Document:

Protocol

Official Study Title:

A Multiple Technology-Based and Individually Tailored Sit Less Program for patients with Type 2 Diabetes: A randomized controlled trial

NCT06457802

Document Date:

May 15, 2024

A Multiple Technology-Based and Individually Tailored Sit Less Program for patients with Type 2 Diabetes: A randomized controlled trial

Principal Investigator:
Chorong Park, PhD, RN
Assistant Professor
School of Nursing, Vanderbilt University
511 Godchaux Hall/21st Avenue South
Nashville, TN 37240
Phone: 615-875-5226
Email: chorong.park@vanderbilt.edu

Co-Investigators:

Soojung Ahn, PhD, RN
Postdoctoral Scholar
School of Nursing, Vanderbilt University

Shelagh Mulvaney, PhD
Associate Professor
School of Nursing, Vanderbilt University

Mary Dietrich, PhD, MS
Associate Professor
School of Nursing, Vanderbilt University

Date: May 15th, 2024

Table of Contents:

1.0 Background

Sedentary behavior (SB) is a strong modifiable risk factor for developing type 2 diabetes (T2D) and cardiovascular disease, even after controlling for daily physical activity.[1-3] During sedentary behavior, there is no muscle contraction of the legs, which causes decreasing insulin sensitivity, glucose uptake, vascular dysfunction, and promotes low-grade inflammatory cascades.[4] Despite the important role of sedentary behavior in managing T2D, people with T2D remain highly sedentary. They spend on average 11-15 hours per day sitting,[5, 6] which comprises 65-75% of waking time.[5, 7, 8] Moderate-to-vigorous levels of physical activity or exercise can attenuate cardiometabolic risk but does not eliminate the increased risk associated with high sedentary time.[1, 9] Considering T2D patients' low cardiorespiratory fitness and low activity levels,[10, 11] they may be at greater risk than others for the negative cardiometabolic consequences of sedentary behavior.[12] Therefore, there is a pressing need to develop novel strategies to reduce SB and improve daily activity in patients with T2D. Targeting SB, which occupies most of a T2D patient's waking time, can be a new target behavior for secondary prevention in this population.

2.0 Rationale and Specific Aims

Frequent standing/walking can reduce the total SB time and change prolonged patterns to interrupted patterns. Since leg muscles do not contract during SB, sedentary breaks such as standing/walking (requiring muscle contractions) may change physiological pathways and improve cardiometabolic outcomes. A recent meta-analysis found that while controlling for total sedentary time and MVPA time, short sedentary breaks (2-5 minutes of standing/walking for every 20-60 minutes of sitting) were beneficially associated with cardiometabolic markers; adding one break decreases 0.05 unit of BMI, 0.2 cm of WC, 0.002 mg/dl of hsCRP, and 1.8 mmHG of systolic blood pressure (BP).[13, 14] Many intervention studies have also shown that breaking prolonged sedentary time with short periods of light PA or standing improves glucose (2-17%) and insulin (15%). [13, 15] Moreover, emerging evidence shows that reducing SB time with frequent breaks is safe[16-18] in other chronic health conditions and applicable to T2D patients.

SB breaks can be achieved through self-monitoring and prompts from a wearable device. In addition, the use of a smart water bottle may be a promising strategy to naturally break sedentary time due to the impact of increased water intake on kitchen and restroom breaks. A smart water bottle can sync with an activity tracker, which could synergistically motivate the T2D patients to reduce SB. This new technique is a potentially low-cost and sustainable strategy to deliver SB reduction interventions.

Because there is no SB reduction program specifically focusing on sedentary breaks in T2D patients, we propose to develop and conduct a pilot study RCT to test a wearable

technology-based SB reduction intervention in T2D patients. The 8-week intervention includes: 1) one instructional and goal setting session; 2) the use of a wearable device (Fitbit) that provides stand/walk prompts and self-monitoring; 3) a smart water bottle (HidrateSpark) that syncs with the Fitbit; 4) weekly tailored text messages for behavior reinforcement and weekly goal monitoring, and 5) one mid-program counseling session. Since text messages and wearable device-based intervention requires a complex and multiple iterative process to customize research participants' needs and refine the contents and frequency of the text messages.
Outcomes will be measured at baseline and post-intervention. Specifically, we aim to:
Aim 1: Determine the acceptability of the SB reduction intervention in T2D patients by evaluating satisfaction and compliance with the intervention.
Aim 2: Evaluate the preliminary efficacy of the SB reduction intervention on changes in total SB time and numbers of prolonged SB bouts.
Aim 3 (Exploratory Aim): Explore preliminary effects of the SB reduction intervention on light physical activity (total standing and stepping times), cardiometabolic markers (24-hour glycemic control, BMI, waist circumference, blood pressure, and patient-centered outcomes (confidence in reducing SB, habit strength for SB, and quality of life).

3.0 Inclusion/Exclusion Criteria

Inclusion criteria: 1) ages 18 and above, 2) diagnosed with type 2 diabetes, 3) self-reported HbA1C<13, 4) self-report of sitting ≥ 8hr/day, 5) ability to stand and walk, 6) ownership of a smartphone.
Exclusion criteria: 1) currently using an activity tracker; 2) currently participating in exercise or other research programs; 3) random blood glucose >300; 4) non-English speaking; 5) patients who are classified as unstable (e.g., heart failure, uncontrolled arrhythmia) or have kidney disease that limits daily water intake; 6) any conditions that prevent standing or walking due to physical or cognitive limitations, such as cognitive impairment, severe pain, problems with lower limbs, or a history of surgeries that limit movement [19, 20]; 7) participation in Sit Less Program V1 (IRB #221566); and 8) currently pregnant.

4.0 Enrollment/Recruitment

We will use three recruitment strategies:

1) **Research Notification Distribution List**
   Email distribution list allows researchers to email IRB-approved participant recruitment announcements to the Vanderbilt community. Members of the distribution list have the option to subscribe/unsubscribe with each email. The

potential participants will click the pre-screening consent. The detailed procedure regarding pre-screening prospective participants is described below

2) **Reporting Workbench**

Reporting Workbench Reports are available/viewable in eStar. These reports are developed using real-time data and can be customized to meet study-specific inclusion/exclusion criteria that are computable in the EHR. The reports often include additional variables to facilitate study team outreach, such as Research OK to Contact status, MHAV account status, contact information, next upcoming appointment in a specific clinic. While the report displays certain variables/data, it provides easy access to a patient's record for additional screening and confirmation of eligibility. Research team members with appropriate eStar access can view/run the reports as frequently as needed.

