Sedentary Behavior in People with Type 2 Diabetes

By

Shaima Abdullah Mohammed Alothman

MSc, Oklahoma State University Center for Health Sciences, 2013
BSPT, King Saud University, 2008

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Patricia M. Kluding, PT, PhD
Chairperson

Jason Rucker, PT, PhD

Jo Wick, PhD

Joseph LeMaster, MD MPH

John Thyfault, PhD

Date Defended: October 31st, 2018

The dissertation committee for Shaima Abdullah Mohammed Alothman
certifies that this is the approved version of the following dissertation:

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Patricia M. Kluding, PT, PhD
Chairperson

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Abstract

Sedentary behavior is a major health issue in people with type 2 diabetes (T2D). Many people with T2D are sedentary despite strong recommendations of regular physical activity. Studies that investigate the complex nature of sedentary behavior in people with T2D are still in their early stages. The overall purpose of this project was to investigate the general health impact of sedentary behavior on people with T2D. Specifically, three areas of research were identified as the primary focus of this dissertation. First, to examine the test-retest reliability of sedentary behavior measured via objective measures that are uniquely capable of detecting postural allocation (i.e. sitting vs standing or walking). Second, to assess the association of objective modifiable factors, glycemic control and physical function, and subjective health perception, fatigue and well-being, with sedentary behavior. Lastly, the feasibility and effectiveness of behavioral interventions aimed to decrease sedentary behavior in people with T2D were tested.

Chapter one describes the results of a systematic review of randomized clinical trials (RCTs) that used objective measurement of activity to determine the outcome of interventions promoted daily physical activity in sedentary people with T2D. Two databases, PubMed and CINAHL, were searched for eligible studies using the following search terms: sedentary, diabetes, pedometer, physical activity, and accelerometer. A total of 15 RCTs were identified that investigated objectively measured daily physical activity in people with T2D. Multiple interventions such as behavioral/cognitive consultation and motivational phone calls promoting physical activity demonstrated improvement in physical activity level during the intervention period. The results of this review indicated that different interventional strategize can leads to

temporary improvement in physical activity, however, interventions that produce long-term increases in physical activity and decreases in sedentary behavior are still scarce.

Building upon the results from the above systematic review and the recommendations of a four session workshop sponsored by the National Heart, Lung, and Blood Institute and National Institute on ageing entitled Sedentary Behavior: Identifying Research Priorities (Rosenberg et al., 2015; Thyfault, Du, Kraus, Levine, & Booth, 2015); we surmise the importance of establishing the test-retest reliability of activity monitors, activPAL™, in measuring habitual sedentary behavior and physical activity. Chapter two describes the result from examining the test-retest reliability of an activPAL™ activity monitor in measuring sedentary behavior and physical activity in people with T2D aged 50 to 75 years old. Habitual sedentary behavior and physical activity data from two 7-day time periods of assessment separated by at least one week were obtained and intraclass correlation coefficient (ICC) was utilized to compare the two time points. Thirty participants completed the study. Both sedentary time and standing times exhibit high reliability, while step count and transitions from sit to stand demonstrated very high reliability. These results indicate stability in the measurement of sedentary behavior and physical activity in people with T2D over time using an activPAL™ activity monitor. Thus, we concluded that activPAL™ devices might be used as objective assessment of sedentary behavior and physical activity and detect changes in activity level in pre-post intervention designs.

Examining sedentary behavior in further detail, multiple linear regression models were built to investigate the relationship between sedentary behavior and number of transitions from sit to stand with glycemic control, physical function, fatigue, and well-being in people with

T2D. As described in chapter three, sedentary behavior data measured using activPAL^{TM} obtained from 59 individuals with T2D, aged 50 to 75 years old. Analysis of the data demonstrated the significant positive association of glycemic control with sedentary behavior independent of moderate to vigorous physical activity (MVPA). Furthermore, it showed that higher physical function levels tended to predict the association with higher number of transitions from sit to stand. Fatigue and well-being showed no significant association with either sedentary behavior or transitions from sit to stand. The results from this chapter demonstrated that glycemic control predicted sedentary behavior level. Furthermore, it highlighted the need to establish the direction of the association between glycemic control and sedentary behavior. In addition, there is a need to identify other modifiable health factors as these variables could be used as a main target for interventions aimed to improve health outcomes in people with T2D.

In the last experimental chapter, chapter four, the results from the feasibility and efficacy of combined sedentary behavior counseling and vibrotactile sensory feedback on sedentary time and physical activity (steps count) in people with T2D are described. Ten community-dwelling sedentary adults completed the 3 months intervention consisting of sedentary behavior counseling (SB education and a motivational interviewing-informed) aided by an activity monitor with vibrotactile feature (activPAL3^{TM}). Participants received sedentary behavior counseling at the end of weeks one, five, and nine; while they received the vibrotactile sensory feedback from the activity monitor at weeks five and nine. After study completion the intervention appeared to be feasible with 100% compliance and only 2 out of 10 participants reporting mild to moderate issues with activity monitor tolerability such skin irritation.

However, these tolerability concern did not lead to either serious adverse events or the removal of the activity monitor. Furthermore, the pre – post assessment analysis of sedentary behavior and physical activity via paired t test or Wilcoxon matched pair signed-rank test showed that the intervention was effective in decreasing sedentary behavior and increasing physical activity, in addition to improvements in glycemic control. These findings suggested the promising effect of intervention aimed to decrease sedentary behavior in people with T2D in improving health outcomes. Larger sample size and randomized clinical trial design studies are warranted to examine the full extent of the intervention in the future.

In summary, the results from this dissertation project found that people with T2D demonstrated stable levels of sedentary behavior and physical activity over 2-time periods. These stable levels of activity can be improved after the completion of 3-months behavioral modification intervention. Furthermore, sedentary behavior and glycemic control demonstrated a positive relationship independent of MVPA, and glycemic control improved after the compilation of a behavioral intervention aimed to decrease sedentary behavior and increase physical activity. Overall, sedentary behavior appears to negatively influence glycemic control and short-term intervention can offset the effects of sedentary behavior. However, the long-term effect of this intervention is still unclear. The obtained results indicate the need for future research investigating the full impact of sedentary behavior in people with T2D independent of physical activity, as being physically active does not necessary exclude high levels of sedentary behavior. Further, there is a need to investigate possible clinical applications for managing T2D and preventing detrimental health complications associated with T2D and sedentary behavior.

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This work is dedicated to my parents, for fostering the love of science in me since I was a child and for their unquestionable believe in me.

The Prophet Muhammad (peace be upon him) said: “He who does not thank the people is not thankful to Allah”

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Table of Contents

Dissertation Introduction

Theoretical Framework of Aims Development

Objective and accurate measures of SB have been validated through use of devices such as ActiGraph and activPAL™.[1, 2] ActivPAL™ is a small motion sensor which classifies human physical behavior to 3 categories: sitting/lying, standing, and stepping.[3] Compared to other motion sensor devices designed to measure SB, a unique feature of the activPAL™ is the ability to detect postural allocation. It contains both accelerometer and inclinometer sensors which can discriminate between sitting vs standing by detecting static acceleration in relation to thigh orientation in space. It can also measure steps by detecting dynamic acceleration.[4] In general activPAL™ has shown higher accuracy in detecting SB compared to other monitors.[4-7]

Reliability is defined as the ability of an instrument/behavior to produce stable and consistent results. In this work our main method of measuring SB was through the analysis of activPAL™ output data. Although the activPAL™ has been established as a valid measurement tool of SB in several studies[1, 5], the test-retest reliability of SB captured via activPAL™ has not been established. Previous studies that examined the reliability of activPAL™ in adults employed methodologies, one week of measurement or testing under controlled laboratory conditions, that limit the applicability of the findings to habitual SB in free-living conditions.[8, 9] In order to evaluate the test-retest reliability of habitual SB via an objective activity monitor, the 1st aim of this dissertation was to examine the test-retest reliability of ActivPAL as objective measure of SB in people with T2D. Investigating SB relationship with health outcomes is dependent among other factors on establishing the nature of habitual SB nature.

SB is a serious health issue in people with T2D where the majority of people with T2D are considered sedentary.[10-12] For the 2nd aim of this project we investigate four possible modifiable health variables (glycemic control, well-being, fatigue, and physical function) that can predict SB level in people with T2D. These variables were identified as most likely to affect SB based on previous studies in SB or T2D literature.

Multiple studies have shown that SB is associated with T2D and it negatively affects glucose and insulin metabolism in both healthy and people with T2D.[13-16] Studies examining the effect of acute episodes of SB on glucose and insulin metabolism have confirmed that SB has negative impacts on both biomarkers. Fortunately, glucose and insulin control were improved significantly by incorporating light activities into the testing protocol.[17-20] Decreasing SB by light activities means that the human body experiences frequent alternating muscle activities. During active muscles contraction insulin action improves, resulting in increased glucose uptake. These studies examined the acute effect of SB on glycemic control. In addition, the relationship between glycemic control and SB can be bi-directional as no study has established cause and effect yet. Thus, in aim 2 we examined the relationship between long-term glycemic control with SB.

Well-being can be defined as the individual's feeling, function, and evaluation of their life. How people with T2D perceive their overall well-being can greatly influence their health outcomes. For example, Petterson et al. [21] showed that patients with diabetes who are insulin dependent have significantly lower well-being scores compared to patients with diabetes who control their diabetes by diet or oral medication only. Another study[22] showed that in people with T2D, a higher perception of general well-being is associated with improved glycemic control. These studies show that well-being correlates with better health outcomes in people with T2D. In addition to the correlation between well-being and better health outcomes, a perception of positive well-being can be influenced by activity levels. Buman et al. [23] showed that objectively measured light-activity was positively associated with well-being in 862 older adults even after adjusting for covariates (age, gender, race, educational status, income, and neighborhood walkability index). Another study by Shiue[24] showed that TV/screen time of 2 hours or more was associated with metabolic disorder, diabetes, poor mental health, and poor well-being in adults age 18-98 years. These studies suggest that there is a need to investigate perception of well-being as possible predictor of SB in people with T2D.

Fatigue has been reported as a frequent complaint in sedentary adults as well as in people with T2D. In sedentary literature, fatigue was identified as key barrier to decreasing SB in overweight/obese adults [25] and lower fatigue levels were associated with less time spent sedentary.[26, 27] Similarly, people with T2D report higher levels of fatigue and are 10 times more likely to experience fatigue compered to healthy adults.[28, 29] High levels of fatigue can cause people to avoid activities that they perceive will make them more fatigued. This can have negative impacts on metabolic and overall well-being and spur a vicious cycle of SB exacerbating feelings of fatigue. In summary, the current evidence highlights the prevalence of fatigue in people with T2D as well as the link between SB and fatigue. Additionally, evidence also supports that perceptions of well-being can impact a person's level of engagement in SB. However, the relationship between fatigue, perception of well-being, and SB in people with T2D is still in need of investigation.

In older adults, declines in physical function contribute to increases in SB. Furthermore, physical function influences quality of life, health care cost, and mortality.[30] A study by Sardinha et al. showed a significant association between breaks in SB and lower physical function in older adults after adjusting total time toward SB and/or MVPA. Furthermore, it showed that participants with the lowest physical function scores were the least likely to break-up their SB and engage in more than 30 minutes of MVPA per day.[30] Another study by Gennuso et al. showed breaks in SB patterns were more important than total time spent sedentary in determining physical function levels in older adults.[31] These studies are limited to older populations; however, they reveal a critical link between physical decline and SB.

Muscle strength and balance are physical function parameters that can be affected by T2D and can lead to further complications.[32-35] People with T2D have higher risk of falling compared with healthy, aged-matched individuals.[36, 37] Additionally, a study by Maurer et al. showed that balance and gait are significantly and independently associated with a higher risk of falls in older adults (>60 years) with T2D. Strengthening and balance exercises are known to decrease falls in people with T2D.[38] However, it is unknown whether people who experience falls tend to be sedentary or not. Furthermore, diabetes cannot alone explain all the changes observed in physical function.[39] Thus, It is important to understand the relationship between SB and physical function in people with T2D.

Studies targeting SB as their main intervention goal are relatively new. Furthermore, only few studies have used SB counseling, without any specific exercise prescription, as a strategy to decrease SB. The first study assessing the effect of SB counseling found that a single session of face-to-face SB counseling decreased SB by 33 minutes compared to the control group.[40] A randomized control study found that 4 sessions of SB counseling over a 6 months period significantly increased total standing time and decreased fasting serum insulin and waist circumference post intervention.[41] These studies indicate the potential effectiveness and feasibility of SB counseling for the general population. However, no study published to date has focused on people with T2D. SB counseling showed promising results in decreasing SB for the general population. Therefore, the 3rd aim of this project was designed to test the feasibility of a combined approach to treat SB in people with T2D. The combined approach consisted of SB counseling (SB education + motivational intervewing) and vibrotactile sensory feedback using the vibration feature in the used activity monitor, activPAL™.

Significance and Innovation

This work is significant in three aspects: First, testing the test-retest reliability of habitual sedentary behavior (SB) via activPAL™ (PAL Technologies, Glasgow, Scotland, UK) is important to determine the effectiveness of any proposed intervention to reduce SB over time. Establishing a reliable and valid objective measure of SB is one of the recommendations of a four session workshop sponsored by the National Heart, Lung, and Blood Institute and National Institute on ageing entitled Sedentary Behavior: Identifying Research Priorities.[42] Second, understanding the relationship between SB and physical function in people with type 2 diabetes (T2D) is important in designing and implementing interventional programs. Lower physical function is associated with higher SB in older adults independent of moderate to vigorous physical activity (MVPA).[31] However, the relationship between SB and physical function in the presence of T2D is still unknown. In addition, understating the relationship between SB and patient perception of their health in people with T2D is important in designing strategies and approaches to increase patient participation, education, and adherence to prevention programs. Third, the SB intervention approch tested in this project is unique because of the combination of SB counseling (SB education + motivational intervewing) and activity monitor vibrotactile feedback. All these aspects target important prevention and wellness areas in improving general population health especially for individuals with T2D.

This dissertation project is the first to attempt to understand the complex nature of SB and its association with long-term glycemic control, physical function and patient's perception of their health in people with T2D. This understanding has several possible clinical applications in managing T2D and the prevention of detrimental health complications associated with T2D and SB. For example, understanding the effect of physical function level and fatigue on SB could lead to the development of SB intervention program that focus on improving physical function by using light exercises that avoid any significant increase in the participants fatigue level. Furthermore, this work is innovative due to 1) the use of an objective method, activPAL^{TM}, to detect postural allocation allowing the differentiation between SB and physical activity; and 2) the use of objective data generated by this activity monitor to facilitate SB education and counselling is an innovative approach

Specific Aims:

Sedentary behavior (SB) has harmful effects on multiple systems in the human body. SB is defined as "*any waking behavior characterized by energy expenditure less than 1.5 METs while in a sitting or reclining posture.*"[43] Recent studies have shown that the deleterious effects of SB are magnified in disease states, such as type-2-diabetes (T2D). In contrast to SB, physical activity (PA) can be defined as any movement other than sitting that requires skeletal muscle activation and causes energy expenditure. It is important to distinguish SB from PA because people can meet the PA recommendations and still have extended periods of SB.

Objective measures of SB such as inclinometers (e.g. ActivPAL) can differentiate between sitting, standing, and walking. The ActivPAL is a valid measure of activity. However, the device's test-retest reliability as indicative of habitual SB in adults under free living conditions is unknown. Thus, use of the ActivPAL in interventional studies is limited.

Several health domains appear to be affected as SB increases, however, their link with the presence of T2D remains unclear. For example, physical function is known to be decreased in people with T2D and individuals' perceptions influence disease status. It is uncertain if physical function level and individual perception would explain SB level in people with T2D or not.

The overall purpose of this project is to investigate general health impacts of SB on people with T2D. The central hypothesis is that there will be a negative relationship between SB, physical function and perceived factors in people with T2D that can be ameliorated with SB intervention. This study has 3 specific aims and 7 hypotheses:

Aim 1: Examine test-retest reliability of the ActivPAL in measuring total sitting time (TST) as function of sedentary behavior (SB) in people with T2D. We hypothesize that the ActivPAL will have at least moderate reliability in quantifying TST across two one-week periods of measurement separated by one week of rest (H1). Interclass correlation will be used to test H1.

