THE EFFECT OF INTERRUPTING PROLONGED SITTING WITH RESISTANCE EXERCISE BREAKS ON CARDIOVASCULAR AND METABOLIC OUTCOMES

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Resistance exercises to break up prolonged sitting have only recently been studied with promising results. However, it remains unclear if a more feasible, guidelines-based approach can yield acute health benefits. **Purpose:** To compare resistance exercise breaks (REX) to prolonged sitting (SIT) in a simulated office environment for effects on cardiometabolic and other health outcomes over a simulated work period. **Methods:** Fourteen adults (age: 53.4±9.5 years, BMI: 30.9±4.8 kg/m^2) completed two 4-hour conditions in random order: prolonged sitting (SIT) and resistance exercise breaks (REX). Glucose, triglycerides, blood pressure and heart rate, discomfort, fatigue, and sleepiness were measured at baseline and every hour after (5 total). Pulse wave velocity (PWV) was measured before and after each condition. Acceptability of REX programming was measured using 5 Likert scale questions. Linear mixed models were used to analyze differences for overall condition effect for all outcomes and differences at each hour (post hoc), with Cohen's d reported to display magnitude when necessary. **Results:** Overall differences between conditions in favor of REX were approaching significance for discomfort, mental fatigue, and physical fatigue ($p<0.10$). Heart rate was significantly higher in the REX vs. SIT condition (3.3 bpm, $p<0.001$, $d=0.35$). A post hoc analysis for individual time points for each outcome observed statistically significant differences for glucose (hour 1: -12.5 mg/dL, $p=0.004$, $d=1.02$) and mental fatigue (hour 4: -0.48 log-points, $p=0.016$, $d=0.37$) in favor of the REX condition and a difference in favor of the SIT condition for heart rate (all time points, ≤4.2 bpm, $p \leq 0.044$, $d \leq 0.45$). For questions on acceptability of the program, the majority (>50%) of participants rated acceptability/feasibility for implementation of the REX program in their own office environment as "high" or "very high" for all questions. **Conclusion:** This study provides evidence that low intensity, once per hour, resistance exercise activity breaks can potentially be beneficial to several acute health outcomes and have promising ratings of acceptability. However, this can potentially increase resting heart rate, acutely. These findings suggest that resistance exercise breaks may be a feasible, health-enhancing intervention in desk-based employees that warrant further long-term research.

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PREFACE

"The difference between a successful person and others is not a lack of strength, not a lack of knowledge, but rather in a lack of will."

-Vince Lombardi

I would like to thank everyone, both personally and professionally, who has been a part of this process and their willingness to spend the time and knowledge in mentorship and support to help achieve my goals. No words can do justice to how thankful I am, and because of you, we are truly successful.

1.0 INTRODUCTION

1.1 BACKGROUND

Cardiovascular disease (CVD) is the leading cause of death in the United States with prevalence at a staggering 84 million people and costs totaling $315 billion per year.[1] Diabetes is prevalent in 20 million individuals, costs $245 billion per year, and is the 7th leading cause of death.[2] Additionally, 78 million people with high blood pressure and 87 million with pre-diabetes are at high risk for developing these conditions.[1,2]

Fortunately, lifestyle interventions (e.g., exercise and diet) can substantially reduce the risk of CVD and diabetes.[3] Achieving exercise at the recommended levels can decrease blood pressure and arterial stiffness, maintain healthy glucose levels, and improve cholesterol and lipids (e.g., triglycerides), decreasing the long-term risk of developing CVD and diabetes.[4-7] Current exercise recommendations to achieve these benefits have two components: 1) aerobic exercise - 150 minutes per week accumulated in bouts of at least 10 minutes and 2) resistance exercise - strengthening exercises targeting 8-10 major muscle groups on 2-3 days per week.[8] Despite the known benefits of exercise, only 43.5% of adults in the United States achieve aerobic exercise guidelines and only 21.9% meet resistance exercise guidelines.[9] Thus, innovative strategies are needed to increase physical activity participation and realize potential population-level reductions in CVD and metabolic diseases.

Concurrent with this trend of inactivity, adults in the United States are engaging in increasing amounts of sedentary behavior, which is typically defined as any awake, sitting or reclining behavior with low energy expenditure (<1.5 METs).[10] Occupational sedentary behavior has increased due to more desk jobs and technology which, in many cases, have limited movement due to the use of emails, digital document storage and video conferencing.[11] Sedentary behavior has been independently associated with an increased risk of diabetes, arterial stiffness, CVD and mortality, even when participation in moderate-to-vigorous intensity physical activity is taken into account.[12-14] Thus, reducing and breaking up prolonged sitting at work is a proposed strategy to reduce cardiovascular and metabolic risk.[15] However, there is not yet a consensus for the optimal strategy to break up sitting at work that is feasible and improves health.

Most studies evaluating whether interrupting sedentary behavior yields immediate health benefits have only examined the influence of walking breaks (e.g., 3-minute walks every 20 or 30 minutes) on cardiovascular and metabolic risk factors. These studies have found reduced same day glucose, blood pressure, and triglycerides, but have not measured arterial stiffness, a more global measure of vascular health.[16-19] Fewer studies have evaluated interrupting sitting with resistance exercise, though this type of break may have advantages. Resistance exercise has greater benefits compared to aerobic exercise such as greater muscle mass and improvement in glucose control through allowing more glucose uptake into muscle tissue.[20] Resistance exercises can also be performed at a workstation, thus limiting work disruptions or the need for a place to walk. In addition to breaking up sedentary behavior, using resistance exercise breaks could also facilitate achievement of current guidelines for resistance exercise which have a lesser time requirement compared to aerobic recommendations.