We plan to use the results from our custom Reporting Workbench report to facilitate outreach in the following way: To send My Health at Vanderbilt (MHAV) recruitment requests, as detailed below in recruiting strategy 3. KSP do not have an existing provider relationship with the patients being approached about study participation. Results will be restricted to those marked as 'OK to Contact'. We will not be reaching out to employees or persons of interest.

3) **My Health at Vanderbilt (MHAV) Recruitment Requests**

Participants will be recruited through My Health at Vanderbilt. My Health at Vanderbilt (MHAV) is VUMC's patient portal where the patient may sign up and participate in managing his/her health care. MHAV can also be used for sending recruitment requests to a predefined cohort of patients who meet certain study-specific inclusion/exclusion criteria, have an activated MHAV account and are marked as OK to Contact in eStar. The recruitment requests are sent by a central VICTR team on behalf of the study team. The notification preferences for the recruitment requests can be managed by the patients in MHAV. The system default is an email notification like clinical notifications (see attached MHAV Recruitment Request messaging). If the patient has turned off notifications, the study will just be listed on their research studies page in MHAV.

Once the Recruitment Requests are sent, the patient's enrollment status is automatically updated to (IT Use Only) Identified - RWB Recruitment Message or

Auto DL. If the patient clicks '**No Thank You'**, the patient's enrollment status in eStar is automatically updated to **(IT Use Only) Not Interested - Pt. answered in MHAV**. The study team does not get a notification in Epic In-Basket or in REDCap.

If the patient clicks '**I'm Interested**', the designated KSP (with eStar access) receive an In Basket message in eStar indicating the patient is interested

The patient's enrollment status is automatically updated to **(IT Use Only) Interested - Pt. answered in MHAV**. The REDCap Participant Updater Module looks for the patient's MRN in the study specific database. If a matching MRN is not found, the Participant Updater Module creates a record in the study-specific database with the following information from eStar:

1) Patient's MRN
2) Patient's enrollment status - (IT Use Only) Interested - Pt. answered in MHAV
3) Study ID (IRB#)

REDCap CDIS is then triggered to pull in the patient email address from eStar if available for all patients who click I'm Interested. This will trigger an email from REDCap to the patient which contains a link to the IRB approved pre-screening and eConsent surveys on REDCap.

If the patient responds to the email from REDCap or completes a pre-screening survey or eConsent, the study team will update the patient's enrollment status accordingly in eStar or REDCap. Once the patient's enrollment status has been updated in the study specific record in REDCap, the Participant Updater Module will automatically update the enrollment status in eStar. The study team will contact the interested patient by telephone call or email to confirm their eligibility and schedule an in-person baseline visit

5.0 Study Procedures

5.1 Baseline visit 1: Initial contact, screening, and consent

Interested respondents will be screened by a trained research staff over the phone or in-person, depending on the recruitment methods. For this research, no aspect of the participant's diabetes treatment regimen will be modified.

Those who are eligible for the study will be invited to the in-person visit. The first visit (i.e., Baseline visit 1) will be conducted at VUSN (Vanderbilt School of Nursing)'s lab at Wesley building.

At the Baseline visit 1, individuals will check their blood glucose level via finger prick. If their random glucose levels are between 80-300, they will complete the informed consent with assistance from the trained research staff. The trained research staff will complete baseline biometric assessment, including measure of height, weight, waist circumference, and blood pressure. Those who are consented will participate in: 1) completing survey questionnaires (30 minutes), 2) a baseline biometric assessment, 3) brief instruction regarding the wear of activPAL and continuous glucose monitoring (CGM) devices (30minutes), and 4) start to wear two devices for 7 days. The activPAL3 device (PAL Technologies Ltd., Scotland, UK) will be worn on the thigh and a CGM (Abbott FreeStyle Libre) will be attached to the upper arm. The research staff will provide: 1) a copy of the informed consent form; 2) instructions with photos and 5 waterproof dressings (Tegaderm) for attaching the activPAL on the thigh; 3) information about the CGM; and 4) daily sleep diary and wear log for 7 days. Participants will receive $25 for baseline visit 1.

1. **Biometric assessments**
   Participants will undergo a basic physical examination (e.g., height, weight, blood pressure, hip circumference, waist circumference) and blood collection.
   A) **Anthropometrics:** Height, weight, and waist and hip circumferences will be measured using a validated stadiometer, digital scale, and flexible tape measure, respectively. All measurements will be recorded to the nearest 0.1 cm and 0.1 kg.
   B) **Blood pressure:** Blood pressure will be measured using an automated and validated BP monitor. In a private room, participants will be seated comfortably for 5 minutes with feet flat on the ground prior to measurements.32 The device will take three readings at 2-minute intervals and the mean of three BP readings will be recorded.[21]

2. **Questionnaires**

Participants will be given an iPad to answer questions about their demographics, socioeconomic characteristics, and a series of questionnaires detailed below. All responses will be recorded in REDCap.

A) **Demographics**: demographics and socio-economic status will be self-reported by the patients.

B) **Health behavior**: Questions about their tobacco use, alcohol intake, physical activity will be measured using the 27-item International Physical Activity Questionnaire (IPAQ)[22], and diet measured using the 16-item Rapid Eating and Activity Assessment for Participants Short Version (REAP-S)[23]. Sleep quality (measured using the 10- item Pittsburgh sleep quality index)[24] will be answered with the assistance of the study team member.

C) **Confidence in reducing SB and increasing PA**: Confidence in reducing SB and increasing physical activity will be measured using 12 items from the Self-Efficacy Questionnaire for Physical Activity and Sedentary Behavior (Cronbach's alpha = 0.79).[25]

D) **Habit strength for SB**: Habit strength for SB will be assessed by using a validated measure, Self-Report Habit Index (Cronbach's alpha = 0.91).[26] This 7- item index was adapted to sedentary breaks (standing/walking) to assess the degree to which sedentary breaks become habitual.