Aim 2: Examine the association between SB (TST) and physical function, glycemic control, fatigue, and well-being in people with T2D. We hypothesize that lower physical function test scores (H2), higher glycemic control levels (H3), higher scores on a fatigue scale (H4), and lower scores on a well-being questionnaire (H5) will explain significant portions of the variability in TST independent of age and MVPA. Independent variables: Physical function will be tested using senior fitness; Glycemic control will be tested using HbA1c. Fatigue will be assessed using Fatigue Severity Scale (FSS); and well-being will be assessed using Well-Being Questionnaire (WBQ-22). Dependent variable: TST. Multiple-linear regression will be used to test H2 to H5.

Aim 3: examine the feasibility of a sedentary behavior intervention on TST in people with T2D. We hypothesize that participants will tolerate ActivPAL wear (H6), be able to adhere to the intervention protocol (H7). SB intervention will be considered as feasible if we achieved 70% ActivPAL tolerability and adherence to the intervention protocol.

These aims will advance the field of SB and T2D in the following ways: 1) Establishing the reliability of ActivPAL as an objective measure of habitual SB will facilitate its use in measuring the effects of SB interventional studies. 2) Understanding the link between SB and physical function, higher glycemic control, fatigue, and sense of well-being in people with T2D may lead to targeted SB interventions that enhance long term benefits. 3) Establish the feasibility of our novel SB intervention.

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Chapter 1: Effectiveness of Interventions for Promoting Objectively Measured Physical Activity of Adults with Type 2 Diabetes: A systematic review

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Abstract

BACKGROUND: Many people with type 2 diabetes (T2D) are sedentary despite strong recommendations of regular physical activity (PA). Objective measures of PA provide accurate reflection of daily PA level. The purpose of this review was to analyze studies used pedometers or accelerometers to determine the outcome of interventions promoted daily PA in people with T2D.

METHODS: An electronic literature search was conducted using the PubMed and CINAHL databases (2000 – 2016), with search terms: sedentary, diabetes, pedometer, physical activity, and accelerometer. Only peer-reviewed, randomized clinical trials (RCTs) that utilized objective measurement of daily PA level were included. All studies design, participant characteristics, intervention, and key findings were evaluated systematically and summarized.

RESULTS: A total of 15 RCTs were identified investigated objectively-measured daily PA in people with T2D. A significant increase in PA was found following exercise consultation, behavioral/cognitive consultation, continuous glucose monitoring counseling, and motivational phone calls promoting PA. However, this increase in daily PA level was evident only during the intervention period.

CONCLUSION: Our systematic review of the literature indicated that a variety of interventions approaches were effect in increasing PA temporarily during the intervention period. Interventions that utilize objective methods in measuring PA and have long term improvement in overall PA are needed.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease with significant morbidity and mortality rates. In 2014, the CDC reported that the prevalence of type 2 DM is around 10 % in the United States.[2] Several factors such as the aging population, higher obesity rates, and sedentary lifestyle are expected to increase the prevalence of DM to 30% by 2050.[3] Among these factors, obesity and lifestyle are considered to be modifiable. Therefore, interventions that increase physical activity and reduce sedentary time are crucial to offset the increase in DM prevalence and to decrease the burden of DM worldwide. Evidence has shown that regular physical activity is a vital aspect in managing DM and delaying its complications.[4, 5] However, many people with type 2 DM remain sedentary or inactive despite the strong recommendations of regular physical activity.[6-8]

Previous systematic reviews have examined interventions to promote physical activity in a variety of populations, with 2 focused on people with type 2 DM. One review concluded that exercise had a positive effect on glycemic control, visceral adipose tissue and plasma triglycerides, but not plasma cholesterol.[9] The other found that interventions to promote physical activity in older adults (>65 years) with type 2 DM, were effective when assessed using subjective measures.[8] However, they only identified 6 studies out of 21 that had adequate methodological quality. One limitation of both of these previous systematic reviews is that studies using only subjective, self-reported physical activity outcomes were included. Sedentary adults have been shown to overestimate their physical activity level; thus results from subjective physical activity measures need to be interpreted with caution.[10, 11]

Objective measures of physical activity such as pedometers and accelerometers have been shown to be valid and reliable in measuring physical activity in a variety of populations.[12, 13] Even though pedometers are inexpensive and valid tools for measuring physical activity, they do have some disadvantages: they must be reset every day, people must remember to wear them while active, and they only measure step count and distance.[14] Accelerometers are also valid and may be more appropriate for measuring physical activity for longer time period of time, up to 10 days.[15] However, a disadvantage of accelerometers is that the data is not readily available during wearing time, as it must typically be processed and interpreted.[14] Overall, pedometers and accelerometers are convenient and accurate tools in measuring physical activity in people with chronic diseases such as diabetes.[16]

To the best of our knowledge, no systematic review has focused exclusively on evaluating interventions promoting objectively-measured physical activity in people with type 2 DM. As objective measures have greater validity than self-reported measures of physical activity, there is a critical need for researchers to use objective tools to measure physical activity for accurate comparisons of interventions. The purpose of this systematic review was to analyze studies that used pedometers or accelerometers to determine the outcome of interventions designed to promote daily PA in people with type 2 DM. The information provided by this review will help clinicians identify the most appropriate interventions to improve physical activity for their patients with type 2 DM.

Methods

Data Sources and Searches

An electronic literature search was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines using the PubMed and CINAHL databases.[17] The following terms were used to conduct the search in different combinations: sedentary, diabetes, pedometer, physical activity, and accelerometer. Search criteria were specified to include randomized clinical trials, studies written in English (due to limited resources for translation), human subjects, and studies published from 2000 to 2016. Older studies were not included in the search, because the first use of objective measures such as pedometers and accelerometers in diabetes research occurred around the year 2000.

Study Selection

Only peer-reviewed published randomized clinical trials that utilized objective measurement of physical activity level were included in this review. Included studies were required to include an intervention designed to increase daily physical activity level or reduce sedentary time in type 2 diabetes individuals. There were no restrictions on participant's age, disease duration, type of intervention, and disease severity. Studies other than randomized clinical trials were excluded from screening. Studies were excluded if the physical activity level was not measured with objective tools such as accelerometer or pedometer.

All titles, abstracts, and full-text of every study retrieved from the search were screened by two independent reviewers (S.A. and A.Y.) using the eligibility criteria. If one of the two reviewers were in doubt of the eligibility of any screened studies, a third independent reviewer (P.K.) assessed the study using the same eligibility criteria and the decision of the third reviewer was final.

Data Extraction and Quality Assessment

All retrieved studies were evaluated systematically and summarized according to previous published methods.[18] This included study objective (effect of physical activity intervention); targeted health domain (self-management, cognition, physical activity, and combination of cognition and self-management); characteristics of the study (study design, participant's demographics, and sample size); characteristics of the intervention(s) (intervention procedures, length, and follow-ups); targeted outcome(s); and the study main results.

Included studies were evaluated for their methodological quality using a list of 13 criteria questions modified and adopted from other sources (Table 1).[8, 19] All criteria were scored as (yes), (no), or (unclear) and resulted in total score between 0 and 13. Although no standard guidelines exist to use these criteria to identify a study as good or poor methodological quality, we considered studies with total score of 9 or higher to have good methodological quality based on previous recommendations.[8, 19]

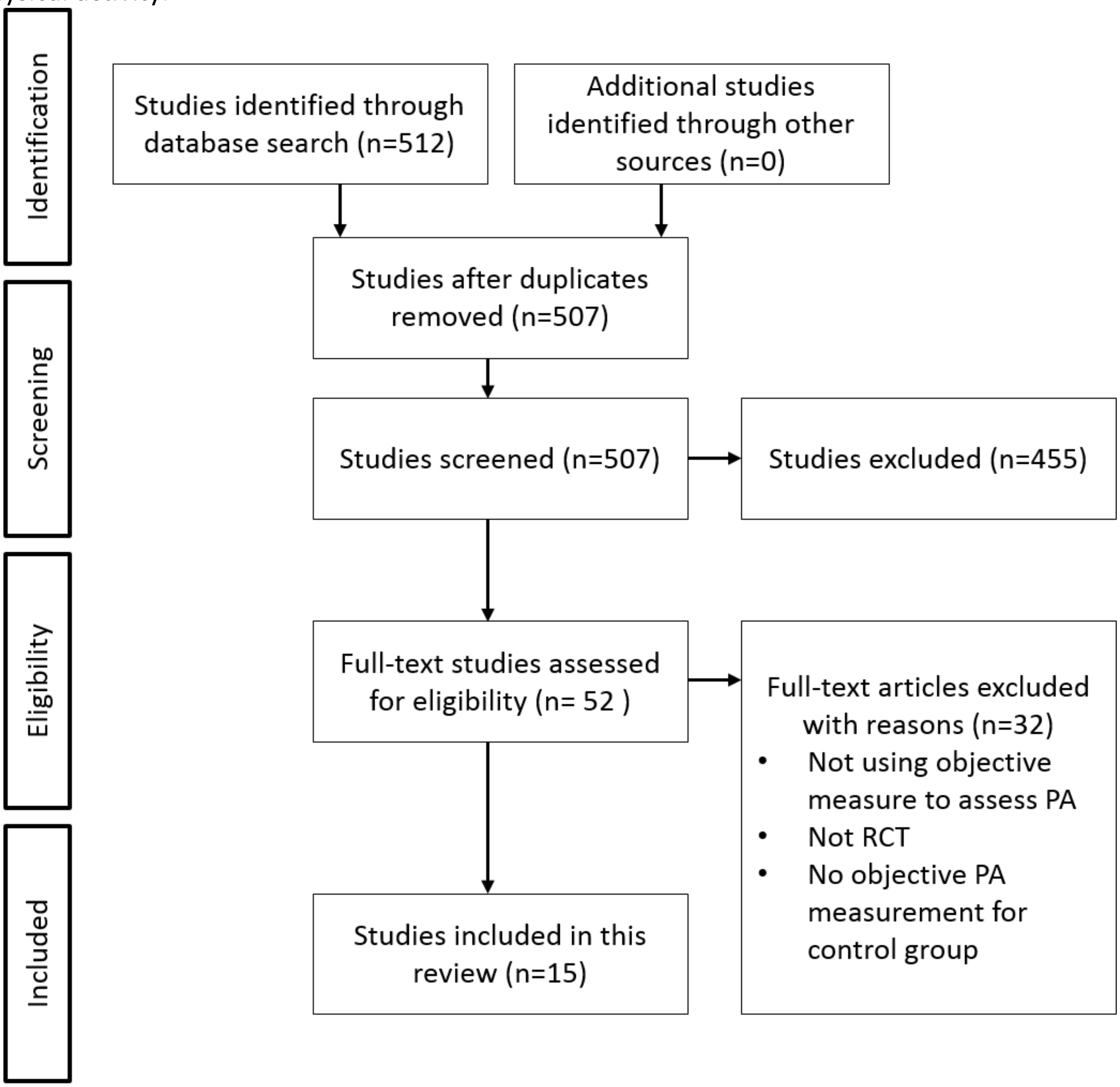
Table 1. Methodological quality criteria
1. Documentation of inclusion and exclusion criteria
2. Description of randomization method
3. Random allocation masked to study personnel
4. Groups are similar at baseline regarding important prognostic indicators
5. Intervention and control approach description is clear
6. The explanation of compliance or adherence with the interventions
7. Outcome assessor(s) is (are) blinded to the intervention's allocation
8. The description and comparison of dropout rate and characteristics of dropouts compared with completers of the study
9. Incorporation of long-term follow-up measurement (> 6 months)
10. Outcome measurements were assessed at comparable time in all groups
11. Sample size description by means of power calculation for each group
12. Intention-to-treat analysis
13. Point estimates and measures of variability description for the primary outcome measure
Modified from: Sazlina et al, 2013 [8]

All studies were also assessed by 2 independent reviewers (S.A. and A.Y.) for risk of bias using Cochrane collaboration assessment tool.[20] If the 2 reviewers were in disagreement, a 3rd independent reviewer (J.R.) assessed the study using the same method, and the decision of this reviewer was final. The following categories were used to assess bias: 1) sequence generation; 2) allocation concealment; 3) blinding of participants, personnel and outcome assessors; 4) incomplete outcome data; 5) selective outcome reporting and 6) any other sources of bias. Each category was individually judged as follows: 'Yes' (i.e. all category criteria met; low risk of bias), 'No' (i.e. one or more category criteria not met; high risk of bias), or 'Unclear' (i.e. one or more category criteria not adequately described or partially met; uncertain risk of bias). The results of Cochrane collaboration assessment tool for each category were reported across studies as follows: If all the studies were judged as 'Yes' for the evaluated category, this category was considered to have a low risk of bias. If one or more studies were judged as 'Unclear', the evaluated category was deemed to have an unclear risk of bias. If one or more of the studies were judged as 'No', then the evaluated category was considered to have a high risk of bias.

Results

The initial search identified 507 potential studies from the databases search. From these articles a total of 455 studies were excluded during the initial screen, and another 37 were excluded after detailed review as illustrated in Figure 1. The characteristics of the 15 included studies are described in table 2. Six studies used accelerometer as their physical activity objective measure;[21-26] 6 studies used pedometers to measure steps/day as indicator of physical activity;[27-32] and 3 studies used both accelerometer and pedometer to objectively measure physical activity.[33-35]

Figure 1. Flow diagram of study selection according to PRISMA. RTC: randomize clinical trial, PA: physical activity.



The reviewed studies focused on promoting change in physical activity behavior using several types of interventions. Seven out of 15 studies utilized cognitive consultation based on the principles of cognitive-behavioral therapy.[29-35] Five studies out of 15 utilized exercise consultation based on the trans-theoretical model and designed to educate, strengthen motivation and develop realistic strategies to promote exercise.[22-26] One study utilized exercise intervention,[28] and one study utilized DM education in addition to continuous glucose monitoring.[21] Twelve studies utilized individual intervention sessions, and 3 studies utilized a combination of group and individual sessions. In addition, 4 studies utilized follow-up and motivational methods like phone calls or mailed post cards.[24, 25, 32, 35] All studies utilized a control group at the same time of intervention (e.g. standard care) or waiting list group. Most of the reviewed studies included a long-term (> 6 months) follow-up assessment session; 10 out of 15 had a follow up period longer than 12 weeks.

The majority of reviewed studies reported a significant increase of physical activity level in intervention groups compared to control groups. Only 2 studies reported no change in daily physical activity level after interventions.[23, 31] Both studies had good methodological quality and large sample size. The first study by Kirk et al. employed personal physical activity education twice during a 6-month intervention period compared to printed educational material delivered at the beginning of the intervention period.[23] The 2nd study by Plotnikoff et al. used telephone counseling with printed individualized physical activity information as educational tools compared to standard printed physical activity educational material.[31]

The increase in physical activity level was evident only in the intervention period for the majority of studies. During the follow-up assessment, physical activity level in the intervention group was not significantly different from control group, with one exception.[29] This study by De Greef et al. assessed the effect of 7 cognitive behavioral sessions and telephone support on daily physical activity at 24 and 52 weeks. The result showed that the physical activity level increase found in the intervention group at 24 weeks compared to control was retained at the follow-up assessment.

Methodological quality was judged to be good in 8 out of 15 RCTs, and individual study scores are shown in table 2. Within individual studies, the risk of bias assessment showed 8 studies out of 15 to have a low risk of selection bias, with the remaining studies demonstrating an unclear risk. Six out of 15 studies were identified as having a high risk of performance and detection bias, and the risk of such bias was unclear in the remainder. For attrition bias 8 studies showed low risk, 2 studies showed high risk, and 5 studies showed unclear risk. All studies showed low risk of reporting bias. Only 2 studies showed high risk of other sources of bias. Although the majority of the reviewed studies appeared to demonstrate a relatively low risk of bias on the Cochrane Assessment Tool, the overall risk of bias should be considered unclear, as most authors did not provide methodological descriptions that adequately addressed the criteria specified by this tool (Figure. 2).