Only one study has evaluated the effect of interrupting sitting with resistance exercise breaks and found same day improvements in blood pressure, triglycerides and glucose uptake. [21,22] In this study, Dempsey et al., demonstrated that interrupting sitting with lower body resistance exercise breaks improved glucose (+9.5 mmol · h · L−1) and triglyceride (+1.9 mmol · h · L−1) uptake from the from the blood [21] and decreased blood pressure (systolic blood pressure: -16 mmHg, diastolic blood pressure: -10 mmHg) among subjects with type II diabetes over a simulated workday. [22] Despite these promising initial proof-of-concept results, this study had several limitations. These include: 1) a high frequency of breaks (3-minute bouts every 30 minutes) that is likely infeasible for most desk workers; 2) a routine that rotated through lower body exercises rather than targeting major muscle groups as recommended in resistance training guidelines; 3) lack of measurement of the effect resistance exercise breaks on arterial stiffness, and 4) lack of measurement of discomfort, fatigue, sleepiness, or acceptability. Since the resistance training guidelines recommend 8-10 exercises using different muscle groups, we proposed to break up sitting once per hour (8 breaks in a typical workday) with resistance exercises using different muscle groups during each break. Thus, this research evaluated whether a more feasible, evidence and guidelines-based approach to resistance exercise breaks during sedentary work can induce meaningful, immediate benefits in vascular and metabolic risk factors.

1.2 SIGNIFICANCE AND THEORETICAL RATIONALE

Physical activity is known to improve CVD and metabolic risk factors including blood pressure, arterial stiffness, glucose, and lipids (triglycerides and HDL cholesterol). [4,23,24] Specific to this proposed research, these benefits have also been observed with resistance exercise. [23,25,26] It should be noted that 21.9% of adults in the United States do not meet resistance exercise guidelines,[9] therefore a need to find new strategies to facilitate exercise participation. Incorporating resistance exercises throughout the workday is one potential strategy. Furthermore, prolonged sedentary behavior has been associated with similar adverse effects on cardiovascular and metabolic risk factors, independent of physical activity participation.[27] Resistance exercise breaks are a potential strategy to increase adherence to exercise guidelines, decrease prolonged sedentary behavior, and potentially improve vascular and metabolic health.

The influence of resistance exercise on metabolic outcomes is mostly due to its influence on muscle activation. Muscle fiber activation has a beneficial effect on blood glucose levels by taking glucose from the blood into the working muscles to be used as fuel.[28] Normally, insulin is primarily responsible for facilitating the uptake of glucose from the blood into the muscle for use, maintaining healthy glucose levels.[29] However, in persons with impaired metabolic function, high levels of glucose in the blood are common and can lead to damage and thickening of the artery walls and increased CVD risk.[30] Increased muscle activation during resistance exercise has the beneficial effect of activating the GLUT4 pathway in muscle tissue that allows uptake of blood glucose without the need of insulin as well as improving insulin-mediated glucose uptake.[31] The GLUT4 pathway can be stimulated by either insulin or exercise to translocate to the edge of a cell to allow for glucose uptake into the tissue. An improved glucose disposal response has been observed with walking[18] and resistance exercise breaks,[21] yet whether our proposed, less intense program is sufficient to elicit enhanced glucose uptake is unclear.

Another metabolic benefit to resistance exercise is its influence on lipids (i.e., triglycerides). Resistance exercise has been shown to increase lipoprotein lipase activity,[32] which is an enzyme responsible for the breakdown of triglycerides. Triglycerides are responsible for transporting fat throughout the blood to be stored or utilized as energy. Increasing breakdown of triglycerides into usable energy decreases lipid levels in the blood. Research is still unclear on how high triglyceride levels influence CVD risk, but there is strong evidence demonstrating that lowering triglyceride levels even by 1% reduces CVD risk by 2-3%.[33] Studies have found that more breaks in sedentary behavior are cross-sectionally associated with lower triglycerides[34] and that high frequency resistance exercise breaks lower triglycerides,[21] but it is not clear whether our intervention will result in this benefit.

Formerly, resistance exercise was thought to be dangerous to individuals with elevated blood pressure due to acute increases in blood pressure. However, recent research has shown that resistance exercise is not contraindicated and, in fact, has a beneficial effect on blood pressure.[25] A meta-analysis published in 2000 demonstrated that resistance exercise results in a 2% and 4% decrease in systolic and diastolic blood pressures, respectively.[35] Importantly, even small reductions in blood pressure are associated with decreases in CVD incidence and death.[35] The primary pathway through which high blood pressure causes increased CVD is by damage to the artery walls. This damage can lead to compensatory arterial stiffness in the arteries and development of blockages and narrowing of the arteries. Both can cause excess stress on the heart in its attempts to supply sufficient blood to tissues beyond the stiff, narrowed vessels[36] Studies interrupting sitting with walking and a single study using resistance exercise have found immediate decreases in all-day blood pressure ranging from 2-16 mmHg.[22,37,38] Our study will evaluate whether hourly resistance exercise breaks result in a blood pressure benefit.

Resistance exercise has also been shown to have a beneficial effect on arterial stiffness. Arterial stiffness is best measured as PWV, which is the noninvasive, gold standard measurement that can assess both central and peripheral stiffness.[39] Higher arterial stiffness has a harmful impact by increasing the amount of work for the heart to pump blood. The stiffer an artery is, the harder the heart works to deliver blood to the rest of the body. Over time, an excessively stressed heart can lead to heart failure and other CVD outcomes.[40] A 2013 study in pre-hypertensive individuals demonstrated a reduction in arterial stiffness (measured by PWV) following only 8 weeks of resistance exercise.[41] Though no studies have evaluated whether active sedentary behavior breaks can reduce arterial stiffness, we hypothesize that breaking up sedentary behavior could reduce PWV. Our rationale is that PWV is known to decrease immediately after an aerobic exercise bout[42] and has been related to sedentary behavior in observational studies.[13,14] The proposed research will be the first to evaluate this novel hypothesis.

Additionally, it is important to understand how using a resistance exercise break strategy influences physical discomfort, fatigue and sleepiness. Of significance, presenteeism seems to be vital for productivity at work,[43] so strategies to improve physical discomfort and level of sleepiness at work are needed. Therefore, we will evaluate whether interrupting sedentary behavior with resistance exercise breaks can improve feelings of fatigue, sleepiness, and discomfort, which is an interesting new area of research and can inform the acceptability of sedentary behavior interventions in the workplace for employees and employers.