E) **Quality of life**: Quality of life will be measured using the Patient-Reported Outcomes Measurement Information System (PROMIS)-Global Health, a 10-item measure developed by the NIH as an indicator for Healthy People.[27]

F) **Medical history and current medication**: Medical history and current medication will be self-reported by the patients through the Self-Administered Comorbidity Questionnaire (SCQ).[28]

G) **Diabetes self-management**: Self-efficacy of diabetes self-management will be measured by the Diabetes Self-Management Questionnaire (DSMQ).[29]

H) **Diabetes-related emotional distress:** The emotional impact of living with diabetes will be assessed using the Diabetes Distress Scale (DDS)[30].

I) Barriers to Physical Activity: Barriers to PA will be assessed using 11 items from the Barriers to Physical Activity in Diabetes (BAPAD1) questionnaire which asks about various factors such as the fear of hypoglycemia, concerns about losing control over diabetes, fear of fatigue, fear of injury, and other perceived barriers related to diabetes and physical health[31]. Participants will

be asked to rate the likelihood of each item impeding their regular physical activity over the next 6 months on a scale ranging from 1 (extremely unlikely) to 7 (extremely likely).

3. **ActivPAL**

   The activPAL is a non-invasive method of monitoring activity and rest cycles through an inclinometer. The device will be worn on the anterior upper thigh of the dominant leg and kept in place by an adhesive pad (Tegaderm). If the participants have hair on the upper thigh, shaving an area of the thigh will be considered; we will provide a disposable shaving razor and foam as well as a private room with a sink. The participant will apply the device by themselves in a private room. The participants will wear the activPAL 24hours over a 7-day period. There is no need to charge the device. The activPAL monitor has been validated against direct observation and is the most sensitive device to detect sitting-to-standing transitions.[32] At a follow-up visit (Baseline visit 2), the activPAL data will be downloaded to the secured PI's computer and summary reports will be reviewed by the study team member and the participants.

4. **Continuous Glucose Monitor (CGM)**

   The device (FreeStyle Libre Pro™; Abbott Diabetes Care, Witney, Oxon, UK) will be worn on the back of the upper arm to measure their 24-hours glucose levels for 7 days. The CGM has one sensor applicator, one sensor, and one reader. Skin will be prepared using an alcohol wipe and the sensor applicator will be placed over the application site. The research staff will press firmly, hold for a few seconds, and gently pull the sensor applicator away from the site. A sensor applicator has an introducer needle which will be retracted after application. Only a thin, flexible filament will remain under the skin and the sensor is held in place by an adhesive. The sensor applicator serves as a container for disposal. The water-proof sensor, worn on the upper arm, is factory calibrated. The reader is retained by the PI and data are not visible to participants during sensor wear. The sensor automatically captures and stores glucose data every 15 min (96 glucose readings/day).

5. **Sleep diary and wear log**

   The participants will be asked to complete a daily sleep diary each morning while they are wearing the monitor, which takes about 2 minutes. The participant will

also complete a daily wear log each evening. The information about sleep onset and offset and wear time will be used to validate the activPAL wearing protocol.

Once they complete the 7 days of activPAL and CGM monitoring, they will be scheduled for the in-person visit (Baseline visit 2) and will return the devices and log to the study team at the visit.

6. Fitbit
   We will provide Fitbit (Inspire 3) to each participant. The Fitbit is not intended to be used as a medical device. All participants will have the ability to monitor physical activity, sleep, and heart rate with the Fitbit. All data from the Fitbit will be continuously streamed to the secure Fitbit servers. The study team member will assist participants in downloading the app and creating an account and will instruct them on how to use the device, with the official Fitbit user manual. When we create Fitbit accounts for research subjects, we do not use their real name or email address and default their account settings to the most privacy-protective option available.
   Fitbit accounts require a unique email address for each user. To ensure participants' anonymity and privacy when creating Fitbit accounts, we will (1) set up anonymous Gmail accounts and (2) set up de-identified Fitbit accounts for the purpose of the study. This individualized email address will then be linked to a Fitbit account in which personal identifiers should not be used. Importantly, research staff and participants will be advised that the email and Fitbit accounts should be used strictly for the study's purpose.
   Moreover, account information will be stored in protected PI's computer within encrypted documents. Once the intervention is concluded, Fitbit data will not be collected. Also, Fitbit and Fitbit app will be reset for the participant to keep using the Fitbit after study completion.

5.2 Baseline visit 2

5.2.1 Baseline assessment

The in-person baseline visit 2 will take place at the VUSN Clinic in the Wesley building. Participants will return the activPAL and the continuous glucose monitoring devices at Baseline visit 2. Participants will receive $25 for baseline visit 2.

1. **ActivPAL data download**

The 7 days of activPAL data will be downloaded and stored in the secured PI's computer. The variables of interest from the activPAL data are listed below:

A) **Sedentary behavior**: SB will be objectively measured as time spent sedentary (sitting or lying, minutes/day) and number of prolonged sedentary bouts (>30 minutes and >60 minutes) using the activPAL3. ActivPAL data will be downloaded and processed using activPAL software.
B) **Physical activity**: Time spent standing and walking (stepping), number of sitting- to-standing transitions, and daily step counts will be measured using the activPAL.

2. **Continuous glucose monitoring data download**

The 7 days of CGM data will be downloaded via Libreview and stored in the PI's computer. The variables of interest from the CGM data are listed below:
The 24-hour glucose control: the 24-hour glucose control will be evaluated by mean 24-hour glucose levels and numbers of events and time in hypoglycaemia (glucose < 3.9 mmol/l), euglycaemia (glucose 3.9–7.8 mmol/l), hyperglycaemia (glucose > 7.8 mmol/l) and above target (glucose > 9 mmol/l).

5.2.2 Randomization

Once the data is downloaded and reviewed by the PI, the Study Team Member will use the REDCap randomization function and will inform participants of their group assignment (1:1 ratio).

5.2.3 Blinding

Participants, the interventionist and the PI will be aware of the participants' treatment assignments. However, data collectors will be blinded.

5.3 Intervention

The 8-week intervention will consist of four components. After the intervention, the intervention group will keep their Fitbit and the HidrateSpark smart water bottle.

