c).

RT-CGM. Dexcom G6 CGM

Questionnaire data related to physical activity.