In summary, resistance exercise breaks could have a beneficial physiological effect on blood pressure, arterial stiffness, glucose, triglycerides, sleepiness, and discomfort and might be a more acceptable strategy to break up sedentary behavior compared to previously studied interventions. An initial study of resistance exercise breaks suggests improvements in cardiovascular and metabolic risk factors, but the high frequency of breaks, training only in lower body muscles, and failure to assess arterial stiffness (PWV), effects on perceptions, or acceptability preclude ready translation of a strategy using resistance exercise breaks to reduce sedentary behavior. Addressing these gaps with a feasible, guidelines-based, hourly resistance exercise routine and analysis of its effects on glucose and triglyceride uptake, blood pressure, PWV, feelings, and the acceptability will inform future research and recommendations using this strategy.

1.3 SPECIFIC AIMS

This study will engage subjects in their own work in an office setting where they will be exposed to a control and experimental condition in randomized order:

1. Prolonged Sitting (SIT)
2. Prolonged Sitting with Recommendations-based Resistance Exercise Breaks (REX)

These conditions will be used to address the following aims.

1. The first aim is to evaluate the effect of breaking up prolonged sitting with recommendation-based resistance exercise breaks (REX) on metabolic function (glucose and triglyceride disposal) compared to prolonged sitting (SIT).
2. A second aim is to evaluate the effect of REX vs SIT on vascular function (blood pressure and arterial stiffness as measured by PWV).
3. A third aim is to evaluate the influence of REX vs SIT on ratings of physical/mental fatigue, physical discomfort and sleepiness.
4. A fourth aim is to evaluate the acceptability of REX in an office setting.

1.4 HYPOTHESES

1.4.1 Metabolic outcomes

It is hypothesized that metabolic function measured as postprandial area under the curve for glucose and triglyceride (representing disposal) will differ between groups with REX < SIT.

Rationale: Metabolic function has been shown to improve with physical activity, and specifically with resistance training, for both glucose and triglyceride area under the curve. Additionally, area under the curve for glucose and triglycerides might be worse with prolonged sitting. Due to the SIT condition having no engagement in physical activity throughout the session, we hypothesize that the REX condition will result in significantly lower (better) area under the curve for glucose and triglycerides compared to a sitting condition.

1.4.2 Cardiovascular outcomes

It is hypothesized that vascular function presented as blood pressure and arterial stiffness (PWV) will differ between groups with REX < SIT.

Rationale: Blood pressure is known to be reduced following acute bouts of physical activity including resistance training. Furthermore, prolonged sedentary behavior increases blood pressure throughout the day. PWV measures are lower following acute bouts of exercise. This research will add to previous studies on the influence of using resistance exercise to break up sedentary behavior on blood pressure and the novel outcome, arterial stiffness.

1.4.3 Discomfort, fatigue, and sleepiness outcomes

It is hypothesized that self-reported ratings of sleepiness, physical discomfort, and mental and physical fatigue will be lower in the REX vs. SIT conditions for sleepiness, physical discomfort, mental fatigue and physical fatigue.

Rationale: Research has demonstrated that presenteeism is vital for productivity at work and sleepiness, physical discomfort and fatigue play an important role in presenteeism. Previous studies have demonstrated improvements in these measures with other sedentary behavior interventions. Individuals participating in a sedentary behavior intervention have reported reduced pain and improved mood states.[44] Low levels of added activity have been shown to improve daytime sleepiness in older adults,[45] which is important due to the link of daytime sleepiness to mortality and CVD in older adults.[46] Preliminary data from our laboratory suggests the beneficial impact of using a sit-stand desk versus continuous sitting on these measures and demonstrated improvements in sleepiness and physical discomfort over an eight hour workday. Another study found that breaking up sedentary time with simply having participants stand every 30 minutes reduced fatigue and physical discomfort in office workers.[47] This study will extend these findings with a unique sedentary behavior intervention using resistance exercise breaks and will study the effects on daytime sleepiness, physical discomfort, and fatigue in relation to activity breaks in working-aged adults.

1.4.4 Acceptability outcomes

It is hypothesized that acceptability of the REX condition would be ≥4 on a 5 point Likert scale.

Rationale: No study has evaluated the acceptability of using resistance training exercises in the workplace to break up sedentary behavior. We believe this novel approach will be highly acceptable due to the low time requirement to complete the exercises and the ease of being able to perform these exercises at the desk or workspace.

2.0 REVIEW OF LITERATURE

2.1 CARDIOVASCULAR DISEASE

Cardiovascular disease (CVD) is a collection of pathological processes related to the heart and blood vessels that includes atherosclerosis, stroke, heart failure, peripheral artery disease and coronary artery disease. Even though CVD is a major health burden in the United States and globally, it is a disease that is in many cases preventable with healthy lifestyle choices.

The 2016 update by the American Heart Association attributes 223 deaths per 100,000 people to CVD.[48] Stratified by gender, annual death rates for males and females were 269.8 and 184.9 deaths, respectfully, per 100,000 people.[48] When further stratified by race, non-Hispanic black males (356.7) had the highest CVD death rates per 100,000 people followed by non-Hispanic white males (270.6), non-Hispanic black females (246.6), Hispanic males (197.4), non-Hispanic white females (183.8) and finally Hispanic females (136.4).[48] From 2003 to 2013, death rates that were attributed to CVD actually declined by 28.8%. However in 2013, a large proportion (30.8%) of all deaths was still due to CVD.[48] Thus, even though CVD mortality rates are improving, there is still a great burden of CVD and a need for better preventive strategies.

CVD also has a high economic burden. For 2011 to 2012, the estimated costs for CVD in the United States were $316.6 billion. Of this total, $193.1 billion was associated with the direct costs of CVD,[48] and an additional 123.5 billion was related to losses in future productivity.[48] Reducing the number of new and recurrent cases of CVD would also decrease the substantial cost associated with CVD.