5.3.1 Instructional/goal setting session

The study team member will provide an orientation at the baseline visit 2. The study team member will review the activPAL data and identify targetable prolonged SB bouts. The study team member and the participant will set two goals:

1) a SB reduction goal will be set as reducing daily sedentary time gradually until they reach the goal of ≥ 120 minutes SB reduction; and
2) a sedentary break goal will be set as 3 minutes of standing/walking every 1 hour and then increasing its duration to 5 minutes and its frequency to every 30 minutes.

These goals were feasible in stroke patients and T2D patients.[16, 33] The participant will enter the goal into the Fitbit for self-monitoring and fill out the first worksheet in the Ten Top Tips (TTT). The TTT is a booklet developed from the Habit Formation Theory and includes 10 tips to add SB breaks into their daily routine.[34] The ten tips are modified to eight in our study. See Appendix for the TTT and worksheet. This goal session will last approximately 1 hour.

5.3.2 Fitbit

Intervention group participants' Fitbits will be programmed to provide the 'Reminder to Move' or 'Move Alert'. The move alert is a notification that cues the participant to walk at least 250 steps per hour. The Fitbit will vibrate when they have been sitting for 60 minutes. Participants can select the days and the time ranges to receive the move alerts. Patients will be encouraged to review their daily summary before they go to bed.

5.3.3 Smart Water Bottle

We will provide a HidrateSpark water bottle, and the study team member will assist participants in downloading the app and creating an account. The study team member will instruct participants on how to use the bottle, with the official user manual. The device alerts participants with a color change and message on the Fitbit to keep them hydrated. The device provides the daily water intake summary in the Fitbit app. We will advise participants to drink 4.5 – 6 bottles (500ml/bottle) of water per day based on current recommendations by the U.S. National Academies of Medicine.[35] The HidrateSpark accounts require a unique email address for each user and the same email which is used to Fitbit account will be used to the HidrateSpark app. The same rules will be applied to the HidrateSpark account, and the account information will be stored in protected PI's computer within encrypted documents. Once the intervention is concluded, HidrateSpark data will not be collected. Also, the HidrateSpark bottle and the app will be reset for the participant to keep using the bottle.

5.3.4 Text Messages

Text messages will be provided to support and enhance the habit formation process. Text messaging has shown effectiveness in many exercise studies.[36-38] There are three weekly default text messages which will be sent. Participants will also receive up to one text message per day providing a daily tip, which will be tailored to participants based on preferred message frequency and activity choices. In addition, the interventionist will offer weekly personalized feedback on the participant's progress towards goal achievement and helpful tips. The first default text message will be sent on Thursday to provide feedback on their progress for the week. The second default text message will be sent on Saturday morning to encourage them to sync their Fitbit to the Fitbit app.

The third text message will be sent on Monday morning to prompt participants to report their weekly activity. Participants will be instructed to open their Fitbit app, tap on 'Hourly Activity', and navigate to their data from the previous week. They will then respond to the survey text message with their average daily active hours from the previous week. Based on the participants' responses, the interventionist will propose an adjustment to the goal, either by suggesting a new lower goal or recommending the same goal. Participants will then respond to either accept the proposal or reject it. They will also get an introductory video explaining Fitbit app navigation.

When participants take an SMS survey, questions are asked one at a time as an SMS text message conversation/thread. We will ask three questions (three SMS text messages). Participants may respond with any kind of alpha-numeric text for SMS survey. Only REDCap administrators are allowed to enable the Twilio option to initiate a survey as an SMS conversation. All messages and Fitbit data will be managed in REDCap. After week 6, participants will set a new goal with the interventionist as part of the mid-program counseling session (described below, in 5.3.5 Mid-Program Counseling Session).

Below is the process of developing and providing text messages:

1. Creation of weekly text message template: Dr. Mulvaney (Co-I), an expert in effective health communication, and the PI co-created the weekly message template with Dr. Mulvaney.
2. Fitbit data transfer: We will transfer the Fitbit data from the participants' Fitbit accounts to REDCap by developing our own data collection interface using Fitbit's Web Application Programming Interface (API). This platform provides

secure data acquisition and management tools that facilitate remote data collection from Fitbit without the need for study participants to return the devices to researchers for data extraction.

3. Integration of Fitbit data into the text message template. The collected Fitbit data from REDCap will be integrated into our weekly text message template.
4. Send text messages using Twilio and Redcap. The customized text message will be sent using the Twilio plug-in for REDCap. Twilio module enables our study to make and receive SMS text messages, both to and from study participants. A REDCap and Twilio account are linked together. When a user indicates that an SMS (text) or a call should be sent to a cell phone, REDCap requests that action through Twilio. When a user responds, Twilio relays that information back to REDCap. The data is stored in the REDCap database. Twilio does not store any data, nor does it keep a log of its actions.

5.3.5 Mid-Program Counseling Session

At the halfway point of the intervention (after week 4), a focused counseling session will be conducted to re-evaluate and adjust the participants' activity patterns and sedentary break schedules. This interventionist-assisted session represents a critical touchpoint in the intervention, offering participants an opportunity to recalibrate their targets and enhance the positive behavioral changes initiated in the program. The session is outlined as follows:

1. Prior to the scheduled Zoom meeting, study participants will be mailed an activPAL device to their home address. Instructions will be provided to participants to ensure correct usage of the activPAL device, which they will wear for a period of one week. Participants will be informed of the procedures for returning the device using a prepaid express mail envelope for overnight shipping.
2. Upon receipt of the returned activPAL devices, the study team will promptly download and analyze the collected data. The interventionist will then utilize the data from the activPAL to assess the participant's activity patterns during the mid-program review.
3. During the Zoom meeting, the interventionist and participant will review the activity data together. The interventionist will facilitate a discussion to reflect on the participant's progress and challenges encountered in meeting the established goals. Personalized feedback will be provided, and the sedentary break schedules

will be adjusted based on the insights from the activPAL data. Goals and expectations for the remainder of the program will be discussed, reset, and agreed upon, ensuring they are realistic and achievable for the participant. Participants will be encouraged to incorporate the revised goals into their daily routine using their Fitbit for self-monitoring.

4. The audio will be recorded to guarantee consistent adherence to the protocol and to maintain inter-rater reliability among the interventionists. The audio recorded files and transcripts will be saved in the secured computer at a locked office.