Figure 2. Review authors' judgements about each risk of bias item presented as percentages

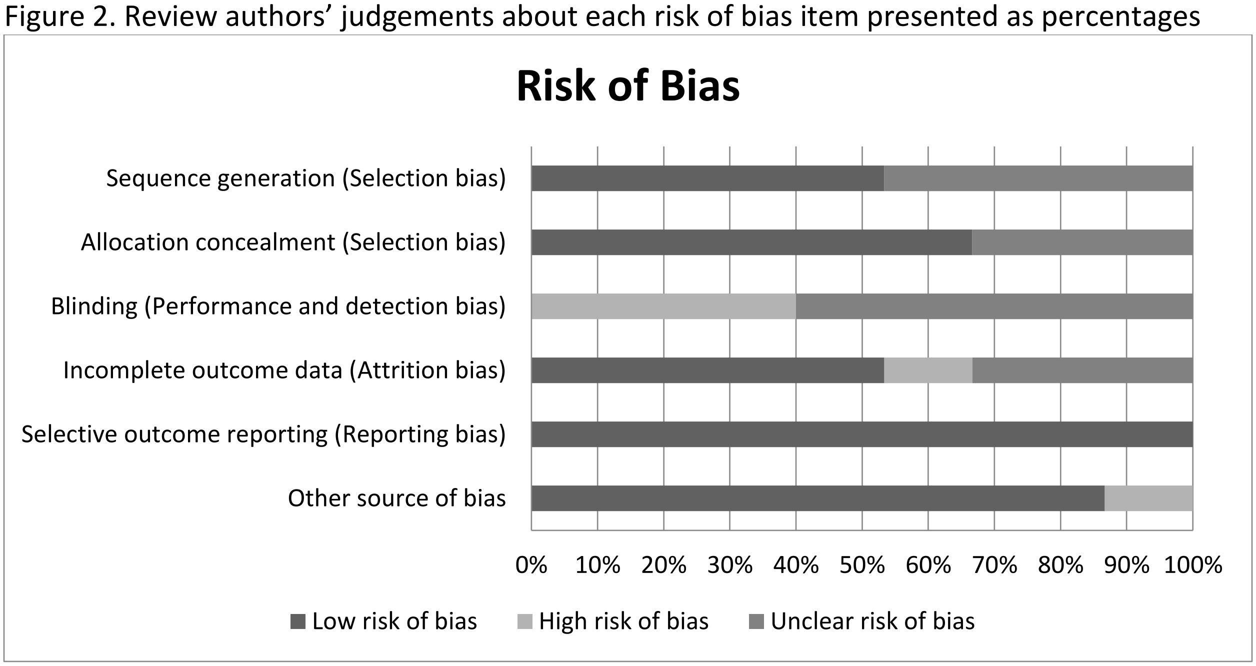


Table 2. Characteristics of selected studies

Study	Design and quality	Participants	Objective PA measure	Intervention	Summary of key findings
Keysirling 2002 [22]	3 Arm RCT 13	N=200 African-American women with type 2 DM, ≥ 40 years	Accelerometer (7 days) at baseline, 6 and 12 months	4 clinic visits in 4 months Exercise consulting, community-based intervention (2 support group sessions in 6 months, and monthly phone call (IG1) vs clinic only intervention (IG2) vs minimal intervention (mailed educational pamphlets) (CG)	PA levels increase in the IG1 (P = 0.0055) and IG2 (P= 0.029) compared to CG
Plotnikoff 2013 [31]	3 Arm RCT 12	N=287 adult with type 2 DM	Pedometer step/day (3 days) at baseline, 6, 12, and 18 months	telephone counseling (once a week in 1st month, biweekly 2nd month, once a month the reminder of intervention), print based materials and pedometer vs Print based materials and pedometer vs standard PA printed education	No significant effect of either intervention on PA levels compared to standard PA printed education
De Greef 2011 [34]	3 Arm RCT 11	N= 67 < 81 years with type 2 DM	Pedometer steps/day (7 days) Baseline and 12 weeks	Individual behavioral/ cognitive consultation (three 15 min	Significant increase of steps/day (1,706 steps) over baseline

Study	Design and quality	Participants	Objective PA measure	Intervention	Summary of key findings
				sessions during 12 weeks) vs group consulting (three 90 min sessions during 12 weeks) vs no intervention	in the group consulting arm group
De Greef 2010 [33]	RCT 11	N= 41 Inactive with type 2 DM	Pedometer steps/day & Accelerometer minutes/day (5 days including 1 weekend day) at baseline, 12 and 52 weeks	5 cognitive behavioral session and a poster session during 12 weeks (IG) vs standard care in addition to one group session on the effect of PA on diabetes care (CG)	IG improved PA at week 12 but not 52 weeks compared to CG
Kirk 2009 [23]	3 Arm RCT 11	N=134 Inactive with type 2 DM	Accelerometer steps/day and (minutes/day (7 days) at baseline, 6 and 12 months	Person delivered PA consultations vs written delivered PA consultations vs standard care During the intervention (6 months) period consultations were delivered twice	No between-groups difference in PA levels
Van Dyck 2011 [35]	RCT 10	N= 92 Overweight with type 2 DM	Pedometer steps/day & Accelerometer minutes/day (7 days) at baseline, 24 and 52 weeks	Social-cognitive constructs face to face session (30 min) and telephone follow up (2 phone calls in the 1st 4 weeks then one phone call every 4 weeks the reminder of the intervention	At 24 weeks IG improved their PA level compared to CG and the improvement were mediated by coping with relapse, change in

Study	Design and quality	Participants	Objective PA measure	Intervention	Summary of key findings
				(20 weeks)) (IG) vs standard care (CG)	social norm and social modeling
Kirk 2004 [25]	RCT 10	N=70 inactive with type 2 DM	Accelerometer minutes/day (7 days) at 6 and 12 months	exercise consultation (one session) and standard exercise leaflet (IG) vs standard exercise leaflet only both groups received follow up phone call at 1, 3, 6, and 9 months	Significant increased PA in IG from baseline to 6 months, no different between 6 and 12 months
Kirk 2001 [26]	RCT 9	N=23 with type 2 DM, in contemplation or preparation of exercise behavior	Accelerometer minutes/day (7 days) at baseline and 5 weeks	exercise consultation (30 min session) and standard exercise information (IG) vs standard exercise information only (CG)	IG significantly increased their PA levels compared to CG with 4% PA increase in IG compared to 9% decrease in CG
Van Dyck 2012 [30]	RCT 8	N= 92 (IG:60, CG:32), Overweight with type 2 DM	Pedometer steps/day (5 days that include at least 1 weekend day) at baseline, 24 and 52 weeks	Face to face consultation (30 min session) and 7 phone calls (12-20 min spread over 24 weeks) vs control	Intervention increased step/day count People who increased their daily steps by 4000 step showed significant

Study	Design and quality	Participants	Objective PA measure	Intervention	Summary of key findings
					improvement in HbA1c
De Greef 2011 [29]	RCT 8	N= 92 (IG:60, CG:32), inactive and overweight with type 2 DM	Pedometer steps/day & Accelerometer minutes/day (7 days) at baseline, 24 and 52 weeks	Cognitive behavioral session (30 min) and 7 telephone support (spread over 24 weeks) vs standard care	Significant PA level increase post intervention and retained at follow up (52 weeks) compared to standard care group
Tudor-Locke 2004 [32]	RCT 8	N= 47 Overweight or obese inactive adults with type 2 DM	Pedometer steps/day (3 days including 1 weekend day) at baseline, 16 and 24 weeks	4 group meetings (week 1-4), individually record pedometer values (week 1-16) (IG) vs wait-list (CG) Both IG and CG received motivational cards at week 6 and 10	IG increased their PA by 3000 steps/day during the intervention ($p<0.0001$)
Kirk 2003 [24]	RCT 8	N=70 Inactive with type 2 DM, in contemplation or preparation of exercise behavior	Accelerometer minutes/day (7 days) at baseline and 6 months	exercise consultation (30 min session) and standard exercise leaflet (IG) vs standard exercise leaflet only both groups received follow up phone call at 1 & 3 months	PA, exercise duration and peak gradient increased in IG compared to CG at 6 months ($P < 0.001$)
Allen 2008 [21]	Pilot RTC 7	N= 52 Adults with type 2 DM	Accelerometer minutes/day (7 days) at baseline and 8 weeks	90 min of individualized diabetes education session and received	IG had higher increase minutes in MVPA levels

Study	Design and quality	Participants	Objective PA measure	Intervention	Summary of key findings
				continuous glucose monitoring counseling (3 days in week 1) (IG) vs 90 min of individualized diabetes education (CG) both groups received follow up phone call at week 4	compared to CG
Araiza 2006 [27]	Pilot RTC 7	N=30 Adults with type 2 DM	Pedometer daily steps for 6 weeks	Active group instructed to walk 10000 steps/day on 5 days or more/week vs control group instructed to maintain normal PA	Active group increased their daily step counts by 69% compared to their baseline steps counts No change observed in the control group activity level
Bjorgaas 2005 [28]	Pilot RTC 6	N=29 Overweight adults with type 2 DM	Pedometer steps/day (3 weekdays) at baseline and 12 weeks	Aerobic exercise (twice a week for 12 weeks) vs control	Improvement in IG pedometer activity correlate with decreases in HbA1c compared to baseline levels
PA, physical activity; IG, intervention group; CG, control group; BMI, body mass index; WC, waist circumference; HbA1c, glycosylated hemoglobin; MVPA, moderate to vigorous physical activity; a quality of methods score of 9 or higher indicate good methodological quality					

Discussion

The objective of this review was to systemically evaluate studies that utilized pedometers or accelerometers to determine the outcome of interventions promoting daily physical activity in people with T2D. Our initial search identified a large body of literature investigating interventions to promote daily physical activity; however, the majority of these studies measured daily physical activity subjectively, and we were only able to find 15 RTC that met our criteria.

Interventions used in the reviewed studies had a wide variety of approaches, including educational approaches, behavioral modification, and physical exercise. The intervention dose (duration and intensity), methods of intervention delivery, length of the follow-up period, and the sample size differed greatly between studies. Furthermore, these studies were conducted in different parts of the world with different socio- psychological factors. All together these factors produced heterogeneous results and hinder the absolute generalizability of daily physical activity improvements. However, it gave us a unique perspective on how different interventions protocols can lead to similar improvements in daily physical activity in different subgroups of people with type 2 DM. Improvement of daily physical activity seen in the reviewed studies demonstrated a clear example of the benefits of personalized health care.

The most effective intervention in terms of a long-term effect was seen in the De Greef et al. study.[29] In this study the investigators tested the effectiveness of behavioral modification program on the physical activity behavior in people with type 2 DM. The behavior modification program included face to face 30 minutes sessions focused on motivational strategies and lifestyle change plan individualized for each participant, 7 supportive phone calls over the intervention period of 24 weeks and wearing a pedometer while keeping records of daily steps to track progress. This combination of interventions appeared to be effective in long term maintenance of improvements in physical activity for one year from the baseline assessment. This is in contrast with several studies that utilized only one of these interventions in isolation. For example, Kirk et al. did not see any improvement in physical activity when educational strategies were utilized alone,[23] and Plotnikoff et al. study did not see any improvement in physical activity after telephone counseling alone.[31]

The quality of the reviewed studied were good in 8 out of 15 RCTs. However, the amount of daily physical activity improvements in these studies varied. Again, the variability of the employed methods in each study makes it hard to compare the outcomes produced by these interventions directly. Thus, there is a critical need to conduct comparable RCTs studies looking at different interventions that promote daily physical activity utilizing a similar dose and objective outcome measures. For example, a RCT to compare the effectiveness of individualized consultation sessions vs supervised exercise for the same amount of active intervention period and long-term follow-up period will establish the best intervention option between these approaches. Risk of bias assessment indicated that, as a whole, the reviewed studies demonstrated a low risk of bias in most areas. However, a high risk of performance and detection bias was identified. This is not surprising due to the fact that it is often difficult to blind subjects in behavioral and educational intervention studies.

Our systematic review showed higher percentage (86.6%) of studies with effective interventions in improving PA compared to previous published reviews. For example Cotter et al[36] reviewed 9 studies that utilized Internet interventions to support lifestyle modification for diabetes management found out that 22.2% of the reviewed studies showed improvement in PA. Cassimatis et al[37] reviewed 8 studies that examined the effects of type 2 diabetes behavioral telehealth interventions on PA showed that 62.5% of these studies were effective in improving PA. Furthermore, Lewis et al[38] reviewed 9 studies that evaluate the use of electronic activity monitor devises as an intervention modality reported 55.5% of the reviewed studies demonstrated significant pre-post improvement in overall PA. Our results compared to the above mention reviews indicate that incorporating the use of objective measures of PA in the intervention approch might be superior in producing improvements in overall PA.

Limitations

This review included extensive and systematic literature search strategy in major databases. However, there are few limitations to this review. A meta-analysis could not be performed due to two reasons: 1) the interventions used in the included studies varied greatly which made it clinically inappropriate to combine these studies in one analysis; and 2) only 8 out of 15 studies were considered to have good methodological quality which might result in a low-quality meta-analysis. Only English peer-reviewed studies were included in the data extraction; therefore, a selection bias might exist. Furthermore, although the search was completed in a major database, there is a possibility that some studies were not included due to the search inclusion and exclusion criteria. In addition, even though 2 independent reviewers assessed the studies for eligibility, some risk of evaluation bias might exist.

Future directions

Our systematic review of the literature indicated the need for further investigational research in several areas such as the long-term benefits of existing and new interventions aimed to increase overall PA and the translation of existing interventions from the research setting into clinical practice. Thus, systematic reviews that compare cost and feasibility of the effective interventions in improving overall PA in both research and clinical sitting are needed.

Conclusion

In conclusion, the reviewed studies employed several types of interventions ranging from cognitive and behavioral approaches to exercise consultation and prescription. Most of the reviewed RTCs were effective in increasing PA temporarily during the intervention period. Furthermore, they emphasize the importance of implementing objective measures of daily physical activity to produce consistent and accurate results in research and patient care. Thus, interventions that utilize objective methods in measuring PA and have long term improvement in overall PA are needed. Objective measures such as pedometer and accelerometer provide accurate reflection of daily PA level during the assessment period which will help researchers avoid speculation about the results of PA interventions, and eliminate the uncertainty associated with recall questionnaires.

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Chapter 2: Test-Retest Reliability of ActivPAL in Measuring Sedentary Behavior and Physical Activity in People with Type 2 Diabetes

Abstract

Objective: Sedentary behavior is a major health issue in people with type 2 diabetes. To investigate how changes in sedentary behavior relate to health outcomes, it is important to establish the test-retest reliability of activity monitors in measuring habitual sedentary behavior as a prerequisite. Thus, our objective was to examine the test-retest reliability of a common activity monitor (activPAL^{TM}) in measuring sedentary behavior and physical activity in people with type 2 diabetes. Methods: Sedentary time, standing time, stepping time, step count, and sit to stand transitions were obtained from two 7-day assessment periods separated by at least one week in people with type 2 diabetes. Test-retest reliability was determined with the intraclass correlation coefficient (ICC) to compare activity measures between the two time points. Results: Thirty participants completed the study; mean age was 65 ± 6 years, 63% of the participants were women, and mean BMI was 33.3 ± 5 Kg/m^2. Sedentary time showed high test-retest reliability (ICC=0.79, 95% confidence interval [CI]: 0.61-0.89), standing time showed high test-retest reliability (ICC=0.74, 95% CI: 0.53-0.87), stepping time showed very high test-retest reliability (ICC=0.90, 95% CI: 0.81-0.95), step count showed very high test-retest reliability (ICC=0.91, 95% CI: 0.83-0.96), and sit to stand transitions showed very high test-retest reliability (ICC=0.90, 95% CI: 0.79-0.95). Conclusion: the ActivPAL^{TM} device showed high to very high test-retest reliability in measuring all tested activity categories in people with type 2 diabetes. Thus, it may be an optimal assessment tool to measure changes in activity level in pre-post interventions designed to decrease sedentary behavior.