2.1.1 Pathophysiology of CVD

Of importance to this study, CVD such as atherosclerosis, stroke, heart failure, coronary artery disease and peripheral artery disease are often preceded by cardiovascular risk factors. These risk factors identify high risk individuals that may especially benefit from lifestyle or other interventions. Below, the pathologies leading to different types of CVD are discussed to demonstrate the importance of reducing these risk factors.

Atherosclerosis is a type of arteriosclerosis (hardening of arteries) and is the result of plaque build-up in the walls and lumen of the artery.[49] Plaque consists of cholesterol, fatty substances, collagen and cellular waste. Atherosclerosis typically develops over time through a series of events to the artery walls which lead to partial or complete blockage of the artery. Initially, development starts with damage occurring to the artery walls, due to hypertension or high lipids for example, resulting in the recruitment of inflammation cells from the blood into the artery walls.[50] This influx of inflammation cells, along with cholesterol, eventually forms fatty streaks in the artery wall. Over time, these streaks calcify, becoming hard protrusions into the lumen of the artery. These protrusions cause blockages of blood flow, which increases workload on the heart and can also be damaged and rupture.[51] A rupture develops into an embolism, further blocking the flow of blood. If this embolism breaks free and travels down the blood stream, it can cause complete blockage in smaller arteries in areas such as the lungs, brain or heart. A similar process to more distal arteries and localized to the extremities is the pathological process leading to peripheral artery disease. Like atherosclerosis in more central vessels, peripheral artery disease is a strong predictor of future CVD outcomes and mortality.[52]

Strokes are the result of blockage of blood flow to the brain and can cause varying degrees of irreversible damage to brain tissue that is restricted from blood flow.[53] One cause of strokes is embolisms from more central vessels migrating up the blood stream and creating a blockage in smaller arteries that supply the brain tissue. Another form is hemorrhagic strokes that are caused from weakened blood vessels that rupture and cause pooling of blood that compresses the surrounding brain tissue.[54] This condition stems from atherosclerosis of the arteries that weakens the vessels. If severe enough, a stroke can result in permanent brain damage affecting muscle control, speech, and memory. In the most severe cases, strokes can result in death.[55]

Coronary heart disease is a blockage of the coronary arteries that supply the heart.[56] These small arteries are highly susceptible to blockage, which results in diminished or complete stoppage of blood flow to muscle tissue in the heart. Incomplete blockages can manifest as angina or chest pain. More severe blockage can result in a myocardial infarction that could end in death.[57]

Heart failure is a chronic and progressive condition where the heart is not able to keep up with the demand of blood needed throughout the body.[58] At first, the body can compensate by enlarging the heart chambers, developing more myocardial muscle mass, or by pumping faster. Over time, these mechanisms cannot be sustained and the individual will begin to experience symptoms such as fatigue and breathing problems.[59] Typically, heart failure develops from conditions such as coronary heart disease, hypertension, arterial stiffness, left ventricular hypertrophy or a heart attack.[59] Standard treatment includes cardiac rehabilitation (physical activity training), lifestyle modifications and medications.[59] Heart failure has a poor long term prognosis with 37% of men and 33% of women dying within 2 years of diagnosis.[60] Six-year mortality rates are 82% for men and 67% for women.[60] Prevention of heart failure, therefore, is an important priority to reduce CVD mortality rates.

2.1.2 Risk factors

Several risk factors being assessed in this study have been linked to the development of CVD and are described in further detail below. Elevated blood pressure and arterial stiffness are major CVD risk factors that are important targets for the primary prevention of CVD.[61]

2.1.2.1 Elevated blood pressure

An established risk factor for CVD is elevated resting blood pressure, which corresponds to a systolic blood pressure of ≥120 mmHg or a diastolic blood pressure of ≥80. Table 1 displays the cut-points established by American Heart Association for better treatment of hypertension and are associated with increased risk.[62] Elevated blood pressure is known as the “silent killer” because it has no signs or symptoms and will go undiagnosed without regular monitoring of blood pressure. Elevated blood pressure is highly prevalent in the United States with about 1 in 3 adults having hypertension and an additional 1 in 3 adults having prehypertension.[63,64]

Table 1. Blood Pressure Cut-points

Category	Systolic (mmHg)	Diastolic (mmHg)
Normal	Less than 120	Less than 80
Pre-hypertension	120 to 139	80 to 89
Stage 1 hypertension	140 to 159	90 to 99
Stage 2 hypertension	160 or higher	100 or higher

2.1.2.2 Physiology of elevated blood pressure

With each contraction of the heart, blood is pumped throughout the body via arteries. These arteries transport blood and are responsible for the delivery of oxygen and other nutrients that the organs and tissues require.[54] One way to measure the health of these arteries is to measure the pressure, or force per unit, exerted on the artery walls as blood is pumped through the body.[54]

Arteries are made up of several layers that include the tunica intima, tunica media and tunica externa.[54] The inner-most layer is the endothelium which is a single cell layer made up of simple squamous cells.[54] The middle layer is composed of smooth muscle and elastin with the outer layer being mostly collagen fiber.[54] This design, under normal circumstances, allows for an elastic-like property of the vessels to permit for expansion and contraction during the cardiac cycle and allows for more space for blood to flow when needed. As the blood exits the heart and flows through the arteries, the blood exerts a force (pressure) on the walls which is known as blood pressure and reported as millimeters of mercury (mmHg).[54] The less compliant the arteries are, the higher the pressure that will be exerted upon them as blood is pumped through. Chronic exposure to elevated blood pressure results in damage to the artery walls, leading to more overt CVD. One such manifestation of this would be the development of atherosclerosis.[65]

Elevated blood pressure is related to several modifiable and non-modifiable risk factors including age, gender, race, activity level and diet. With increasing age, structural changes occur to the arteries, making them less compliant, and resulting in elevated blood pressure.[66] When men and women are compared at the same age, men typically have higher blood pressure and are therefore at increased risk for CVD as compared to women.[67] When stratified by race, blacks typically have higher blood pressure than their white counterparts.[68] As for modifiable risk factors, diet and exercise along with weight loss have been strongly linked to the reduction and control of blood pressure.[69,70]