5.3.6 Control Group

The control group will receive the American Heart Association's Healthy Living booklet. Control group participants will receive all study assessment but will not be instructed to monitor sitting time. The Fitbit move alert setting will be disabled for the control group.

5.4 Post-Intervention Visit

After 8 weeks, all participants will be invited to an in-person visit (post-intervention visit). During the visit, all the above parameters will be re-measured by the same trained research staff. The visit will take about 1 hour including the completion of a series of questionnaires (which participants may complete beforehand) and biometric assessments. All participants will wear the activPAL3 and the CGM for 7 days to examine their post-intervention activity and glycemic control. They will return the devices via pre-paid mail. All participants will receive $50 for the post intervention visit, and an additional $50 for mailing back the devices to the study team.
Therefore, total compensation would be $150 for each participant. Also, all participants will be informed of their 24-hour glucose results and activity patterns retrieved from the activPAL device.

1. **Questionnaires**
   Participants will answer the same questions about their demographics, socioeconomic characteristics, medical history and current medication, health behaviors, and patient-centered outcomes (e.g., confidence in reducing SB and increasing PA, habit strength for SB, quality of life, and diabetes self-management). Participants will have a choice to complete these questionnaires during the post-intervention visit in person or to receive paper copies of the questionnaires by mail. Printed copies will be identified by the participant's

REDCap record ID number; there will be no additional identifying information on the printed questionnaires. If a participant chooses to receive the questionnaires by mail, he or she will be asked to complete them using a blue or black ink pen no sooner than 2 days prior to their scheduled post-intervention visit and will bring the completed surveys to their post-intervention visit. After the post-intervention visit is completed, the study team will enter their responses manually into REDCap and upload a scanned PDF version of the paper questionnaires to their REDCap record. Paper copies of the surveys will be kept in a locked cabinet in the study team's office at the Vanderbilt School of Nursing. Alternatively, participants may opt to receive an email invitation that contains a unique link to a REDCap survey. REDCap ensures that all data transmitted during the survey completion process is secure and that participant privacy is maintained. The system is compliant with standards for sensitive data, such as HIPAA in the United States. In addition, participants will answer questions (Table 2) about feasibility and acceptability of the intervention. Level of satisfaction with the intervention will be assessed by using 23 items from the questionnaire developed by Lyons, Swartz, Lewis, Martinez and Jennings[39] and Burner, Zhang, Terp, Bench, Lee, Lam, Torres, Menchine and Arora[40]. We will also use the 10-item System Usability Scale[41] to assess usability. The scale is considered as "industry standard" and provides a global measure of satisfaction[42].

2. **Biometric Assessment**
   Participants will undergo the same physical examination (e.g., height, weight, blood pressure, hip circumference, waist circumference). The same protocol and instruments will be used.
3. **activPAL data download**
   The 7 days of activPAL data will be downloaded and stored in the PI's computer.

6.0 Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

Consent

For the pre-screening activity, potential participants recruited from the email distribution list will sign an e-consent in REDCap. Participants will be given information about what questions we will ask. There are no benefits or side effects related to this prescreening activity. Once they meet all the eligibility criteria, they will be invited for

the in-person baseline visit. At the visit, participants are given as much time as they would like to consider participation from the initial invitation to participate until they sign the "main" consent form. Participants are encouraged to ask as many questions as possible and reminded that participation is completely voluntary and will not affect their medical rights. They are also told that they have the option to discontinue participation at any time for any reason.

Finger Prick Random Blood Glucose Test

Risks associated with the finger prick include temporary discomfort from the needle prick, bruising, and rarely (<1%) infection. These risks will be minimized by using a sterile technique and applying sustained pressure to the site.

activPAL

The activPAL activity tracker is a safe, non-invasive method to capture information about activity cycles. Participation in this study requires that participants wear an activPAL tracker adhered (using Tegaderm adhesive dressing) to the front of the right thigh during waking hours for a minimum of 7 consecutive days (baseline and follow-up). The Tegaderm adhesive dressing used to apply the activPAL devices is hypoallergenic and consists of a dual layer hydrogel that does not pull at the skin or hair. There are few risks associated with wearing the activPAL device and include slight discomfort, such as light pressure from the activPAL or irritation from the waterproof dressing.

Continuous Glucose Monitor

The FreeStyle Libre Pro Flash Glucose Monitoring System is an FDA-approved, professional continuous glucose monitoring device indicated for detecting trends and tracking patterns in persons (age 18 and older) with diabetes. After application of the sensor, only a thin, flexible filament will remain under the skin and the sensor is held in place by an adhesive. The following are possible adverse effects of inserting a sensor and wearing the adhesive patch: local erythema (redness), local infection, inflammation, pain or discomfort, bleeding at the glucose sensor insertion site, bruising, itching, scarring or skin discoloration, and adhesive irritation. There is a remote risk of sensor or needle fracture during insertion, wear or removal, with fragments retained under the skin.

Fitbit

Participants will wear an additional wrist-worn activity tracker for 8 weeks during waking hours. There are few risks associated with wearing the device and include slight discomfort, such as light pressure from the wristband or irritation from wearing a damp band after showering or swimming. There is a possible risk of confidentiality loss. To reduce the risk, we will create an anonymous email account for the Fitbit app. All identifiable data will be kept on password-protected computer systems in a locked office.

Smart Water bottle

Participants will use the smart water bottle to increase the frequency of standing and moving by frequently going to the restroom and kitchen for refills. There is no risk associated with using the smart water bottle. To reduce the possible risk of confidentiality loss, we will create an anonymous email account for the HidrateSpark app. All identifiable data will be kept on password-protected computer systems in a locked office.

8-Week Sedentary Behavior Intervention

Participants will gradually decrease their sedentary behavior and replace the sedentary behavior with a short period of light intensity physical activity such as 2 to 3 minutes of standing or walking over 8 weeks. While participating in this intervention, there is a potential risk of experiencing physical discomfort or symptoms that may include back pain, muscle ache, knee pain, and other discomforts arising from increased activity levels. Additionally, participants may also experience annoyance or inconvenience associated with receiving the tailored text messages. These symptoms or discomforts may occur during the course of the study, but the study team will take measures to minimize any adverse effects and ensure participants' safety and well-being throughout the research process. The level of risk associated with these symptoms or the risk of falling or injury is similar to the risks associated with day-to-day activity. Trained research staff members will instruct participants to make sure there are no hazards within the walking path and surrounding area.