Keywords: Sitting, Standing, Stepping

Introduction

Sedentary behavior is a growing epidemic[1] in both prevalence and severity. A population based study (n=6,329) showed that people spend on average 7.7 hours engaged in sedentary behavior each day.[2] The prevalence of sedentary behavior is exacerbated by declines in both leisure and occupational energy expenditure.[3, 4] A meta-analysis showed that all-cause-mortality significantly increased by 5% for each one hour increase in total sitting time when individuals sit for more than 7 hours per day, independent of physical activity level.[5] A growing body of literature has identified sedentary behavior as a factor associated with at least 35 diseases, including diabetes and cardiovascular diseases.[6, 7]

Sedentary behavior is a major health issue in people with type 2 diabetes (T2D).[8, 9] T2D is a chronic metabolic disease characterized by abnormal insulin signaling that leads to an accumulation of high levels of glucose in circulating blood. T2D is a serious health condition that, if not managed properly, leads to devastating health complications with significant morbidity and mortality rates.[10] Furthermore, the majority of people with T2D are considered sedentary.[11, 12] Fortunately, a sedentary lifestyle is modifiable. However, before the effectiveness of any intervention aimed to decrease sedentary behavior and increase physical activity can be determined in people with T2D, the stability of sedentary behavior over time must be assessed via objective measurement tools.

Establishing a reliable and valid objective measure of sedentary behavior has been recommended as a research priority by a panel of experts that participated in a four session workshop sponsored by the National Heart, Lung, and Blood Institute and National Institute on Ageing entitled Sedentary Behavior: Identifying Research Priorities.[13] Objective and accurate measures of sedentary behavior have been validated through the use of activity monitoring devices such as ActiGraph (Actigraph LLC, Pensacola, Fla, USA) and activPAL™ (PAL Technologies, Glasgow, Scotland, UK).[14, 15] ActivPAL™ is a small motion sensor which classifies human physical behavior in to three categories: sitting/lying, standing, and stepping.[16] This device has the unique feature to detect postural allocation to distinguish between sitting and static standing.[14, 17] In general activPAL™ has shown higher accuracy in detecting total sitting time and breaks in sitting time compared to other activity monitors. [18-21]

The validity and reliability of any given instrument in research are of the utmost importance in producing clinically meaningful results. The validity of activPAL™ measurements have been established against video recordings of activities as well as against other validated measures of sedentary behavior (i.e. Actigraph),[14, 18] although step count during slow walking (≤ 0.47 m/s) may be underestimated in individuals with impaired function.[17] However, relatively few studies have examined the reliability of activPAL™ measurements. Reliability is defined as the ability of an instrument or behavior to produce stable and consistent results in different situations. Test-retest reliability is one of four reliability classes and is designed to test the consistency of measurement or behavior from one time point to another.

Sedentary behavior and physical activity levels are subject to natural variation from day to day influenced by weather,[22, 23] day of the week,[24] and seasonal variation.[25, 26] Multiple studies have attempted to establish the length of time needed to capture habitual sedentary behavior and physical activity level in healthy adults. Results from these studies specify that three and a half to five days are needed to measure habitual sedentary behavior, while three to four days of measurement are required to establish physical activity level.[27-29] All of these studies indicated that the length of sedentary behavior and physical activity assessment should be based on the population of interest, the main study's outcome (i.e. sedentary behavior vs light physical activity), and the type of measurement used (i.e. subjective vs objective).

Although two studies examined the reliability of activPAL^{TM} in adults, both studies employed methodologies that limit the applicability of the findings to studies of habitual sedentary behavior in free-living conditions. One study examined the test-retest reliability of activPAL^{TM} under laboratory conditions in young adults and showed high reliability for treadmill walking (ICC:0.88), jogging (ICC: 0.81), and self-paced walking (ICC:0.69).[30] However, these results were obtained under well-controlled conditions and thus do not translate to free-living conditions. The second study examined the day-to-day individual variability of sedentary behavior and physical activity in women, and determined the reliability of sitting time and moderate-to-vigorous physical activity bouts. [31] The study results showed high variability in day-to-day total sitting time and, based on a generalized analysis of variance, determined that four days of valid recording is needed to achieve a reliability coefficient of 0.80. Day-to-day reliability could be affected by routine weekly events such as shopping or weekend activities, and thus may not accurately reflect sedentary behavior patterns. Because this study measured only day-to-day reliability rather than habitual sedentary behavior, examining activPAL^{TM} reliability over at least two different time periods is needed to establish activPAL^{TM} reliability in measuring habitual sedentary behavior.

From these reviewed studies we concluded that 1) activPAL^{TM} is a valid measure of sedentary behavior with unclear test-retest reliability, and 2) studies examining the reliability of habitual sedentary behavior using objective activity monitors in people with T2D are needed.

The objective of this study was to examine the test-retest reliability of activPAL^{TM} as a measure of habitual sedentary behavior in people with T2D. We hypothesized that the activPAL^{TM} device will have at least moderate reliability in quantifying measures of sedentary behavior and physical activity across two distinct one-week periods of measurement separated by at least one week of non-wear time.

Methods

Design and Participants

This study utilized a test-retest reliability, repeated measure design. The study took place from March 2017 to May 2018 in the Department of Physical Therapy and Rehabilitation Science at the University of Kansas Medical Center. The study was approved by the University of Kansas Medical Center's Institutional Review Board and Human Subjects Committee. Informed consent was obtained in writing from each participant prior to the study. No person was excluded on the basis of sex, race, or ethnicity. Interested participants underwent a structured screening interview to determine their eligibility for the project.

Potential participants were included in the study if they were English speakers between 50 – 75 years of age, had a self-reported a diagnosis of T2D, and were able to ambulate independently without an assistive device for at least 50 meters. Individuals were excluded if they reported any one of the following exclusion criteria: 1) neurological conditions that interfere with mobility or cognition such as Parkinson disease, Alzheimer's disease, or multiple sclerosis, 2) foot ulcers and/or a history of lower extremity amputation (great toe or above), 3) morbid obesity (i.e., BMI > 45 kg/m^2), 4) major depressive disorder, 5) any cardiovascular or vestibular impairments that would interfere with testing, 6) uncontrolled hypertension (BP >

190/110mmHg), and 7) inability to understand or cooperate with testing procedures. All interested individuals were screened for eligibility via phone or in person using the above inclusion/exclusion criteria. If eligibility criteria were met, participants were scheduled for their first testing session.

Study Protocol

Participants in this study underwent a total of four testing sessions which lasted 30 to 60 minutes each. Figure 1 outlines the objectives and assessments that occurred at each session. During session 1, written informed consent was completed, and subsequently demographic information, employment status, medical history, and a concomitant medication list were collected. The activity monitor (activPAL^{TM}, PAL Technologies Ltd. Glasgow, UK, http://www.paltechnologies.co.uk) and sleep\non-wear time diary were given to the participant to wear for seven days along with instructions for use.

The activPAL^{TM} is a small (5 cm × 3.5 cm × 0.7 cm) lightweight monitor worn, per manufacturer instructions, on the mid-line of the thigh, one-third of the way between hip and knee. The activity monitor has a sampling frequency of 10 Hz, with a recording interval of 0.1s. Participants were asked to wear the activity monitor for seven consecutive days and to remove the monitor only if the device would be fully submerged in water (e.g., while swimming). Participants were asked if they planned to engage in any non-routine physical activity such as traveling during the week that they would be wearing the activity monitor. If they answered yes, then a different measurement week was selected. Also, the participants were asked to maintain their normal level of activity while wearing the activity monitor. This was done to ensure the capture of habitual behavior.

The next session (session 2) was scheduled 7 – 14 days later, at which time the participant returned the activity monitor and sleep\non-wear time diary. The activity monitor data was downloaded and assessed to ensure that sufficient data was obtained, defined as at least four days with 10 hours per day of activity data.[31] If the activity monitor data was not sufficient, the participant was asked to wear the activity monitor for another week and an extra session was scheduled to repeat session 2 activities. The next session (session 3) was scheduled occur at least after 7 days after the second session. During session 3, the activity monitor and sleep\non-wear time diary were given to the participant to wear for 7 consecutive days with instructions for use. The final session (session 4) was scheduled 7 – 14 days later, with a repeat of the procedure for session 2. In addition, individualized counseling to reduce sedentary behavior and increase physical activity, based on the participant's activity monitor results, was provided during session 4. Only participants who completed all aspects of this study were included in the final analysis.

Data Acquisition

Sedentary behavior (average duration of total sitting time in minutes per day) and physical activity (total standing time, total stepping time, step count, and sit to stand count per day) were estimated from the activity monitor data. For data analysis, the time-stamped "event" data file generated by the activPAL™ software (version 7.2.32) was exported as a .csv file for further cleaning and analysis in RStudio. R is an open-source computing language and statistics package available for free at www.r-project.org.[32] A freely available custom R package developed by Lyden et al. was used to extract the outcomes of interest from the activity monitor data.[33] Using the package, we ran the function *process.AP* to batch process all event.csv activPAL^{TM} files and produced three .csv files that summarized 1) sleep/wake time and wear/non-wear time, 2) physical activity (stand time, step time, step count) and sedentary behavior (sitting time excluding sleep and non-wear time) results per day and 3) mean physical activity and sedentary behavior variables by visit. We used the physical activity and sedentary behavior results per day .csv file to exclude any days with less than 10 hours of wear time. Mean values for minutes/day or count/day for week 1 and week 2 were calculated for all variables of interest.

Statistical Analysis

Descriptive statistics included means and standard deviations for continuous variables and frequencies for categorical variables. A power analysis was conducted to determine the necessary sample size using SAS software. It was estimated that 29 participants would be required to test our hypothesis at 80% power with a significance level of 0.05, null hypothesis = no change, alternative hypothesis = 50% change, and 2-sided test. [34, 35] The test-retest reliability of the study outcomes from week 1 and week 2 was determined by use of the intraclass correlation coefficient (ICC) with an estimation model.[36] The correlation strength was interpreted as 0.90–1.00 = very high correlation, 0.70–0.89 = high correlation, 0.50–0.69 = moderate correlation, 0.26–0.49 = low correlation and 0.00–0.25 = little, if any correlation.[30] Statistical evaluation was done using RStudio Team (version 3.5.10, RStudio: Integrated Development for R. RStudio, Inc., Boston, MA URL http://www.rstudio.com/) and GraphPad Prism (version 7.04 for Windows, GraphPad Software, La Jolla California USA, www.graphpad.com).

Results

A total of 38 participants consented to participate in the study. Eight participants opted to not complete the study after signing informed consent: 4 were lost to follow up, 2 did not wish to continue the study due to lack of time, and 2 did not like wearing the activity monitor. As shown in Table 1, thirty participants (63% women) completed the study. Participants were 64.9 ± 6 years old and overweight or obese. Demographic characteristics did not differ between completers vs non-completers.

Figure 1. Study session outline. Study sessions were separated by at least 7 to 14 days.

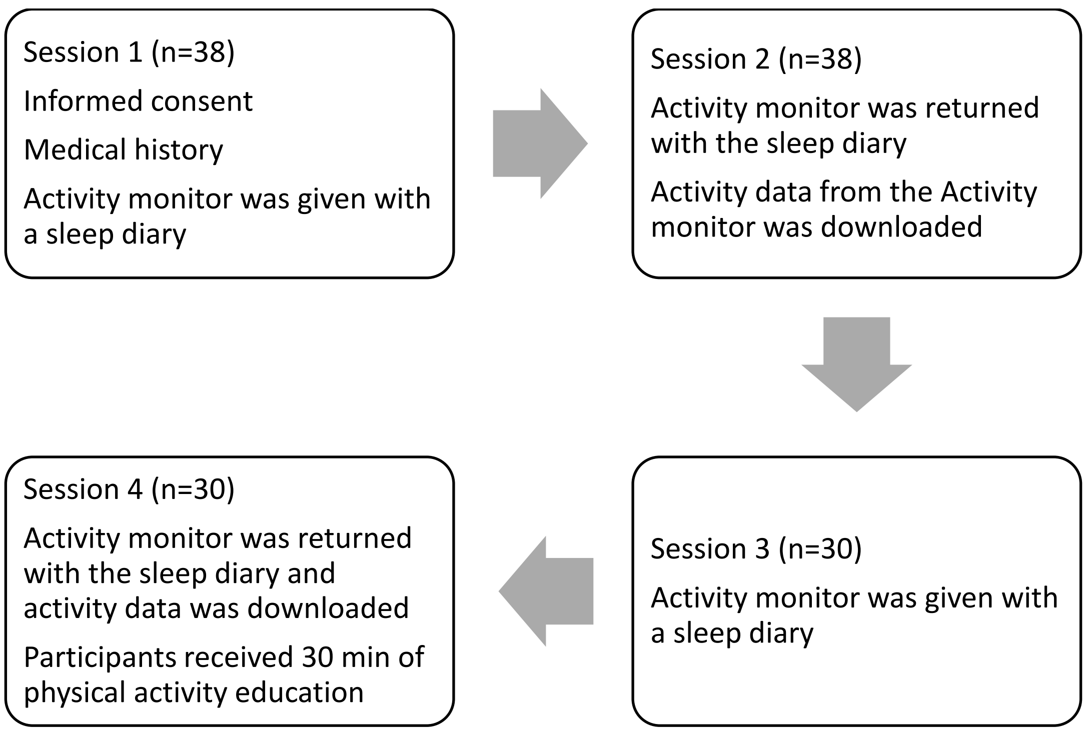


Table 2 shows the mean (average minutes/day or count/day for week 1 and week 2 for days with > 10 hours of wear time) and standard deviation for each activity category in the first and second week of assessment, the absolute difference between the two weeks of assessment, and the estimate of the test-retest reliability. Sedentary time showed high test-retest reliability (ICC=0.79) with a 95% confidence interval (CI) ranging from moderate to high (0.61 to 0.89). All other activity categories also showed high to very high test-retest reliability (ICC > 0.70), with 95% CIs ranging from moderate to very high (0.53 to 0.96). Figure 2 shows individual variation between week 1 and 2 for sedentary time (A) and step count (B).

Table 1. Participant's Demographics. Data reported as mean ± SD or frequency.

Characteristic	Completed Study (n=30)
Age, y	64.87 ± 5.99
Gender, Women	19 (63.3%)
BMI, Kg/m^2	33.30 ± 4.97
Race	
Caucasian	22 (73.3%)
African American	7 (23.3%)
Asian	1 (03.3%)
Retired, Yes	18 (60%)

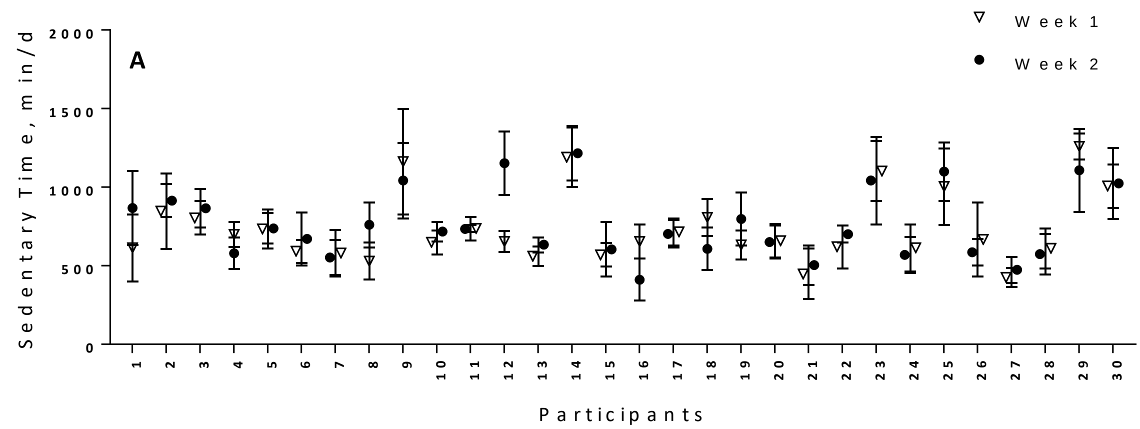
Table 2. Average duration of activity categories (min/d or count) for both week (each week was the average of days with at least 10 hours of wear time) with the absolute difference between them. CI= confidence interval, ICC= intraclass correlation coefficient. Data reported as mean ± SD or mean (95%CI).