2.1.2.3 Methods for assessment of blood pressure

Blood pressure is typically measured one of two ways: auscultation or oscillometry methods. Auscultation utilizes a cuff to occlude the brachial artery in the arm and pressure is slowing released and is the standard way to measure blood pressure.[71] The noise emitted from the artery wall can be detected by a stethoscope and is known as Korotkoff sounds. Identification of the systolic and diastolic pressures is determined from when the first detectable sound is obtained (systolic), which is when blood starts to flow, and when sounds cease (diastolic), signifying when the minimum arterial pressure is less than the pressure of the cuff.[71] As for oscillometry, a cuff is similarly inflated to occlude blood flow and then pressure is slowly released. When the pressure of the cuff becomes lower than the systolic pressure, the arteries begin to pulsate against the cuff pressure with the return of blood flow.[72] The machine detects the maximum oscillation and estimates systolic and diastolic blood pressure using proprietary formulas. The oscillometric method has been validated for the assessment of resting blood pressure.[73] Auscultation allows for precise, direct measurements, but is susceptible to user error and expectancy bias. Oscillation has excellent reliability between measurements and is objective, but does not directly measure systolic blood pressure and diastolic blood pressure. Both methods are considered indirect whereas the direct method would be the insertion of an arterial line.

2.1.2.4 Arterial stiffness

Arterial stiffness refers to the compliance of the artery walls to expand and retract in response to increased or decreased blood pressure and blood flow. Arterial stiffness has been established as an independent predictor of CVD risk and is a subclinical indicator of such CVD endpoints as stroke and heart failure.[74]

2.1.2.5 Pathophysiology of artery stiffness

Arterial stiffness can occur throughout the vasculature of the body, but typically increased stiffness of the central arteries is more consistently linked to increased CVD risk.[75,76] Newer research also suggests that more peripheral measures of artery stiffness may predict CVD, but further research is warranted.[77]

Within the arteries, collagen and elastin represent the rigid and elastic properties of the artery and are balanced to allow for a properly functioning artery wall. When the arteries are exposed to stress, typically from high blood pressure or inflammation, collagen production increases and elastin production is reduced.[78] This increased collagen results in a "hardening" or "stiffening" of the artery wall. With increased stiffness of the arteries, the heart must work harder to facilitate the flow of blood throughout the body. This structural change to the arteries is known to occur with aging;[79] however, arterial stiffness also results from chronic exposure to oxidative stress, hyperglycemia and hypertension.[80]

Of importance, arterial stiffness is most closely related to excess stress on the heart and CVD endpoints such as heart failure and hemorrhagic stroke.[74] Increased stiffness increases the demand on the heart to supply blood throughout the body, which results in ventricular hypertrophy, for example.[81] This process, although distinct from atherosclerosis, can occur alongside atherosclerotic processes which can also harden arteries. These stiff arteries can result in vascular damage, atherosclerotic plaques, and atherosclerotic CVD.[82]

2.1.2.6 Methods for assessment of arterial stiffness

Arterial stiffness can be measured by several different noninvasive techniques that include PWV, ultrasound, pulse waveform analysis and pulse pressure.[75] The gold standard for arterial stiffness assessment is carotid-femoral pulse wave velocity (cfPWV).[75] This measurement captures the transit time of a pressure waveform as it travels throughout the body to superficial points on the carotid and femoral arteries. As the left ventricle of heart contracts (systole), a pressure wave is generated and is sent throughout the arterial circulatory system.[75] The speed that the wave travels represents arterial stiffness. PWV can also be used to measure stiffness along the pathway to more distal arteries (peripheral PWV). Whereas cfPWV is a marker of central artery stiffness (aorta), peripheral PWV signifies the arterial stiffness more systemically.[75] The link to CVD and peripheral PWV is not as strong as with cfPWV, but measurement of both cfPWV and peripheral PWV are each important to understand how CVD development occurs throughout the body.

PWV is the gold standard and most common assessment technique for arterial stiffness because it is noninvasive, accurate, and relatively simple to perform. PWV is assessed by applanation tonometry.[75] This technique captures pulse waveforms at superficial sites on the body that can include carotid, femoral, radial and posterior tibialis artery points. Sensors that are placed against the skin or over thin cloth are able to measure the difference in transit time between arterial sites. For the measurement of the transit time component of the velocity measurement (the denominator), a foot-to-foot method is used, which refers to the beginning of each wave (foot) as the point for transit time calculations. For the distance component of the velocity measurement (the numerator), lengths are estimated between sites using a tape measure outside of the body in a supine position.[75] Of note, though this is the recommended measurement method, error is potentially introduced (e.g., in cases of abdominal obesity).

Other methods include pulse pressure, pulse waveform analysis and ultrasound. Pulse pressure is the crudest form of measurement that uses the difference between the diastolic blood pressure and systolic blood pressure measurements as an estimation of artery stiffness.[83] Even though this technique is easy to administer, it only estimates arterial stiffness rather than more direct measurement. Pulse wave analysis also uses tonometry of the forward pressure waveform, as well as the portion of the wave reflected back towards the heart to estimate the stiffness of the arteries through augmentation index.[75] However, augmentation index is less related to long-term CVD outcomes as compared to cfPWV.[75] Lastly, ultrasound is a more expensive alternative that can assess arterial stiffness by capturing images of the vessel wall and its response to changes in volume and diameter.[75] This is a highly sophisticated technique requiring a skilled technician and expensive equipment.