Suicidal ideation or severe distress

Research has confirmed that simply asking a participant about whether they have thoughts of suicide is not a likely trigger of such an event[(43)]. It is usually only when the

person reports ideation as well as an intent, plan, and/or means to commit suicide that risk for immediate suicide is considered to be more acute.

If a participant reports severe distress or suicidal ideation during the survey administration (Baseline visit 2 or Post-intervention visit), the research staff will immediately notify the PI. The PI will provide the participant with help to get treatment. This may include:

- working with the participant to contact his/her doctor,
- contacting a trusted family member, or a therapist to discuss his/her thoughts,
- or working with the participant on a plan that may include getting him/her to a hospital for safety.

7.0 Study Withdrawal/Discontinuation

Taking part in this study is voluntary, and the participant has the right to refuse to take part in the study. The participant can withdraw from the study at any period and should notify the PI or a study staff member. The decision to withdraw will not affect the participant's ability to get healthcare at the institution, or their enrollment in any health plans or benefits. The investigator may decide to discontinue a participant's participation without permission because she may decide that staying in the study will be harmful for the participant, or the sponsor may stop the study. A participant's decision to withdraw from this study will not be retroactive. For example, if a participant provides consent and completes the baseline visit but then decides to withdraw from the study at the post-intervention visit, the data collected from the baseline visit, which was collected in good faith, will not be destroyed.

Criteria for Discontinuation of Individual Participants

Subjects can decide to discontinue entirely from the study at any time for any reason. Subjects can also be discontinued from the study or discontinued from the study treatment due to Investigator decision as detailed below.

1. Withdrawal of consent.
2. At the Investigator's discretion in certain situations such as lack of compliance or serious adverse event.
3. One DKA event or one episode of hyperglycemic, hyperosmolar nonketotic syndrome (HHNS)

4. Dangerous hypoglycemia (glucose <54mg/dl after three treatments or unable to function due to low blood glucose during study visits)
5. Continuous hyperglycemia (random blood glucose >300mg/dl two times in a row during study visits)

Protocol for hypoglycemia

During any study visits, if the study participant develops any of the symptoms below, the study team member will check glucose levels immediately. The symptoms are

- Weakness and tiredness
- Sweating
- Fast breathing
- Shakiness, nervousness, and or anxiety
- Nausea
- Confusion and problems communicating
- Light-headedness, dizziness

If the glucose level is below 70mg/dl, one of the following options will be administered.

1. 2 oz (60ml) juice
2. 15mg of glucose tables

After 15 minutes, the study team member will re-check glucose level. If the glucose level is still below 70mg/dl, the treatment will be repeated up to 2 times.

If the participant's glucose level is still below 70mg/dl after three treatments, the study team member will notify the PI and ask participants to call healthcare provider. If the participant's glucose level is still below 54mg/dl or the participant is unable to function because of mental or physical changes due to low blood glucose, call 911 immediately and notify the PI.

Protocol for hyperglycemia

During the first visit, the finger prick random glucose level of potential participants is 300 mg/dl or higher two times in a row, the RA will notify PI immediately. The potential participants will be informed of their glucose levels and asked to contact their healthcare provider immediately. The PI will withdraw the study participant to prevent severe hyperglycemic events and/or DKA.

Adverse events (AEs) will be reported according to IRB policies. Any adverse event requiring reporting will be reported no later than 10 working days to the IRB using the IRB form "Report of Unanticipated Problem Involving Risk to Participants or Others" (IRB Form #1105). Reporting will depend on adverse event severity:

Grading of Severity

0: No AE or within normal limits.

1: Mild AE.

2: Moderate AE.

3: Severe AE resulting in inpatient hospitalization, or a persistent or significant disability/incapacity.

4: Life-threatening or disabling AE.

5: Fatal AE.

8.0 Statistical Considerations

Based on Sit Less V1's (IRB #221566) effect size of 0.71 for reducing sitting time, we estimated a minimum sample size of 66. To assess the scalability of Sit Less V2, we aim to recruit 80 patients. Eligible participants will include T2D patients from VUMC who report sitting for over 10 hours daily, own a smartphone, and do not currently use an activity tracker. We will screen potential participants using VUMC's electronic health records (EHR) and send recruitment messages via the My Health at Vanderbilt app. According to our EHR search, we have 2,125 eligible patients, and with a 4% recruitment rate — as seen with enrolling 7 participants monthly from Sit Less V1 — reaching a target of 80 participants within 12 months is achievable.

Analysis Strategies

Aim 1: Acceptability outcomes will be reported as percentages or averages.
Aims 2 & 3: Descriptive analyses are planned to characterize the study sample on all measures including baseline demographics and covariates. For this pilot study, exploratory linear mixed modeling will be used to provide descriptive statistics relative to treatment effects, both within- and between-groups effects on the primary and secondary outcomes over time. We will also estimate effect sizes for those outcomes.

9.0 Privacy/Confidentiality Issues

All Personal Health Information (PHI) and Personal Identifying Information (PII) will be kept confidential, unless release is required by law. Release of PHI/PII information will only be allowed if it is legally required by law. The PI and staff have been trained in confidentiality and HIPAA requirements and will conduct the study using Good Clinical Practice guidelines.
Upon enrollment, participants will be assigned a unique study ID number and anonymous email account that will be used to label all research data including Fitbit data, CGM data, questionnaires, and activPAL data. The study ID and the anonymous email will serve as the only identifier used on all study-related documents. Informed consent will occur at the time of recruitment once eligibility verification is completed. The participant identifiers will be stored in the Master List, which will include full name and contact information (e.g., phone number, email address) and will be used for administrative purposes only. The Master List will be maintained by study staff and stored in a file separate from the coded study dataset on a password-protected computer. Only individuals directly involved with the study (e.g., PI or her staff) will have access to this file.

This individualized email address will then be linked to a Fitbit account in which personal identifiers should not be used. Importantly, research staff and participants will be advised that the email and Fitbit accounts should be used strictly for the study's purpose. Moreover, account information will be stored in protected PI's computer within encrypted documents.