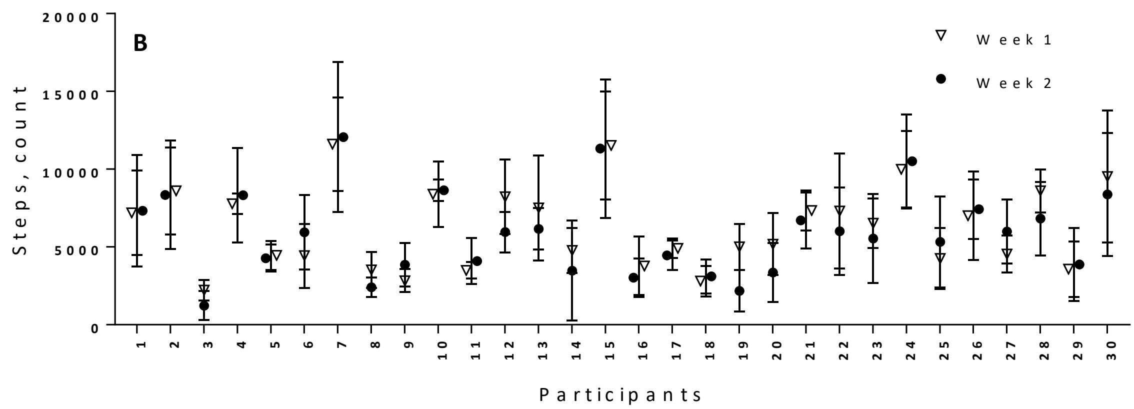
Activity Category	Mean ± SD		Absolute Difference (95% CI)	ICC	95% CI	P value
	Week 1	Week 2				
Sedentary Time, min/d	738.3 ± 219.2	763.4 ± 220.8	98.93 (60.15, 137.7)	0.79	0.61, 0.89	<0.001
Stand Time, min/d	220.9 ± 90.33	216.6 ± 96.86	43.33 (23.91, 62.75)	0.74	0.53, 0.87	<0.001
Step Time, min/d	82.45 ± 31.41	79.68 ± 33.75	11.96 (8.43, 15.49)	0.90	0.81, 0.95	<0.001
Step, count	6231 ± 2604	5870 ± 2709	933 (685, 1180)	0.91	0.83, 0.96	<0.001
Sit to Stand, count	47 ± 14	45 ± 15	5.6 (4.2, 7.2)	0.90	0.79, 0.95	<0.001

Discussion

To the best of our knowledge, this study is the first to examine the test-retest reliability of a specific activity monitor device (activPAL™) to measure habitual sedentary behavior and physical activity in people with T2D. The study results indicated that this activity monitor provides high to very high test-retest reliability in measuring sedentary time, standing time, stepping time, step count, and sit to stand transitions with moderate to very high confidence intervals. Two previous studies that utilized similar methods and activity monitor to our study but with children (one with healthy children and the other with those affected by cerebral palsy) showed that the activity monitor had generally low to moderate test-retest reliability in measuring sedentary behavior, with moderate to high test-retest reliability in measuring physical activity.[35, 37] Both studies indicated that the observed sedentary behavior test-retest reliability values were only moderate in size, and might have been due to changes in activity level between the two weeks of assessment. Thus, our high to very high test-retest reliability values for sedentary behavior and physical activity might be a result of the fact that our participants were sedentary older adults with T2D and who might have more stable level of activity, as compared to children. Another possibility for the observed results might be limited sample variability due to the study exclusion criteria. We also attempted to exclude collecting data on weeks when participants planned to engage in non-routine activities such as traveling. Activity monitors equipped with both accelerometers and inclinometers appear to be reliable in quantifying habitual sedentary behavior and physical activity levels in adults for research purposes, as previously indicated by other research performed under laboratory conditions.[30, 38]

Figure 2. Variation between week 1 and 2 for sedentary time (A) and step count (B). Average duration of activity categories (min/d or count) for both week (each week was the average of days with at least 10 hours of wear time).





Although this study was designed and powered to assess the outcomes of interest, it is not free of limitations. Only people with T2D and between 50 and 75 years of age were included in the analysis. Healthy, active individuals might have higher week-to-week variability in their activity level due to increased leisure activity, occupational demands, and social factors such as childcare. On the other hand, people with different disease conditions might engage in more variable week-to-week activity level as results of symptoms such as pain or fatigue, or other specific disease symptoms. Therefore, future studies to determine test-retest reliability measures of habitual sedentary behavior and physical activity in other populations may be needed before this activity monitor can be recommended for future research in a substantially different population than that from which our study sample was selected. Lastly, our study only assessed habitual sedentary behavior and physical activity at two time points with single objective activity measurement tool; thus, we cannot determine the minimum detectable change with confidence. Larger studies with multiple time points and objective activity measurement tools to assess reproducibility and replicability of habitual sedentary behavior and physical activity are needed to establish true minimal detectable change values for the general population.

Conclusion

This study investigated the reliability of an activity monitor to measure habitual sedentary behavior and physical activity over two separate time periods, each of one week's duration. The study findings showed activPAL™ to have high test-retest reliability in measuring habitual sedentary behavior and very high test-retest reliability in measuring physical activity (standing time, stepping time, steps count, and sit to stand transitions count) in people with type 2 diabetes under free-living conditions. Thus, future intervention studies should consider this activity monitor to assess the effect of their treatment approach on sedentary behavior and physical activity in adults with similar characteristics.

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Chapter 3: Sedentary Behavior and Health Variables in People with Type 2 Diabetes

Abstract

The purpose of this study is to examine the relationships between sedentary behavior (SB), glycemic control, well-being, fatigue, and physical function in people with type 2 diabetes (T2D). These modifiable health variables have been shown to be 1) associated with SB in older adults, and 2) negatively impacted in people with T2D. However, the relationships between these variables and SB in people with T2D are uncertain. Methods: A cross-sectional study design was used to assess the relationship between SB (total sitting time and number of sit-to-stand transitions) with glycemic control (HbA1c), well-being (WBQ-22), fatigue (Fatigue Severity Scale), and physical function (Senior Fitness Test). An activPAL3TM activity monitor was used to assessed SB in people with T2D aged from 50 to 75 years. Results: Data from 59 participants were included in the final analysis. Study participants were obese (33.4 ± 5.5 kg/m2) and sedentary (11.08 ± 2.31 Hours/day). Multiple linear regression examining the effect of the assessed variables on SB showed that poorer glycemic control (β= 0.40; 95% IC: 14.43, 58.13) was associated with higher level of SB, independent of moderate to vigorous physical activity. No other significant relationships were observed. Conclusion: Glycemic control was a significant predictor of SB level. Understanding these relationships is important in designing and implementing interventional programs. Future studies are needed to explore this relationship further, as both glycemic control and SB are modifiable factors and could be used as main target for interventions aimed to improve health outcomes in people with T2D.

Keyword: Sit time, Glycemic control, Fatigue, Well-being, Physical function

Introduction

Sedentary behavior (SB) and its effects on health is an emerging field; however, the majority of studies have been conducted on healthy adults. Only a few studies have focused on the detrimental effects of SB in diseases such as diabetes. Type 2 diabetes (T2D) is chronic metabolic disease that leads to significant morbidity and mortality rates.[1] SB is a serious health issue in people with T2D, with the majority of people with T2D considered sedentary.[2-4] SB is defined as “any waking behavior characterized by energy expenditure less than 1.5 METs while in a sitting or reclining posture”.[5] SB can be accessed via both subjective (self-reported) and objective (activity monitors) measures and it is typically reported as total time spent in SB or number of breaks in SB per day.

Several studies have linked SB to cardiometabolic biomarkers such as glucose level, insulin activity, and lipid metabolism, and have shown that SB is associated with diabetes.[6-9] For example, a study of people with T2D by Van Dijk et al. [10] showed that participants that engaged in light physical activity lowered postprandial glucose by 17% compared to the participants who engaged in SB. In addition, studies examining the effect of acute episodes of SB on glucose and insulin metabolism have confirmed that SB has negative impacts on both biomarkers. Fortunately, glucose and insulin control were improved significantly by incorporating light activities into the testing protocol.[11-14] Decreasing SB through light activity means that the human body experiences frequent, alternating muscle activities. During active muscles contraction glucose uptake increases, and insulin action improves. These relationships can be bi-directional as no study has established cause and effect between physiological factors (e.g. insulin action and glucose uptake) and SB yet. The aforementioned studies demonstrate direct links between SB and T2D metabolic measures of glucose and insulin. However, there is a paucity of research investigating the impact of long-term glycemic control, physical function, or perception of health on SB in people with T2D.

Health related decisions can be influenced by a person's perception of their general health. Several studies that examining the relationship between SB and different general health variables have found that, in general, poor mental and physical health are positively associated with SB.[15, 16] Overall, individuals' perception of health can affect multiple health variables. In this study we aimed to study the effect of individuals' perception of health on SB by evaluating well-being and fatigue in people with T2D. Well-being can be defined as the individual's feeling, function, and evaluation of their life.[17] How people with T2D perceive their overall well-being can influence greatly their health outcomes.[18, 19] These studies show that well-being correlates with health status in people with T2D. In addition to correlations between well-being and health variables, a perception of positive well-being can be influenced by activity levels.[20, 21] These studies suggest that there is need to investigate perception of well-being as possible predictor of SB in people with T2D.

People with T2D often complain of fatigue and they are ten times more likely to experience fatigue compared to healthy controls.[22, 23] Both studies indicate that fatigue is a serious health concern in people with T2D. High levels of fatigue can cause people to avoid activities that they perceive will make them more fatigued. The relationship between SB and fatigue has been explored in several studies. Individuals engaged in longer periods of sitting reported significantly higher levels of fatigue.[24] Furthermore, fatigue has been identified as a key barrier to decreasing SB.[25] In sedentary individuals, decreased sitting time is associated with less fatigue.[26] Current evidence highlights the prevalence of fatigue in people with T2D as well as the link between SB and fatigue. Additional evidence suggests that perceptions of well-being can impact a person's level of engagement in SB. However, the relationship between fatigue, perception of well-being, and SB in people with T2D is still in need of investigation.

A wide variety of medical conditions and diseases can influence physical function. Physical function, in turn, influences quality of life, health care cost, and mortality. [27] A decline in physical function in people with T2D is associated with diabetes severity and duration. For example, six-minute walk distance test is negatively associated with diabetes duration among other factors, And diabetes duration was a significant predictor of walked distance for individuals aged 59 years or older.[28] Furthermore, low cardiorespiratory fitness is associated with worse glycemic control in people with T2D.[29] Diabetes and its complications explained 59 – 72 %[30] and < 60%[31] of the decline in physical function in two large cross-sectional studies. However, diabetes alone cannot explain all the changes observed in physical function.[32] In older adults, declines in physical function contribute to increases in SB.[27, 33] These studies are limited to older populations; however, they reveal a critical link between physical decline and SB.

Beyond the studies described above, there is a lack of informative research examining the relationships between well-being, fatigue, and physical function with SB in people with T2D. Understanding these relationships is an important step towards designing and implementing interventional programs and increasing patient participation and adherence to prevention programs. Thus, the objective of this study was to examine the association between SB (defined as total time spent sedentary and transition from sit to stand) with glycemic control, physical function, fatigue, and well-being in people with T2D. We hypothesized that higher glycemic control levels, lower physical function test scores, higher scores on a fatigue scale, and lower scores on a well-being questionnaire would predict SB variables independent of MVPA in people with T2D.

Methods

Design and Participants

This study utilized a cross-sectional design. The study took place from March 2017 to May 2018 in the Department of Physical Therapy and Rehabilitation Science, University of Kansas Medical Center. The study was approved by the University of Kansas Medical Center's Institutional Review Board and Human Subjects Committee. Informed consents were obtained in writing from each participant prior to the study. No person was excluded on the basis of sex, race, or ethnicity. Interested participants underwent a structured screening interview to determine their eligibility for the project.

Potential participants were included in the study if they were between 50 – 75 years of age, self-reported a diagnosis of T2D, and were able to ambulate independently without an assistive device for at least 50 meters. Participants were excluded if they had one of the following exclusion criteria: 1) neurological conditions that interfere with mobility or cognition such as Parkinson's disease, Alzheimer's, or multiple sclerosis, 2) foot ulcers and/or a history of lower extremity amputation (great toe or above), 3) morbid obesity with a BMI > 45 kg/m^2, 4) major clinical depression, 5) any cardiovascular or vestibular impairments that would interfere with testing, 6) uncontrolled blood pressure with medication (BP > 190/110mmHg), and 7) inability to understand or cooperate with testing procedures. All interested individuals were screened for eligibility via phone or in person using the above inclusion/exclusion criteria. If eligibility criteria were met, participants were scheduled for their first testing session.

Study Protocol

Participants in this study underwent a total of two testing sessions. During the first session, written informed consent was completed, and demographic information, employment status, medical history, and a concomitant medication list were collected, followed by assessments related to study variables (glycemic control, fatigue, well-being, and objective assessment of physical function that includes measures of endurance, strength, mobility, and agility). Participants were given ample time to rest between assessments. Finally, the activity monitor (activPAL^{TM}, PAL Technologies Ltd. Glasgow, UK, http://www.paltechnologies.co.uk) and a sleep\non-wear time diary were given to the participant to wear for 7 days with instructions for use. The activPAL^{TM} activity monitor is a light monitor (5 cm × 3.5 cm × 0.7 cm) worn per manufacturer instructions on the mid-line of the thigh, one third of the way between hip and knee. Participants were asked to wear the activity monitor for 7 consecutive days, removing the monitor only if they were to be fully submerged in water. Participants were asked if they planned to engage in any non-routine physical activities, such as traveling, during the week they would be wearing the activity monitor. If they answered yes, a different measurement week was selected. Also, participants were asked to maintain their normal level of activity during the week the activity monitor was worn. This was done to ensure that habitual SB was captured.

The next session was scheduled 7 – 14 days later, during which the participant returned the activity monitor and sleep\non-wear time diary. The activity monitor data was downloaded and assessed to ensure that sufficient data was obtained, defined as at least 4 days with 10 hours per day of activity data.[34] If the activity monitor data was not sufficient, the participant was asked to wear the activity monitor for another week. In addition, individualized counseling to reduce SB and increase physical activity, based on the participant's activity monitor results, was provided. Only participants who completed all aspects of the study were included in the final analysis.

Study Variables

Glycemic control: was assessed via a disposable finger stick HbA1 kit (A1cNow+). This test measures the level of glycosylated hemoglobin, reflecting average glucose blood levels over the past 6 to 12 weeks.[35]

Well-being: was assessed using a well-being questionnaire (WBQ-22). [18, 36] This questionnaire consists of 22 items, scored on a 0-3 Likert scale, that assess depression (six items), anxiety (six items), energy (four items), and positive well-being (six items). General well-being is calculated by the following equation: General well-being=36-depression-anxiety+energy+positive well-being. Higher scores indicate higher levels of well-being. This questionnaire has been shown to have good internal and external validity in multiple populations, including the elderly and people with diabetes.[18, 37, 38]

Fatigue: was assessed using the Fatigue Severity Scale (FSS). This scale assesses fatigue in daily life and differentiates fatigue from clinical depression. The 9-item questionnaire reflects different domains, including motivation, exercise, and interference with work, family, and/or social life. A score less than 4 indicates no fatigue, a score between 4 and 4.9 indicates moderate fatigue, and a score of 5 or higher indicates severe fatigue. This scale is reliable and valid, and it is recommended to use for people with diabetes.[22]

Physical function: The Senior Fitness Test was used to assess physical function, and has been shown to have good reliability and validity in measuring physical function in older adults.[39, 40] This test measures upper and lower body strength (arm curl and chair stand test), upper and lower body flexibility (back scratch test and chair sit-and-reach test (cm)), and agility\dynamic balance (Time Up and Go (TUG) test), and aerobic endurance (6-minute walk test (6MWT)). Each parameter of the senior fitness test has been shown to be valid and reliable for use in adults of different populations including people with diabetes.[39, 41-43] The result of each test was standardized by gender using a Z-score as follows: Z-score = (observed – sample mean)/ sample standard deviation. The sum of the six Z-scores (6MWT + arm curl + chair stand test – TUG – back scratch – chair sit-and reach) was used to compute an overall continuous measure of physical function.[27]

Activity data acquisition

SB (average duration of total sitting time), breaks in SB (number of transitions from sit to stand), and MVPA were estimated from the activity monitor data. The activity monitor has a sampling frequency of 10 Hz and a recording interval of 0.1s. For data analysis the time-stamped "event" data file generated by the activPAL™ software (version 7.2.32) was exported as a .csv file for further cleaning and analysis in RStudio. R is an open-source computing language and statistics package available for free at www.r-project.org.[44] A freely available custom R package developed by Lyden et al. was then used to extract the variables of interest from the activity monitor data.[45] Using the package, we ran the function *process.AP* to batch process all event.csv activPAL^{TM} files and produced three .csv files that summarized 1) sleep/wake time and wear/non-wear time, 2) SB (sit time and transition from sit to stand) and MVPA results per day and 3) mean SB variables and MVPA by visit. We used the SB and MVPA results per day .csv file to exclude any days with less than 10 hours of wear time. Mean values for minutes/day or count/day were calculated for all variables of interest.