2.2 METABOLIC DISFUNCTION

2.2.1 Diabetes (Type II)

Type II diabetes can also be referred to as non-insulin dependent diabetes. Originally, type II diabetes was referred to as 'adult-onset diabetes' because it only occurred in adults. However, more recently, rates of type II diabetes are increasing in younger individuals, likely as a result of increased obesity in this demographic group.[84] According to the Diabetes Fact Sheet published by the Center for Disease Control and Prevention in 2014,[85] diabetes affects 29.1 million adults in the United States, or 1 out of 11 people. Furthermore, 86 million adults in the United States have prediabetes. Fifteen to 30 percent of individuals with prediabetes will develop type II diabetes within the following 5 years.[85] It is estimated that the total medical cost and lost productivity associated with diabetes is 245 billion dollars per year.[86] Type II diabetes is associated with microvascular and macrovascular complications including an increased risk of stroke, heart disease, loss of vision, kidney failure, peripheral neuropathy and amputation.[87] Thus, diabetes is a growing and expensive public health burden.

2.2.1.1 Pathophysiology of diabetes

Normal blood glucose level is around 90 mg/dl.[88] Though this level can be imbalanced by recent intake or use of glucose, a normal functioning body system will return back to normal quickly by influence of the pancreas. The pancreas contains alpha and beta cells that are responsible for secreting glucagon and insulin, respectively.[88] Of interest to the pathophysiology of diabetes is the role insulin plays in the regulation of blood glucose. When glucose levels in the blood are elevated, insulin is secreted from the pancreas and is circulated throughout the blood stream. Insulin lowers blood glucose by enhancing transportation of glucose across cell membranes, especially into muscle and fat cells.[88] Also, insulin helps lower blood glucose levels by inhibiting processes such as the breakdown of glycogen to glucose and the conversion of amino acids and fats into glucose.[88] At the cellular level, insulin activates its receptor, which starts the cascade eventually leading to increased glucose uptake.

In type II diabetes, insulin is hypoactive and does not engage in its normal role with blood glucose regulation. This is different from type I, where insulin is not secreted by the pancreas. When insulin is not functioning properly, blood glucose levels will rise and remain elevated. Normally in an elevated blood glucose state (hyperglycemia), hormones that are responsible for increasing blood glucose in a low blood glucose state (hypoglycemic) are not secreted. But, when there is a prolonged hyperglycemic state, these hormones are secreted due to a sympathetic response signaling the secretion of these hormones.[54] These hormones are normally responsible for glycogenosis, lipolysis and gluconeogenesis, which are processes for increasing blood glucose and can cause the elevated blood glucose to rise even higher.[88]

Three major signs of diabetes are polyuria, polydipsia and polyphagia.[54] Polyuria is caused by excess glucose in the kidney that acts as a diuretic and causes excess urine output.[54] This surplus of urine output can lead to dehydration and depletion of electrolytes, causing abdominal pains and vomiting. Stemming from the dehydration, polydipsia, or excessive thirst, occurs.[54] Finally, polyphagia is excess food consumption from hunger even though the body has ample blood glucose.[54] This response occurs because blood glucose cannot be utilized. In this state, fat and protein stores are used for energy metabolism, which leads to hyperlipidemia or high levels of fatty acids in the blood. In severe cases, this can lead to a condition known as ketoacidosis that could potentially be life threatening.[88]

The beginning stage of diabetes is known as prediabetes or insulin resistance. Insulin resistance is the inability of tissues to respond to insulin and occurs predominately in muscle and liver tissue.[89] Muscle tissue is the primary endpoint for glucose uptake, so any inhibition in the uptake of glucose by muscle tissue can quickly lead to the development of diabetes. To combat this, muscular contractions can play a key role in facilitating uptake through a separate pathway that will be discussed in Section 2.3.1.

2.2.1.2 Methods of diagnosis of diabetes and pre-diabetes

Diabetes is typically assessed by measurement of blood glucose levels by different methods that have varying accuracy. Common methods include oral glucose tolerance tests, fasting glucose, HbA1c, glycemic clamp, and point-of-care capillary blood testing similar to using a glucometer.[90] Of importance is the accuracy and feasibility of each test in specific clinical settings.

Oral glucose tolerance tests (OGTT) and fasting glucose testing require a patient be in a fasted state at the time of testing. Both tests provide a fasted baseline glucose value. These methods require a skilled phlebotomist to extract blood using a needle via a vein. The OGTT requires ingestion of a sugar solution and periodic subsequent testing over the 2 hours following to quantify glucose disposal from the blood.[91] The difference between these tests are that fasting glucose testing determines impairment of insulin secretion whereas OGTT measures glucose disposal as a function of insulin resistance.[92] Both are considered important for metabolic health.[93] Both of these tests require blood to be drawn. The strengths of these tests are that they are highly accurate for the diagnosis of diabetes, but a limitation is that a fasted state and trained phlebotomists are required and OGTT is not feasible to use for multiple testing throughout the day.

HbA1c is designed to provide an estimate of blood glucose levels averaged over the previous 2 or 3 month period. Glucose binds to the hemoglobin protein in blood cells when glucose levels are high in the blood. Because red blood cells live for about 3 months, they provide an accurate representation of blood glucose levels over a prolonged time. The American Diabetes Association stresses the importance of using HbA1c in conjunction with other testing to evaluate patterns of glucose control.[94] The primary strength of this method is that it provides information on blood glucose levels over an extended time. However, HbA1c is not able to study dynamic changes during an acute period of time. Furthermore, differences in age, ethnicity and medication can influence HbA1c levels.[95]

Glycemic clamps are a highly accurate measure that can be useful for several measurements throughout the day or over several days.[96] However, this method is highly invasive because it requires the placement of a catheter directly into an artery.[96] This method also requires a skilled technician to insert the catheter and is costly.

Capillary testing uses small blood samples extracted from the fingertip to determine blood glucose levels. This method utilizes very small quantities for each measurement and is not as invasive as standard blood sampling. Another benefit is the ability to test blood glucose levels several times throughout the day to determine change without the need for placing an IV. This method has been validated against other methods and has been shown to be a reliable.[97]

2.2.2 Elevated triglycerides

Triglycerides are a form of lipids used by the body to transport fats in the blood to muscle as energy or to adipose tissue for storage.[54] Following food consumption, any unused calories are converted to triglycerides to be stored and released for energy later on by hormones.