All the Fitbit data will be extracted from the Fitbit account to Redcap using the Fitbit web API developed by VU School of Nursing IT team. Fitbit data will be stored on a secure computer at University School of Nursing server and password-protected, only accessible by the PI and/or the IT team. The Fitbit data will be uploaded into REDCap.

To send weekly text messages from REDCap, we will utilize the third-party service Twilio.com which means that all voice calls and SMS messages will be routed through Twilio's servers. However, REDCap goes to great lengths to ensure that voice call records and SMS transcriptions do not stay in Twilio's logs but are removed shortly after being completed. This is done for security and privacy concerns (e.g., HIPAA), in which our survey participants' phone numbers and their survey responses do not get

permanently logged on Twilio's servers but instead remain securely and separately in REDCap. Twilio uses two-factor authentication to access the application administratively. The integrated module can only be turned on by a REDCap Administrator. Twilio configuration is managed by a REDCap administrator. The integration requires 'inspectors' be turned off at the Twilio level to ensure no logging data is retained.

However, this method is limited to two-way interaction, which means that Twilio and REDCap system do not allow research participants to text back to the study team. To facilitate two-way communications, we will have a wireless cell phone and answer any questions if the participants have any.

All hard copy documents (e.g., sleep diary or wear log) will be stored in a locked filing cabinet and office. All electronic records, including the Master List and voice recordings, will be stored on a secure computer at Vanderbilt University School of Nursing and password-protected, only accessible by the PI and/or her staff. No identifiable information will be stored on any mobile devices (laptops, USB keys, CDs, DVDs, etc.). Research files will be kept for 7 years after the study is completed. Data entry will be completed in REDCap by the PI and/or her staff and will be imported to SPSS file format for analysis. Only de-identified data will be used for analysis.

10.0 Follow-up and Record Retention

Raw hard copy research data will be kept in locked file cabinets in a locked office. All electronic records, including the Master List and voice recordings, will be stored on a secure internal Vanderbilt University School of Nursing server and password-protected, only accessible by the PI and/or her staff. After a period of seven years from the end date of the study, all identifying information, including signed consent forms and the Master List, will be destroyed. Anonymous raw data and electronic data will be maintained indefinitely.

References

1. Bellettiere J, LaMonte MJ, Evenson KR, Rillamas-Sun E, Kerr J, Lee I-M, et al. Sedentary Behavior and Cardiovascular Disease in Older Women. Circulation. 2019;139(8):1036-46.
2. Young DR, Hivert M-F, Alhassan S, Camhi SM, Ferguson JF, Katzmarzyk PT, et al. Sedentary behavior and cardiovascular morbidity and mortality: a science advisory from the American Heart Association. Circulation. 2016;134(13):e262-e79.
3. Rezende LFMd, Rodrigues Lopes M, Rey-López JP, Matsudo VKR, Luiz OdC. Sedentary behavior and health outcomes: an overview of systematic reviews. PloS one. 2014;9(8):e105620.
4. Bergouignan A, Latouche C, Heywood S, Grace MS, Reddy-Luthmoodoo M, Natoli AK, et al. Frequent interruptions of sedentary time modulates contraction-and insulin-stimulated glucose uptake pathways in muscle: ancillary analysis from randomized clinical trials. Scientific reports. 2016;6(1):1-13.
5. Hamer M, Hackett RA, Bostock S, Lazzarino AI, Carvalho LA, Steptoe A. Objectively assessed physical activity, adiposity, and inflammatory markers in people with type 2 diabetes. BMJ Open Diabetes Research and Care. 2014;2(1):e000030.
6. Cichosz SL, Fleischer J, Hoeyem P, Laugesen E, Poulsen P, Christiansen J, et al. Objective measurements of activity patterns in people with newly diagnosed Type 2 diabetes demonstrate a sedentary lifestyle. Diabetic medicine. 2013;30(9):1063-6.
7. Loprinzi PD. Accelerometer-determined sedentary and physical activity estimates among older adults with diabetes: considerations by demographic and comorbidity characteristics. Journal of aging and physical activity. 2014;22(3):432-40.
8. Van der Berg JD, Stehouwer CDA, Bosma H, van der Velde JHPM, Willems PJB, Savelberg HHCM, et al. Associations of total amount and patterns of sedentary behaviour with type 2 diabetes and the metabolic syndrome: The Maastricht Study. Diabetologia. 2016;59(4):709-18.
9. Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell KE, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. Lancet. 2016;388(10051):1302-10.
10. Boulé NG, Kenny GP, Haddad E, Wells GA, Sigal RJ. Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in Type 2 diabetes mellitus. Diabetologia. 2003;46(8):1071-81.
11. Kennerly A-M, Kirk A. Physical activity and sedentary behaviour of adults with type 2 diabetes: a systematic review. Practical Diabetes. 2018;35(3):86-9g.
12. Bouchard C, Blair SN, Katzmarzyk PT. Less Sitting, More Physical Activity, or Higher Fitness? Mayo Clin Proc. 2015;90(11):1533-40.
13. Chastin SFM, Egerton T, Leask C, Stamatakis E. Meta-analysis of the relationship between breaks in sedentary behavior and cardiometabolic health. Obesity. 2015;23(9):1800-10.
14. Dempsey PC, Larsen RN, Dunstan DW, Owen N, Kingwell BA. Sitting Less and Moving More: Implications for Hypertension. Hypertension. 2018;72(5):1037-46.
15. Dunstan DW, Kingwell BA, Larsen R, Healy GN, Cerin E, Hamilton MT, et al. Breaking up prolonged sitting reduces postprandial glucose and insulin responses. Diabetes care. 2012;35(5):976-83.