Statistical Analysis

Data analysis was conducted using SPSS 23.0 for Windows (Chicago, IL). Descriptive statistics for continuous variables included means and standard deviations, while frequencies described categorical variables.

Multiple linear regression models (two models) examined the effect of glycemic control, well-being, fatigue, and physical function, along with covariates of age, BMI, and MVPA, on SB (SB min/day or transitions from sit to stand). Univariate analyses were conducted for all covariates and any variable with p-value ≤ 0.1 was included in the adjusted models. The normality and homogeneity of the residual was tested during model development. All independent variables were tested for multicollinearity. An alpha level of 0.05 assessed the significance of all relationships.

Results

A total of 63 participants aged 50 to 75 years, including 36 females and 27 males, participated in the study. Data from four participants was excluded due to insufficient SB data, thus, data from only 59 participants was included in the final analysis. Participants' characteristics are summarized in Table 1. On average, study participants were 64 ± 7 years of age and obese (33 ± 5.5 kg/m^2). More than half of the sample were females (58%), retired

(61%), and had neuropathy (66%). As expected, glycemic control was impaired (Mean: 7.28 ± 1.54, Range: 4.9 – 12.4).

The univariate analysis of covariates indicated that only MVPA had a p-value ≤ 0.1, and this variable was included in the final adjusted model. Multiple regression analyses were performed to characterize the relationships between SB (min/day) and glycemic control (HbA1c), well-being, fatigue level, and physical function composite score, (Table 2l). SB (min/day) showed a significant positive association with glycemic control (β= 0.40; 95% IC: 14.43, 58.13) independent of MVPA.

Table 1. Participant's Characteristic and study variables. Data reported as mean ± SD or frequency (%). BMI: body mass index, 6MWT: 6-minute walk test, TUG: time up and go, MVPA: moderate to vigorous physical activity

Characteristic	**Completed Study (n=59)**
Age, y	63.98 ± 6.79
Gender, % Women	34 (57.63%)
BMI, kg/m^2	33.39 ±5.53
Retired, % Yes	36 (61.02%)
Neuropathy, % yes	39 (66.1%)
HbA1c (%)	7.28 ± 1.54
Well-being Q-22	47.75 ± 9.49
Fatigue severity scale	3.58 ± 1.48
6MWT (m)	405.6 ± 84.1
TUG (sec)	7.37 ± 1.81
Back scratch (cm)	18.6 ± 12.1
Chait-sit-reach (cm)	5 ± 8.6
Arm curl (counts)	19.51 ± 5.19
Chair stand test (counts)	10.24 ± 3.32
Sedentary behavior (min/day)	664.74 ± 138.87
Transitions from sit to stand (counts)	47.55 ± 14.71
MVPA (min/day)	49.83 ± 24.68

A second multiple regression analysis was performed to characterize the relationship between transitions from sit to stand and glycemic control (HbA1c), well-being, fatigue levels, and physical function composite score (Table 2). Physical function showed a trend (p=0.061) toward a positive association with transitions from sit to stand (β= 0.25; 95% IC: -0.044, 1.946) independent of MVPA. Figure 1 provides a graphical representation of these relationships. No other associations were observed between either SB or transitions from sit to stand and any of the other variables assessed.

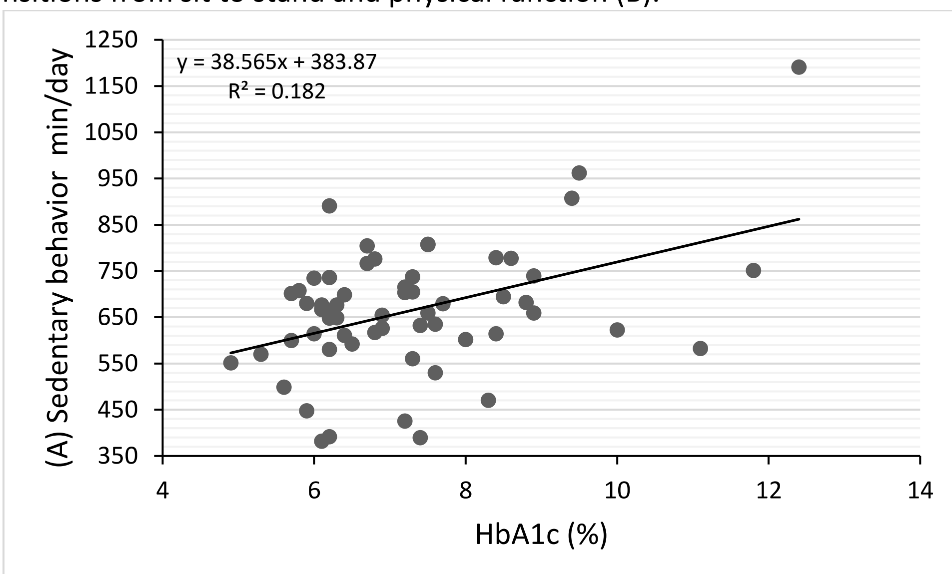
Table 2. Effects of glycemic control (HbA1c), physical function composite score (PF), fatigue (FSS), and Well-being (WBQ-22) on Sedentary behavior (min/day) adjusted for MVPA and transitions from sit to stand (count/day) adjusted for MVPA. *Significant at p<0.05, i p=0.061

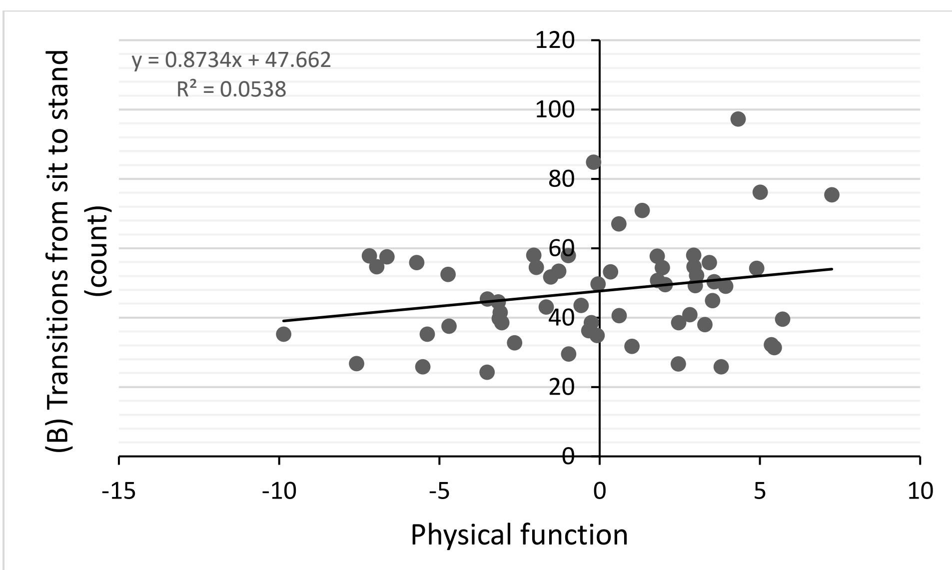
	Sedentary behavior (min/day)			Transitions from sit to stand		
Variable	B	SE B	β	B	SE B	β
HbA1c	36.28	10.89	0.40*	0.1	1.3	0.104
WBQ-22	2.66	1.8	-0.00	0.23	0.22	0.144
FSS	-0.12	12.2	0.018	0.08	1.46	0.008
PF	-1.49	4.15	-0.04	0.95	0.5	0.251[i]
R^2	0.318			0.133		
F statistic	4.848*			1.602		

Discussion

SB is a serious health concern in terms of both its prevalence and severity.[46] Furthermore, the health concerns of SB are exacerbated in the presence of T2D.[2, 4] The objective of this study was to investigate the relationships between modifiable health variables such glycemic control, well-being, fatigue, and physical function with SB and transitions from sit to stand. The study results demonstrated a significant positive association between SB and glycemic control independent of MVPA; indicating that poorer glycemic control predicts longer engagement in SB. Furthermore, the results indicated a possible positive association between transitions from sit to stand and physical function level independent of MVPA; suggesting that participants with higher levels of physical function tended to break their SB more frequently, or vice versa.

Figure 1. Scatterplots illustrating the relationship between (A) sedentary behavior and HbA1c, and (B) Transitions from sit to stand and physical function (B).





Several studies have showed that SB is associated with and has negative impacts on acute glycemic control,[3, 11-14, 47] and incorporating physical activities into testing protocols appears to improve insulin action and glucose metabolism. [11-14] For example, a study of people with T2D by Van Dijk et al. [10] showed that participants that engaged in light physical activity lowered postprandial glucose by 17% compared to participants who engaged in SB. Further, a randomized cross-over study in 19 overweight/obese individuals showed that disrupting SB every 20 minutes with two minutes of light physical activity resulted in decreased postprandial glucose and insulin levels compared to uninterrupted SB.[12] These studies demonstrate one direction of the relationship between SB and acute glucose metabolism. The current study builds on and extends the above studies results as the results from this study establish the relationship between chronic glycemic control and SB in the other direction, indicating that interventions aimed to improve chronic glycemic control may help decrease SB level, and vice versa.

Previous studies have also indicated that, not only is the total time spent in SB is linked to negative health variables, but the way in which this time is accumulated is equally important. [14, 48, 49] The current study suggests that breaks in SB (e.g. transitions from sit to stand) tend to be associated with physical function level. Previous research in older adults has established a link between breaks in SB and physical function level. For example, a study by Sardinha et al. showed that participants with the lowest physical function scores were the least likely to break-up their SB and engage in more than 30 minutes of MVPA per day.[27] Another study by Gennuso et al. showed that breaks in SB patterns are more important than total time spent in SB in determining physical function levels in older adults. [33] However, the relationships between overall time spent in SB, breaks in SB, and physical function in people with T2D needs further investigation.

Research by conducted by Shiue et al has suggested that two or more hours of TV/screen time is associated with poor well-being in adults from 18-98 years of age. However, we found no association between well-being and either SB or breaks in SB, although our participants reported similar levels of well-being to those described previously in people with T2D.[18] It might be that well-being levels are only predictive of passive screen time, rather than SB that includes cognitively engaged activities such as working or reading.

Similarly, our results showed no association between fatigue and either SB variable. However, previous work by Greenwood-Hickman et al.[25] employed semi-structural interviews with 24 overweight/obese adults to determine that fatigue was a key barrier to decreasing SB. Likewise, Thorp et al. showed that frequent breaks in SB during working hours lead to less fatigue and back discomfort in overweight/obese office workers.[24] Furthermore, two studies have reported that more than half of their enrolled participants with T2D reported moderate to severe levels of fatigue.[22, 23] One possible explanation for the lack of association between fatigue and SB we observed is that participants in our study reported lower levels of fatigue than that of other studies. This may reflect limitations in our sample variability and statistical ability to detect associations.

The strengths of this study include the use of objective measures to assess SB and the inclusion of a measure of breaks in SB in people with T2D. However, several factors limit our interpretation of the data. First, we cannot establish the causality of any relationships due to the cross-sectional nature of our study design. Furthermore, while our study sample had high

SB levels, they also exhibited high well-being scores and low fatigue levels, and thus may be somewhat uncharacteristic of the broader population of those with diabetes. In addition, there may have been ceiling effects for SB variable limiting our ability to detect relationships for some variables. Finally, we acknowledge the complex and bi-directional relationships between all study variables, and the need for further studies to determine the direction of these relationships. All in all, future studies with longitudinal or experimental approaches that address these limitations will be needed to confirm or refute our findings.

In conclusion, this cross-sectional study investigated the relationships between objective measures of SB and glycemic control, physical function, and self-reported perception of well-being and fatigue in people with T2D. Multiple linear regression showed that glycemic control (HbA1c) was significantly associated with SB independent of MVPA. Our data also suggest a possible association between breaks in SB and physical function level, independent of MVPA. However, we did not observe significant associations between SB and measures of well-being or fatigue. Future studies should confirm the causality of the observed results using longitudinal or randomized control trial. Furthermore, based on this study results, modifiable factors such as glycemic control and SB might be promising interventional targets.

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Chapter 4: Sedentary Behavior Counseling Intervention in People with Type 2 Diabetes

Abstract

Objective: To examine the feasibility and effect of sedentary behavior (SB) counseling on total sitting time (TST) and physical activity level (e.g. number of steps/day) in people with type 2 diabetes (T2D). Design: Interventional pilot study. Setting: University research center. Participants: Community-dwelling sedentary adults (n=10; 8 women; age 65.6 ± 7.31) with T2D. Intervention: Three months of SB counseling (motivational interviewing-informed education about SB) aided by an activity monitor with a vibrotactile feature (activPAL3™). The monitor was worn for 7 days, on weeks 1 and 13 (without the vibrotactile feature) and during weeks 5 and 9 (with the vibrotactile feature). Objective data from the activity monitor facilitated counseling. Main Outcome Measures: Intervention feasibility was determined by study retention rates and activity monitor tolerability, and differences between pre- and post-intervention average daily TST and number of steps. Paired t test or Wilcoxon matched pair signed-rank test were performed. The effect size (EZ) was calculated using Cohen d. Results: 20% of participants reported moderate issues tolerating the activity monitor, but no serious adverse events occurred. TST time decreased from 11.8 hrs ± 1.76 at baseline to 10.29 hrs ± 1.84 at 3 months' assessment ($p < 0.05$) with a large EZ (Cohen d = 0.88). Number of steps/day increased from 4024 ± 1179.35 at baseline to 4770 ± 1967 ($p < 0.05$) at 3 months' assessment with a medium EZ (Cohen d = 0.46). Conclusions: This study found that 3 months of SB counseling with activity monitor and vibrotactile feedback was feasible for sedentary adults with type 2 diabetes. Furthermore, participants decreased their TST and increased their physical activity level after completing the intervention. Future research with larger,

randomized samples and long term follow up is needed to examine the effectiveness and sustainability of the intervention.

Keywords: activity monitor, feasibility, sitting time

Introduction

Sedentary behavior is a serious health risk for people with type 2 diabetes (T2D),[1, 2] and unfortunately the majority of people with T2D are considered sedentary.[3, 4] T2D is a chronic metabolic disease characterized by abnormal insulin sensitivity and/or impaired insulin secretion that leads to high levels of glucose in circulating blood. T2D results in devastating health complications with significant morbidity and mortality rates.[5] In 2014, the CDC reported that the prevalence of T2D in the United States is around 10%.[5] Factors including an aging population, rising obesity rates, and the ubiquity of sedentary lifestyle are expected to increase the prevalence of T2D to 30% by 2050.[6] Among these factors, obesity and lifestyle are modifiable. Therefore, there is a crucial need for interventions that increase physical activity and reduce sedentary behavior in order to offset the increase in T2D prevalence, and decrease the burden of T2D worldwide.