Triglycerides and cholesterol are commonly discussed together, but it is important to understand the differences in their roles with triglycerides being used to store unused energy and cholesterol being used by the body to build cells and some hormones.[54] Although the evidence is not clear, elevated triglycerides play a role in the development of CVD through mechanisms such as the hardening of arteries and the development of atherosclerosis.[98] High triglycerides are also a component of the metabolic syndrome, which is a cluster of risk factors that elevate an individual's risk for metabolic dysfunction.[99] The most common causes of high triglycerides are obesity and uncontrolled diabetes,[100] but inactivity is also associated with high triglycerides. Increasing physical activity decreases levels of triglycerides and can be part of the treatment strategy to manage high triglycerides.[101] Triglyceride cut-points are displayed in Table 2.

Table 2. Triglyceride Cut-points

Category	*Values*
Normal	*Less than 150 mg/dL*
Borderline high	*150-199 mg/dL*
High	*200 to 499 mg/dL*
Very high	*500 mg/dL or above*

2.2.2.1 Role of triglycerides in metabolic health

Reducing triglyceride levels reduces the risk of CVD and metabolic disease,[101,102] even though the exact mechanism is unclear. Important and relevant to this proposed study, triglyceride reduction has been achieved in sedentary behavior interventions through the use of activity breaks, including resistance training.[21] The potential mechanism for reduced triglycerides by interrupting sedentary behavior with activity breaks is though localized muscle contracting activity that has been shown to increase energy expenditure.[103,104] Long term outcomes in this setting have yet to be established and require further exploration.

2.2.2.2 Methods of assessment for triglycerides

Triglyceride levels in the blood are assessed by analyzing a blood sample, whether it is extracted via blood draw into a vial or from analysis of a smaller blood sample from the fingertip. Both methods have been validated as accurate techniques to determine triglycerides. Typically, blood samples are drawn from the antecubital space on the arm via needle extraction. This method of blood draw is the same process as for venous glucose testing. A capillary sample requires a smaller amount of blood that is extracted from the fingertip. This technique still requires a trained technician, but less training is needed and participant discomfort is decreased as compared to venous blood sampling. This is important when multiple tests will occur in a short time window. A finger lancet is used to draw a blood sample to the surface of the skin and a small tube is used to collect the blood which is then placed in an analyzer to determine triglyceride levels. This method can give point-of-care results whereas blood sampling from the arm requires lab analysis which can take hours or days. Capillary sampling is also cost-effective due to the need of a lesser skilled technician, fewer supplies, and ability to obtain results without a wet lab.

2.3 PHYSICAL ACTIVITY SPECTRUM

2.3.1 Defining physical activity and recommendations

Physical activity is defined as bodily movement that results in energy being expended above resting values.[105] An alternate definition is any movement greater than 1.5 METs (metabolic equivalents). One MET is defined as the amount of oxygen consumed while sitting at rest [106]. Further categorization of physical activity by exertion level classifies activity as light, moderate or vigorous intensity physical activity. MET value cut-points for intensity levels of physical activity are: light intensity from > 1.5 to < 3.0 METs, moderate intensity from 3.0 to < 6.0 METs, and vigorous intensity which is ≥ 6.0 METS (Figure 1).[8] Examples of light intensity activities include washing the dishes and standing, moderate intensity activities include brisk walking and lifting light loads, and vigorous intensity activities includes running and lifting heavy loads. For this proposed research study, the resistance exercises being used are categorized as moderate intensity activity.

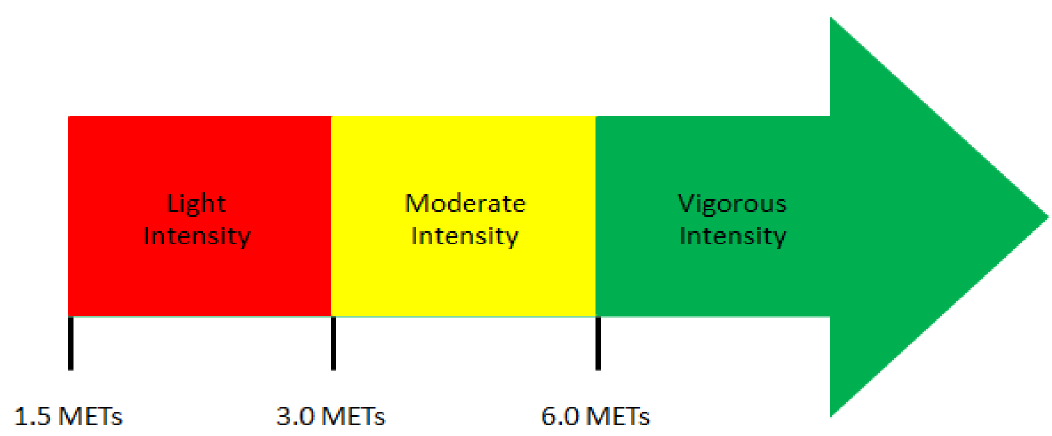


Figure 1. Physical Activity Intensity Levels

Current guidelines for adults in the United States recommend participation in aerobic activity totaling 150 minutes of moderate intensity activity, 75 minutes of vigorous intensity activity, or an equivalent combination of moderate and vigorous intensity physical activity each week, occurring on most or all days of the week, and in at least 10 minute increments.[8] Separate guidelines have been established for resistance exercise stating that adults in the United States should engage in 8-10 exercises on 2 or more days per week that engage all major muscle groups.[8] However, achieving these guidelines is reported by only 43.5% and 21.9% of the population for aerobic and resistance training, respectfully.[9] This low participation highlights a need for novel strategies to increase engagement in both aerobic and resistance exercise physical activity.