Date: May 15th, 2024

16. Ezeugwu VE, Manns PJ. The Feasibility and Longitudinal Effects of a Home-Based Sedentary Behavior Change Intervention After Stroke. Archives of Physical Medicine and Rehabilitation. 2018;99(12):2540-7.
17. Henson J, Davies MJ, Bodicoat DH, Edwardson CL, Gill JMR, Stensel DJ, et al. Breaking Up Prolonged Sitting With Standing or Walking Attenuates the Postprandial Metabolic Response in Postmenopausal Women: A Randomized Acute Study. Diabetes Care. 2016;39(1):130.
18. Lynch BM, Nguyen NH, Moore MM, Reeves MM, Rosenberg DE, Boyle T, et al. A randomized controlled trial of a wearable technology-based intervention for increasing moderate to vigorous physical activity and reducing sedentary behavior in breast cancer survivors: The ACTIVATE Trial. Cancer. 2019;125(16):2846-55.
19. Freene N, van Berlo S, McManus M, Mair T, Davey R. A Behavioral Change Smartphone App and Program (ToDo-CR) to Decrease Sedentary Behavior in Cardiac Rehabilitation Participants: Prospective Feasibility Cohort Study. JMIR Form Res. 2020;4(11):e17359.
20. Patterson K, Davey R, Keegan R, Niyonsenga T, Mohanty I, van Berlo S, et al. A smartphone app for sedentary behaviour change in cardiac rehabilitation and the effect on hospital admissions: the ToDo-CR randomised controlled trial study protocol. BMJ Open. 2020;10(12):e040479-e.
21. Frese EM, Fick A, Sadowsky HS. Blood pressure measurement guidelines for physical therapists. Cardiopulm Phys Ther J. 2011;22(2):5-12.
22. Craig CL, Marshall Al Fau - Sjöström M, Sjöström M Fau - Bauman AE, Bauman Ae Fau - Booth ML, Booth Ml Fau - Ainsworth BE, Ainsworth Be Fau - Pratt M, et al. International physical activity questionnaire: 12-country reliability and validity. (0195-9131 (Print)).
23. Segal-Isaacson CJ, Wylie-Rosett J, Gans KM. Validation of a Short Dietary Assessment Questionnaire: The Rapid Eating and Activity Assessment for Participants Short Version (REAP-S). The Diabetes Educator. 2004;30(5):774-81.
24. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213.
25. Adams MM. On our feet: Feasibility trial of an intervention to reduce sedentary behavior and increase physical activity [Ph.D.]. Ann Arbor: The University of North Carolina at Greensboro; 2012.
26. Verplanken B, Orbell S. Reflections on past behavior: a self-report index of habit strength 1. Journal of applied social psychology. 2003;33(6):1313-30.
27. Hays RD, Bjorner Jb Fau - Revicki DA, Revicki Da Fau - Spritzer KL, Spritzer Kl Fau - Cella D, Cella D. Development of physical and mental health summary scores from the patient-reported outcomes measurement information system (PROMIS) global items. (1573-2649 (Electronic)).
28. Sangha O, Stucki G Fau - Liang MH, Liang Mh Fau - Fossel AH, Fossel Ah Fau - Katz JN, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. (0004-3591 (Print)).
29. Schmitt A, Gahr A Fau - Hermanns N, Hermanns N Fau - Kulzer B, Kulzer B Fau - Huber J, Huber J Fau - Haak T, Haak T. The Diabetes Self-Management Questionnaire

(DSMQ): development and evaluation of an instrument to assess diabetes self-care activities associated with glycaemic control. (1477-7525 (Electronic)).
30. Polonsky WH, Fisher L Fau - Earles J, Earles J Fau - Dudl RJ, Dudl Rj Fau - Lees J, Lees J Fau - Mullan J, Mullan J Fau - Jackson RA, et al. Assessing psychosocial distress in diabetes: development of the diabetes distress scale. (0149-5992 (Print)).
31. Dubé MC, Valois P Fau - Prud'homme D, Prud'homme D Fau - Weisnagel SJ, Weisnagel Sj Fau - Lavoie C, Lavoie C. Physical activity barriers in diabetes: development and validation of a new scale. (0168-8227 (Print)).
32. Mitchell T, Borner K, Finch J, Kerr J, Carlson JA. Using Activity Monitors to Measure Sit-to-Stand Transitions in Overweight/Obese Youth. Med Sci Sports Exerc. 2017;49(8):1592-8.
33. Wadden TA, West DS, Neiberg RH, Wing RR, Ryan DH, Johnson KC, et al. One-year weight losses in the Look AHEAD study: factors associated with success. Obesity. 2009;17(4):713-22.
34. White I, Smith L, Aggio D, Shankar S, Begum S, Matei R, et al. On Your Feet to Earn Your Seat: pilot RCT of a theory-based sedentary behaviour reduction intervention for older adults. Pilot and Feasibility Studies. 2017;3(1):23.
35. Institute of Medicine. Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate. Washington, DC: The National Academies Press; 2005. 638 p.
36. Agboola S, Jethwani K, Lopez L, Searl M, O'Keefe S, Kvedar J. Text to move: a randomized controlled trial of a text-messaging program to improve physical activity behaviors in patients with type 2 diabetes mellitus. Journal of medical Internet research. 2016;18(11):e6439.
37. Pellegrini CA, Hoffman SA, Daly ER, Murillo M, Iakovlev G, Spring B. Acceptability of smartphone technology to interrupt sedentary time in adults with diabetes. Translational Behavioral Medicine. 2015;5(3):307-14.
38. Block G, Azar KMJ, Romanelli RJ, Block TJ, Hopkins D, Carpenter HA, et al. Diabetes prevention and weight loss with a fully automated behavioral intervention by email, Web, and mobile phone: A randomized controlled trial among persons with prediabetes. Journal of Medical Internet Research. 2015;17(10):e240.
39. Lyons EJ, Swartz MC, Lewis ZH, Martinez E, Jennings K. Feasibility and Acceptability of a Wearable Technology Physical Activity Intervention With Telephone Counseling for Mid-Aged and Older Adults: A Randomized Controlled Pilot Trial. JMIR Mhealth Uhealth. 2017;5(3):e28.
40. Burner E, Zhang M, Terp S, Bench KF, Lee J, Lam CN, et al. Feasibility and Acceptability of a Text Message–Based Intervention to Reduce Overuse of Alcohol in Emergency Department Patients: Controlled Proof-of-Concept Trial. JMIR mHealth and uHealth. 2020;8(6):e17557.
41. Brooke J. SUS: A quick and dirty usability scale. Usability Eval Ind. 1995;189.
42. Brooke J. SUS: a retrospective. Journal of usability studies. 2013;8(2):29-40.
43. Gould MS, Marrocco FA, Kleinman M, Thomas JG, Mostkoff K, Cote J, et al. Evaluating iatrogenic risk of youth suicide screening programs: a randomized controlled trial. Jama. 2005;293(13):1635-43.

Date: May 15th, 2024