Sedentary behavior is physiologically and behaviorally distinct from physical activity.[7] Sedentary behavior is defined as "*any waking behavior characterized by energy expenditure less than 1.5 METs while in a sitting or reclining posture*"[8], whereas physical activity is defined by the World Health Organization as *"any bodily movement produced by skeletal muscles that require energy expenditure."* It is important to distinguish sedentary behavior from physical activity because people can meet recommendations for moderate to vigorous (MVPA; 150 minutes of moderate or 75 minutes of vigorous activity per week [9]) and still have extended periods of sedentary behavior.[10-12] Several epidemiological studies have concluded that this sedentary behavior is associated with an increased risk of all-cause-mortality and increased risk of T2D, independent of physical activity levels.[13],[14] Moreover, negative changes in lipid metabolism and insulin sensitivity have been shown to be specifically associated with increased sedentary time.[15-18]

Studies targeting sedentary behavior as a primary intervention goal are relatively new. Generally, sedentary behavior interventions utilizing activity permissive workstations, step counters, and/or face-to-face sedentary behavior counseling using behavior goal setting, self-efficacy, and motivational interviewing techniques have shown promising results by decreasing sedentary behavior in sedentary adults.[19-22] These studies indicate the potential effectiveness and feasibility of several sedentary behavior interventions for the general healthy population. However, no studies published to date have focused on sedentary behavior interventions in people with T2D.

The main objective of this study was to test the feasibility (as determined by study retention rates and activity monitor tolerability) of sedentary behavior counseling using an activity monitor in people with T2D. This counseling consisted of sedentary behavior education informed by a motivational interviewing approach, and vibrotactile feedback provided by an activPAL3™ activity monitor. The vibration feature was intended to promote engagement in physical activity after a specified duration of sedentary behavior. A secondary objective was to test the effectiveness of our approach to decreasing sedentary behavior (total sitting time) and increasing physical activity (total standing time and step counts), and to determine if changes had an impact on improving glycemic control.

Methods

Design and Participants

This study utilized a pilot pre-post intervention design, which is appropriate for assessment of feasibility and effectiveness of a novel intervention. A sample of convenience was used. This study took place from March 2017 to April 2018 in the University of Kansas Medical Center Department of Physical Therapy and Rehabilitation Science. The study was approved by the University of Kansas Medical Center's Institutional Review Board and Human Subjects Committee (STUDY00140490). Informed consents were obtained in writing from each participant prior to the study. Interested participants underwent a structured screening interview to determine their eligibility for the project.

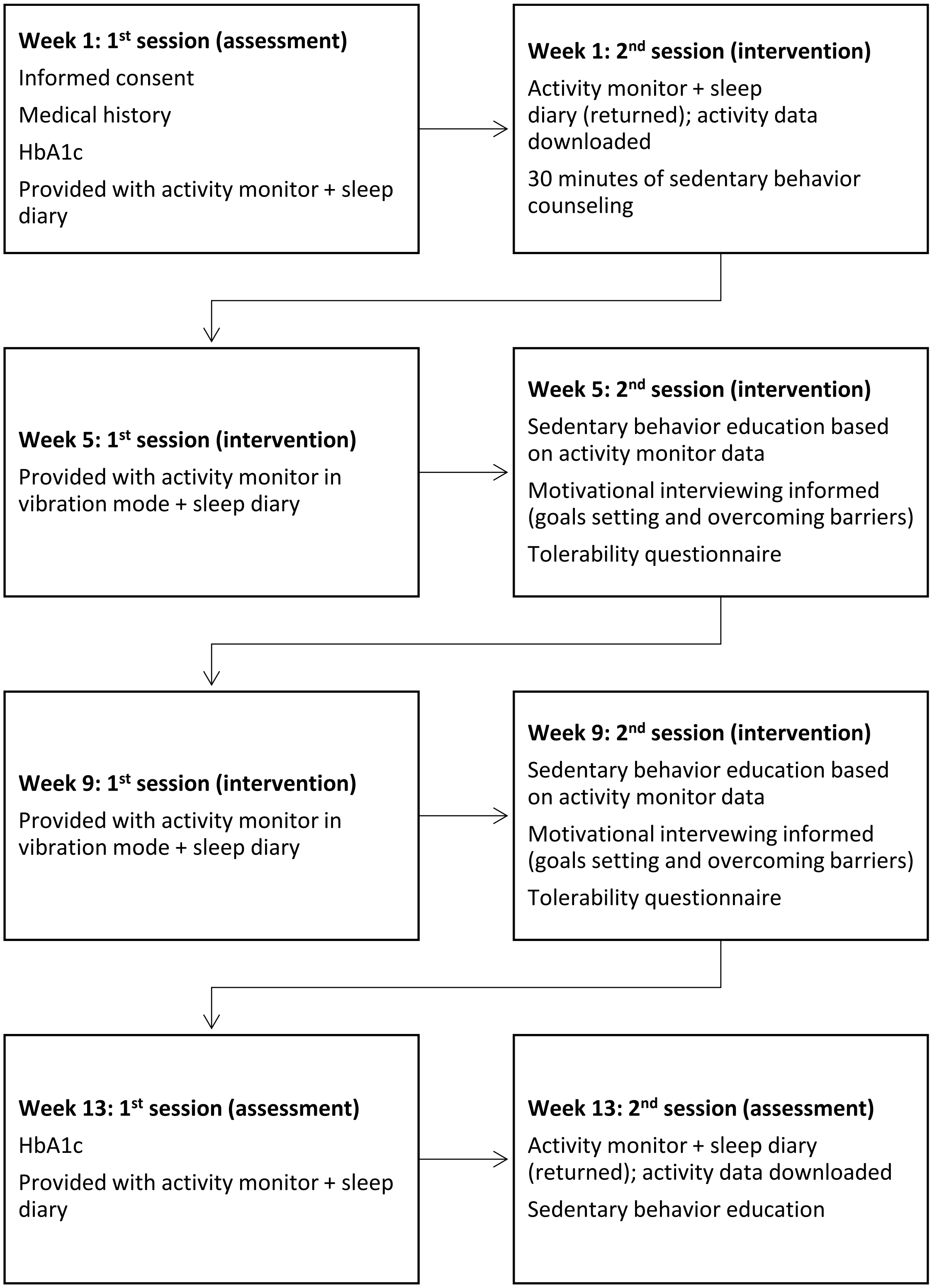
Potential participants were included in the study if they were sedentary (> 7 hours of measured total sitting time per day),[23] between 50 – 75 years of age, self-reported a diagnosis of T2D which was confirmed by reviewing concomitant medications, and able to ambulate independently without an assistive device for at least fifty meters. Individuals were excluded if they had reported any of the following exclusion criteria: 1) neurological conditions that interfere with mobility or cognition, such as Parkinson disease, Alzheimer disease, or multiple sclerosis, 2) foot ulcers and/or a history of lower extremity amputation (great toe or above), 3) morbid obesity (BMI > 45 kg/m^2), 4) major depressive disorder, 5) any cardiovascular or vestibular impairments that would interfere with testing, 6) uncontrolled blood pressure with medication (BP > 190/110mmHg), and 7) inability to understand or cooperate with testing procedures. All interested individuals were screened for eligibility via phone or in person using the above inclusion/exclusion criteria. If eligibility criteria were met, participants were scheduled for their first testing session.

Intervention

This study intervention consisted of three sessions of sedentary behavior counseling delivered at the end of weeks one, five, and nine, and aided by the activity monitor vibrotactile feature at weeks five and nine (Figure 1). Each participant wore the activity monitor with the vibrotactile feature enabled for a 7-day period at weeks five and nine. During waking hours, participants received vibrotactile feedback after 20 minutes of sitting, with the goal of prompting them to stand and/or walk for at least 2 minutes.

Sedentary behavior counseling consisted of sedentary behavior education informed by a motivational interviewing approach. Sedentary behavior education was based on American Diabetes Association lifestyle management (physical activity and sedentary behavior) recommendations published as part of the 2017 Standards of Medical Care in Diabetes.[24] In addition, the activity monitor software produced a single output data sheet that includes activity events (sitting/lying, standing, stepping, and transitioning) per day. This output data sheet was reviewed with each participant as a visual illustration to facilitate sedentary behavior education. As individual sedentary behavior patterns were reviewed, potential strategies to decrease sitting time and increase physical activity as whole were developed. The motivational interviewing informed approach included setting goals for activity, recognizing barriers and resources to decrease sedentary time, and identifying support systems needed to be successful in the intervention. The plan developed at week one was reviewed during the sessions at week five and nine.

Figure 1: Study timeline. 1st and 2nd sessions for each week were separated by at least 7 but not more than 14 days.



Assessment

Written informed consent, demographic information, employment status, medical history, self-reported neuropathy diagnosis, and a concomitant medication list were collected at the baseline (week 1) session. At this baseline session the activPAL3™ activity monitor (PAL Technologies Ltd. Glasgow, UK, http://www.paltechnologies.co.uk) and sleep\non-wear time diary were given to the participant, and instructions were provided for their use. The activity monitor was wrapped in waterproof covering and attached directly to the skin on the front of the right thigh with transparent 3M Tegaderm tape. Participants were asked to wear the activity monitor for 7 consecutive days, removing the monitor only if it was to be fully submerged in water. Participants were asked if they planned to engage in any non-routine physical activity, such as traveling, in the next week prior to being given the activity monitor. If they answered yes, a different measurement week was selected. This was done to ensure the capture of habitual sedentary behavior.

The next session was scheduled 7 – 14 days later and lasted about 30 minutes, at which time the participant returned the activity monitor and sleep\non-wear time diary. The post intervention assessment session was scheduled at week 13 and lasted about 30 minutes, during which time the activity monitor and sleep\non-wear time diary were given to the participant, along with instructions for their use. Again, participants were asked to wear the device for 7 consecutive days. The final session was scheduled 7 – 14 days later and lasted about an hour, repeating the procedure described for session two.

Intervention feasibility outcomes

To assess study feasibility, activity monitor tolerability was determined using a six-question multiple-choice questionnaire. The questions assessed the relative ease of using the monitor, problems wearing the monitor, participants' feelings about wearing the device, the device's impact on daily life, and any complications experienced while wearing the monitor. The results from the questionnaire were classified as: no issues with tolerability, mild issues with tolerability (i.e. the monitor was bothersome, but I did not want to take it off), moderate issues with tolerability (i.e. experience mild complications such as skin discomfort), and severe issues with tolerability (i.e. the monitor was bothersome, I had to take it off).

Sedentary behavior and physical activity outcomes

An activPAL3™ was used to measure sedentary behavior and physical activity. The activPAL3™ directly measures sedentary behavior via postural allocation (e.g. whether the thigh is parallel or perpendicular to the ground). The monitor measures 5 cm × 3.5 cm × 0.7 cm and was worn, as per manufacturer instructions, on the mid-line of the thigh one third of the way between hip and knee. Activity monitor data was downloaded at baseline and weeks 5, 9, and 13, and assessed to ensure that sufficient data was obtained. This was defined as at least 4 days with 10 hours per day of activity data.[25] If activity monitor data was not sufficient, participants were asked to wear the activity monitor for another week.

Glycemic control

At weeks one and thirteen of the study, glycemic control was determined using the HbA1c test via a disposable blood finger stick test kit (A1cNow+). This test measures the level of glycosylated hemoglobin, indicating average glucose blood levels over the past 6 to 12 weeks.[26]

Data Acquisition

For data analysis, the time-stamped “event” data file generated by the activPAL3™ software (version 7.2.32) was exported as a .csv file for further cleaning and analysis in RStudio. R is an open-source computing language and statistics package available for free at www.r-project.org.[27] A freely available custom R package developed by Lyden K was used to extract the outcomes of interest from the activity monitor data.[28] Using the package, we ran the function *process.AP* to batch process all event.csv activPAL3™ files and produced three .csv files that summarized 1) sleep/wake time and wear/non-wear time, 2) physical activity (stand time and step count) and sedentary behavior (sit time) per day and 3) physical activity and sedentary behavior variables by visit.

Statistical Analysis

Descriptive statistics for continuous variables included means and standard deviations, with frequencies used for feasibility and categorical variables. Sedentary behavior and physical activity outcomes were tested for normality via D'Agostino & Pearson normality test. Normally distributed data was tested using one – tailed paired t tests, and Wilcoxon tests were used for non-normally distributed data. The effect sizes for sit time and step count were calculated using Cohen d. Statistical evaluation was done using GraphPad Prism (version 7.04 for Windows, GraphPad Software, La Jolla California USA, www.graphpad.com). Level of significance was set at 0.05.

Results

As shown in table 2, 10 participants completed the study. All participants attended and completed each study session, resulting in a 100% participation and retention rate. All participants completed the tolerability questionnaire. Five participants indicated no issues with tolerability, three participants reported mild issues with tolerability and two participants reported moderate issues with tolerability, including skin irritability or redness due to the 3M Tegaderm tape. No participants reported severe issues with tolerability that necessitated removing the device.

Table 2. Participant's Demographics. Data reported as mean ± SD or frequency.

Characteristic	n = 10
Age, y	65.6 ± 7.31
Gender, Women	80.0 %
BMI, Kg/m^2	32.67 ± 4.89
Race	
Caucasian	80.0 %
African American	20.0 %
Neuropathy, Yes	30.0 %
Retired, Yes	60.0 %

On average, participants spent 11.88 ± 1.1.76 hours/day sitting at baseline and decreased their sitting time to 10.29 ± 1.84 hours/day post-intervention. This yielded a significant mean difference of 1.59 hours/day (p=0.017; Table 3). The effect size for sitting time was 0.88. Concurrently, participants' step counts were 4024 ± 1179 steps/day at baseline and increased to 4770 ± 1967 steps/day post-intervention. This yielded a significant mean difference of 746 steps (p=0.032). The effect size for step count was 0.46. Participants on average increased their standing time from 2.94 ± 1.25 hours/day at baseline to 3.69 ± 1.86 hours/day post-intervention, resulting in a significant mean difference of 44.87 minutes (p=0.069). HbA1c was 7.08 ± 0.86 % at baseline and decreased to 6.57 ± 0.65 % post – intervention, resulting in a significant mean difference of 0.51% (p=0.012; Table 3).

Table 3. Study outcomes: sedentary behavior, physical activity, and glycemic control averages pre and post intervention. [1], data was analyzed via paired t test while; [2], data was analyzed using Wilcoxon non-parametric test. * significant p value. (n)=10 except for HbA1c (n) = 9.

Outcome	Baseline	Post-intervention	P-value
Sitting time (Hours/Day)[1]	11.88 ± 1.1.76	10.29 ± 1.84	0.017*
Steps Count (Step/Day)[2]	4024 ± 1179	4770 ± 1967	0.032*
Standing time (Hours/Day)[1]	2.94 ± 1.25	3.69 ± 1.86	0.069
HbA1c (%)[2]	7.08 ± 0.86	6.57 ± 0.65	0.012*

Discussion

In this study we aimed to test the feasibility and effectiveness of an intervention to treat sedentary behavior in people with T2D. Our intervention utilized individualized, motivational interviewing informed sedentary behavior counseling and vibrotactile sensory feedback. Overall, we found that sedentary behavior counseling and vibrotactile feedback using an activity monitor was a feasible and effective intervention for treating sedentary behavior in people with T2D.

Feasibility was assessed via participant retention and activity monitor tolerability. All study participants completed all study intervention visits and returned for all post-intervention assessments. Similar feasibility studies have reported excellent acceptability and adherence to sedentary behavior reduction aimed interventions.[29-31] One study utilized a single session of goal-sitting to reduce sedentary behavior based on assessed sitting time in older adults, with weekly reminder phone calls. These authors reported 90% acceptability and adherence to the intervention protocol.[31] Another study utilized two weeks of individualized consultation based on activity monitor data to reduce sedentary behavior in older adults. This study demonstrated excellent adherence to study protocol (100% retention) and no issues with activity monitor tolerability.[30] These studies, alongside our results, indicate that sedentary behavior modification interventions are feasible and demonstrate promising potential for impacting sedentary behavior.

Eight out of ten participants in our study indicated either no to mild issues in terms of activity monitor tolerability. Although two participants reported moderate issues related to skin irritation due to use of the Tegaderm tape, neither participant actually removed the monitor. A study by Dall et al.[32] used the same activity monitor affixed with a hypoallergenic adhesive pad and medical grade waterproof dressing. These authors reported that only 8 of the 733 adults that wore the monitor for 9 days removed it due to skin irritation. However, this study did not report whether some participants reported mild skin irritation but did not take the activity monitor off. Regardless, it seems likely that providing multiple options for activity monitor mounting would decrease the possibility of skin irritation.

We also found that a SB intervention decreased sedentary behavior by 95 minutes/day on average in a sample of people with T2D. No previous studies have identified the Minimal Clinically Important Difference or Minimal Detectible Change for this outcome; this is an important area for future research that was beyond the scope of this pilot study. A similar feasibility study with a two-week intervention showed that individualized sedentary behavior consultation based on activity monitor data in older adults decreased sedentary behavior by 24 minutes/day.[30] The greater decrease in sedentary behavior in our study might be due to our longer intervention time, and our utilization of sensory feedback in addition to sedentary behavior counseling. Furthermore, our combined approach showed superior results when compared to a meta-analysis of 15 randomized control trial (total n = 3262) that tested the effectiveness of step counter usage for decreasing sedentary behavior. This analysis revealed a small but significant association between step counter usage and reduction in sedentary behavior (23 minutes/day) compared to control.[20]

After the completion of our intervention participants had decreased their HbA1c by an average of 0.51%. Several studies have shown that an acute reduction in sitting time is associated with positive changes in glucose and insulin metabolism.[16, 33, 34] However, to the best of our knowledge, no studies have previously described the long-term effects of sedentary behavior interventions on glycemic control in people with T2D. Exercise interventions have been reported to decrease HbA1c by 0.66%, while pharmacological agents such as metformin may decrease HbA1c by 0.6%. These changes were associated with positive diabetes and general health outcomes changes.[35, 36] Although it has long been established that exercise interventions have many health benefits, including improved glycemic control, in people with T2D, patient engagement and adherence in these programs are low.[37] Thus, based on our results, further research should examine whether interventions aimed at decreasing sedentary behavior might result in similar changes in glycemic control while fostering greater treatment adherence in people with T2D.

Limitations

This study was not designed or powered to test the efficacy of the sedentary behavior and sensory feedback intervention used here, as we aimed to test the feasibility of this intervention on small sample size. Future studies should utilize randomized clinical trial designs with adequate power to evaluate the true effect of the intervention. Furthermore, this study assessed the feasibility and effectiveness of the intervention on decreasing sedentary behavior immediately after the completion of the intervention. Thus, the long-term effect of the intervention cannot be assessed. These limitations need to be addressed in future research.

Conclusion

This study investigated the feasibility, protocol adherence and tolerability, and the effectiveness of a 3-month sedentary behavior intervention in people with T2D. The results of the study demonstrated that the intervention was feasible and effective. These results indicate promising opportunities for future research to decrease sedentary behavior in people with T2D.

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Chapter 5: Discussion and Conclusion

Summary of findings

The data presented in this dissertation represent one of the first comprehensive analysis of sedentary behavior in people of T2D; examining the stability of sedentary behavior, its associations with modifiable health outcomes, and the feasibility of a behavioral intervention to treat sedentary behavior. Overall, the results of this work demonstrated that individuals with T2D exhibited stable high level of sedentary behavior that were associated with glycemic control. A behavioral intervention was feasible and showed promising results in decreasing sedentary behavior and improving glycemic control. These results confirmed the profound effect of sedentary behavior on health in people with T2D and provided a possible effective treatment to alleviate these effects.

Chapter 1: Effectiveness of Interventions for Promoting Objectively Measured Physical Activity of Adults with Type 2 Diabetes: A systematic review

In the 1st dissertation chapter we completed a systematic review to assess the state of the literature about available interventions aimed to 1) increase physical activity in sedentary people with T2D and 2) assess change in physical activity via objective measures. We searched for randomized clinical trials in two databases (PubMed and CINAHL) with the above criteria using these keywords: sedentary, diabetes, pedometer, physical activity, and accelerometer. We reviewed a total of 15 RCTs using varied interventional approaches, ranging from behavioral or cognitive consultation to motivational phone calls promoting physical activity. In general, 13 out of 15 studies showed immediate improvements in physical activity level post-intervention. This systematic review highlighted the need for interventions that produce long-term improvement in physical activity, as well as the lack of interventions designed to target sedentary behavior change as the main outcome in people with T2D.

Chapter 2: Test-Retest Reliability of ActivPAL in Measuring Sedentary Behavior and Physical Activity in People with Type 2 Diabetes

In our first experimental chapter we wanted to answer the following question: do people with T2D exhibit stable sedentary behavior and physical activity levels that can be measured objectively over time? To answer this question, we collected two weeks of activity data separated by at least one week. The interclass correlation coefficient analysis showed that all sedentary behavior and physical activity variables exhibited high to very high correlations between the two weeks of assessment. Furthermore, we observed that the tested individuals exhibited high levels of sedentary behavior and low levels of physical activity. Overall, our results appeared to confirm that people with T2D exhibit stable sedentary behavior and physical activity over time.

Chapter 3: Sedentary Behavior Relationship with Health Outcomes in People with Type 2 Diabetes

In this chapter, we shifted our focused to examine the relationship between sedentary behavior and transitions from sit to stand with glycemic control, physical function, fatigue, and well-being. These health outcomes were selected for to two reasons; 1) previous studies in general populations indicate that they were associated with sedentary behavior, 2) these outcomes can be targeted in future intervention studies. The results of this chapter showed that higher level of sedentary behavior was significantly associated with worse glycemic control independent of MVPA. Furthermore, transitions from sit to stand were positively associated with physical function at levels that approached statistical significance. However, fatigue and well-being showed no association with both sedentary behavior and transitions from sit to stand.

Chapter 4: Sedentary Behavior Counseling Intervention in People with Type 2 Diabetes

As shown in chapter one, behavioral interventions are effective in increasing physical activity in sedentary people with T2D. However, no intervention to date has focused specifically on treating sedentary behavior and reported reduction in sedentary behavior as a main outcome. Thus, in the last experimental chapter, we examined the feasibility of behavioral intervention to decrease sedentary behavior. The results of this pilot study showed that a behavioral intervention that included sedentary behavior counseling and vibrotactile sensory feedback was feasible. All ten consented participants completed the study, and only two reported moderate issues of activity monitor tolerability such as skin irritability or redness due to the tape. Furthermore, these participants decreased their sedentary behavior, increased physical activity, and improved glycemic control at the end of the 13 weeks study.

Potential Mechanisms

Although beyond the scope of this dissertation, several other studies have linked sedentary behavior to cardiometabolic biomarkers and associated it with metabolic syndrome and diabetes.[1-4] De Rooij et al.[5] study showed that both obese and non-obese metabolically unhealthy adults exhibit higher engagement in sedentary behavior (593.0 and 576.6 minutes) and lower physical activity (105.2 and 115.4 minutes) compared to obese metabolically healthy adults (563.5 minutes of sedentary time and 118.2 minutes of physical activity) and non-obese metabolically healthy adults (553.3 minutes of sedentary time and 125.0 minutes of physical activity). Furthermore, a study by Sisson et al.[6] estimated that people who engage in ≥4 hours of leisure time sedentary behavior have a 1.94 (men) and 1.54 (women) greater odds of having metabolic syndrome compared to people who engaged in ≤1 hours of leisure time sedentary behavior. Finally, another study by Van der Berg, et al.[7] reviewed data from 1,395 participants and concluded that each additional hour increase in sedentary behavior was associated with 22% elevated risk for T2D and 39% increased risk for metabolic syndrome.

Physiological studies have also linked sedentary behavior with glucose and lipid metabolism. For example, a study by Hamburg et al.[8] examined the effect of 5-days of complete bed rest (23.5 hour/day) in healthy adults and showed that lipids, glucose, and insulin metabolism were negatively impacted compared to baseline values. These results were further supported by a study by Stephens et al.[9] that compared the effect of a 1-day of activity vs 1-day of sitting protocol in healthy adults. The results of the study showed that the activity of insulin decreased by 39% in the sitting day, indicating an acute effect of sedentary behavior. Examining whether the same effects of sedentary behavior would be observed in people with T2D, Fritschi et al.[10] followed 86 individuals for 3-5 days and found that sedentary behavior level predicated significant increases in hyperglycemia. Based on these physiological observations, Hamilton et al. [4] hypothesized that T2D might be caused by engaging in long durations of sedentary behavior while being in a hyperinsulinemic postprandial state. Postural muscles are inactive during prolonged periods of sitting potentially leading to reduced glucose uptake and unbalanced regulation of lipoprotein lipase, a key enzyme in lipid metabolism.[11, 12] Previous studies have suggested two pathways by which sedentary behavior may effect metabolic health; via changes in lipoprotein lipase activity[12, 13] and/or changes in muscle glucose transporters.[1]

Previous studies have also indicated that, not only is the total time spent in sedentary behavior linked to negative health outcomes, but that how this time is accumulated is equally important. A study by Takahashi et al.[14] showed that breaking sitting time improved postprandial oxidative stress in 15 young adult men. Furthermore, Henson et al.[15] studied the associations between objectively measured sedentary behavior, breaks in sedentary behavior, MVPA and total physical activity with markers of cardiometabolic health in people with known risk factors for T2D. These authors found that decreased breaks in sedentary behavior are strongly associated with poorer cardiometabolic health in people with higher risks for T2D. Furthermore, breaks in sedentary behavior are stronger indicator of cardiometabolic health than MVPA. This suggest that breaking up sedentary behavior frequently with either light or moderate physical activity is more beneficial for regulating body metabolism and insulin than MVPA alone.[15-17]

Multiple studies have shown that sedentary behavior is associated with T2D independent of body mass index (BMI).[1-4] These studies indicate that there might be additional contributors of T2D beside body composition. For example, a study of people with T2D by Van Dijk et al. [18] showed that participants that engaged in light PA lowered postprandial glucose by 17% compared to the participants who engaged in sedentary behavior. In addition, studies examining the effect of acute episodes of sedentary behavior on glucose and insulin metabolism have confirmed that sedentary behavior has negative impacts on both biomarkers. However, glucose and insulin control were improved significantly by incorporating light activities into the testing protocol.[9, 17, 19, 20] Decreasing sedentary behavior by light activities means that the human body experiences frequent alternating muscle activities. During active muscles contraction glucose uptake increases, and insulin action improves.

Overall, the relationship between sedentary behavior and diabetes is a complex and bi-directional relationship. Previous studies have established one direction of the relationship between sedentary behavior and acute glucose and insulin metabolism. While, we were able to show the other direction of this relationship by demonstrating that long-term glycemic control can predict sedentary behavior level. However, the results from our project is preliminary and in need for further examination.

Limitations

Participant Characteristics and Sample Size

In an effort to collect representative data for people with T2D we did not control for participant characteristics except for age. However, not controlling for variables such as education, socioeconomic, and employment status may have affected our results. Although we attempted to enroll people with variable levels of sedentary behavior and physical activity, most of our participants in the test-retest reliability and cross-sectional studies were sedentary. This was expected as most people with T2D are considered sedentary. [5, 21] However, there may be a ceiling effect of sedentary behavior limiting our ability to detect relationships for some variables. Thus, our results should not be generalized to very active individuals. Despite these limitations, the characteristics of our participants do not appear to have differed greatly from those of other investigations.

We powered the test-retest reliability and cross-sectional studies sample sizes to detect significant variables. However, we designed our intervention aim as a pilot feasibility study and did not power the sample size to detect changes in sedentary behavior. Thus, the observed positive changes in sedentary behavior, physical activity, and glycemic control after the completion of the intervention should be interpreted with caution until these results can be validated by future research.

Study Design

We utilized a study design that answered our specific questions, however, every design has limitations. In our 2nd aim we utilized a cross sectional study design, and thus cannot establish causality. In addition, there might be an unavoidable reverse causation bias between sedentary behavior and glycemic control. In our 3rd aim, we utilized a single group pre-post intervention design with no follow up visits. This might influence the observed changes in study outcomes because it might be due social interaction not the tested intervention protocol. This study design, in addition to the small sample size employed, does not confirm the general effectiveness of our intervention. However, our results can inform the planning off future studies of sedentary behavior interventions in people with T2D.

Comorbidities and Medications

Only people with T2D and between 50 and 75 years of age were included in the study. Many participants did have multiple comorbidities such as osteoarthritis, joint arthroplasty, hypertension, peripheral neuropathy, and other such conditions. However, we did not exclude any participant on the basis of this information unless it was determined to result in significant physical impairment. Furthermore, these participants took a variety of medication including for many different purposes including ant-diabetic medications and/or exogenous insulin. Although we collected these variables, we did not control for any of them due to their high prevalence in adults over the age of 50, and particularly in those with diabetes. Exclusion on the basis of these factors would have made recruitment of our required sample size extremely difficult.

Future directions

In this dissertation project we attempted to answer multiple research questions regarding the stability of sedentary behavior, its associations with health variables, and its treatment in people with T2D. However, a number of questions remain unanswered. We have identified four key questions that should be prioritized in future studies related to the effects of sedentary behavior on T2D mechanisms, its associations with health outcomes, the effectiveness of treatments designed to reduce sedentary behavior, and the clinical applications of such treatments.

Although our results demonstrated positive associations between sedentary behavior and glycemic control, we could not establish causal relationships or the direction of these associations. Future longitudinal studies following newly diagnosed individuals with T2D are needed to understand the relationships between sedentary behavior and glycemic control; and to answer the following questions: do high levels of sedentary behavior lead to worse glycemic control or vice versa? If so, at what level of sedentary behavior does this association become apparent? And what are the additional effects of sedentary behavior on health outcomes such as health quality and/or the rate of functional decline?

Another area of interest is the identification of key health outcomes that influence the level of engagement in sedentary behavior. We propose conducting qualitative studies in which representative samples of sedentary adults with T2D are asked to identify barriers to physical activity and facilitators for sedentary behavior engagement. Other studies might also assess the prevalence of serious diabetes complications such as neuropathy, falls, and depression in sedentary compared to non-sedentary adults with T2D.

Previous research has demonstrated the high prevalence of sedentary behavior and its negative effect on health outcome. Thus, even though we do not completely understand the relationships between sedentary behavior and diabetes, effective interventions with long term effects are needed. In this project we examined the feasibility of such interventions. However, further research is needed before these interventions can be deemed effective. Thus, we propose a three-arm randomized clinical trial examining the effect of sedentary behavior treatment on sedentary behavior outcomes, glycemic control, compliance, and participant acceptance of treatment. The first group would receive the same intervention used in chapter four (sedentary behavior counseling and sensory feedback). The second group would receive exercise counseling. The third group would receive standard of care. Study assessments would occur at the end of the intervention (month 3), and again at months 6 and 12.

A final area of interest is the clinical application of sedentary behavior treatments. Although the American Diabetes Association recommends engagement in 150 to 75 minutes of MVPA per week and has linked this level of exercise to improvement in diabetes outcomes, patients' compliance is generally low. We suggest supplementing these recommendations with behavioral treatments targeting sedentary behavior. Telemedicine is an area of considerable potential with which to test the feasibility and effectiveness of recurrent sedentary behavior counseling sessions on both sedentary behavior and diabetes clinical outcomes.

Conclusion

This body of work confirmed the high prevalence of sedentary behavior in people with T2D. Furthermore, the high level of sedentary behavior observed in our sample was consistence over time and was associated with worse glycemic control. Our results indicated that sedentary behavior was not associated with scores on either self-reported fatigue or well-being questionnaires. Our sedentary behavior counseling and sensory feedback intervention was feasible and indicated possible improvements in sedentary behavior outcomes and glycemic control. Future research should attempt to explore the relationships of other health outcomes with sedentary behavior in people with T2D. Additional studies are also needed to establish and develop effective treatments to reduce the impact of sedentary behavior on health.

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