2.3.2 Physical activity's impact on health

Exercise can be an effective component in the treatment and prevention of CVD and diabetes as well as effective at reducing risk factors associated with CVD and diabetes. These risks include adiposity, hypertension, hyperlipidemia, dysglycemia and arterial stiffness.[8] Early observational research by Paffenbarger and others demonstrated in observational studies the beneficial impact that physical activity can have on health.[107] Both men and women who reported increased levels of physical activity had a reduction in the relative risk of death by 20-35%.[108,109] Recently, a study completed in 2005 determined that individuals who are physically active have a reduced risk of developing diabetes by 30-50% with similar risk reduction for CVD.[110] A dose-response relationship has also been established where greater physical activity leads to greater reduction in the risk of CVD.[111,112]

Experimental studies have also explored the chronic training effect of physical activity and how exercise can reduce risk factors for CVD and metabolic disease. A meta-analysis of controlled experimental studies found that structured exercise in any form (aerobic, resistance training, or combined) improves glycemic control in individuals with diabetes.[113] Another study found that there are significant differences following both aerobic and resistance exercise interventions in HbA1c compared to controls (7.65% vs 8.31%; P<.001).[114] Long-term training reduces mortality due to CVD [115] as well as risk factors associated with CVD.[3]

Of interest to this proposed study is the acute training effect on CVD and diabetes risk factors. Thompson et al., concluded that exercise has an acute benefit on lipids, blood pressure and glucose homeostasis.[6] Exercise of any mode or intensity will recruit muscles and induce glucose uptake into the working muscles independently of insulin.[116] This is a key concept for individuals with impaired glucose regulation or diabetes. In the presence of impaired insulin-driven glucose regulation, exercise provides a different pathway to allow for glucose uptake into the working muscles and can prevent hyperglycemic states independent of the impaired uptake pathway.

During a bout of exercise, or physical activity in general, the contraction of skeletal muscle will cause a rise in the metabolic demand to meet energy needs. To meet these needs, glucose is taken into the working muscles by facilitated diffusion via GLUT4 transports.[117] GLUT4 is responsible for transporting glucose across the plasma membrane. In a healthy individual, insulin binds to the targeting cells membrane and enhances the carrier-mediated facilitated diffusion via GLUT4. However, in the presence of abnormal insulin function, such as pre-diabetes or type 2 diabetes, this process is diminished. Nevertheless, exercise has been shown as an independent factor in stimulating GLUT4 transport.[31] Muscle tissue contains both insulin-responsive and exercise responsive GLUT4 transporters.[117] This is a key process in glucose management for individuals who cannot maintain blood glucose homeostasis normally. Exercise provides a management tool to regulate glucose and reduce chronic hyperglycemia.

Additionally with an acute bout of activity, lipid lipase is activated. Resistance exercises in particular have induced increases in lipid lipase activity,[32] which is responsible for the breakdown of triglycerides for use. This is important for the management of triglycerides and their role in the development of CVD.

Long-term treatment of type II diabetes with habitual exercise provides additional benefits, separate from enhanced glucose uptake by the working muscle. Furthermore, there exists an extensive amount of epidemiological evidence to support that long-term exercise can reduce the risk of type II diabetes.[110,118] As for treatment of diabetic individuals, even one week of aerobic exercise can improve insulin sensitivity throughout the body.[119] Improved insulin sensitivity is due to an increase in expression and/or activation of proteins involved in glucose metabolism and insulin signaling.[119] When combined with obesity, diabetes can be treated with weight loss by exercise and diet and has been shown to improve inflammatory markers and reduce their influence on the development of CVD. Higher intensities and amounts of activity have been shown to be more beneficial in the management of diabetes and obesity, but new evidence suggests that even excessive sedentary time is linked to increased diabetes risk. As such, strategies to reduce sedentary behavior could be advantageous in the treatment and prevention of diabetes.[27]

Long-term exercise is also highly important for the treatment and prevention of CVD. Studies have demonstrated that even moderate intensity exercise for 15 minutes a day can provide reductions in risk.[120] Furthermore, the American College of Sports Medicine recommends reaching 150 minutes per week for risk reduction.[121] Protective mechanisms of exercise include regulating body weight, reducing insulin resistance, triglycerides, and hypertension, as well as enhancing insulin sensitivity and glycemic control.[110]

2.3.3 Sedentary behavior and its impact on health

Emerging research now suggests that sedentary behavior has an impact on health independent from engagement in moderate-to-vigorous intensity physical activity.[122] Sedentary behavior is defined as any waking activity in a seated or reclined position at ≤1.5 METs.[123] Of importance is that the amount of sedentary time that working adults in the United States are engaging in has been increasing due to the increasing number of desk-based jobs and technology that reduces bodily movement during work and leisure.[124]

Early research identified television viewing time as an independent risk factor for CVD and metabolic dysfunction,[125] Even when physical activity levels were taken into account, both men and women reporting more television viewing or sitting time have higher waist circumference, blood pressure, and 2-h plasma glucose.[125] A meta-analysis from 2012 determined that the highest amount of sedentary time compared to the lowest amount was associated with a 112% increase in the risk ratio for diabetes, 147% for CVD events, 90% for CVD mortality, and 49% for all-cause mortality.[27]

When physical activity and sedentary time are objectively measured, the adverse impact of on cardiovascular biomarkers of risk remains.[125] Healy et al., demonstrated that less sedentary time and greater breaks in sitting were associated with several meaningful benefits including lower waist circumference, BMI, triglycerides and 2-h plasma glucose.[34] What remains to be investigated is the feasibility of programs in various settings (e.g., the workplace) and the type, amount, and intensities of sedentary behavior breaks required to elicit a meaningful benefit without unacceptable interruptions to daily activities. Sedentary time accounts for about 77% of work hours in office workers, signifying a great need to reduce sedentary behavior in this environment.[126]

2.4 SEDENTARY BEHAVIOR WORKPLACE INTERVENTIONS

Recently, a growing body of research has attempted to identify the best strategy to break up sedentary behavior for acute benefits to health including energy expenditure, metabolic function, musculoskeletal pain, and vascular function. Previous research has shown that breaking up sedentary behavior acutely reduces cardiovascular and metabolic risk factors, but the strategy that provides the most benefit that is also feasible has yet to be established.[125] Strategies include the use of sit-stand desks, other active workstations, and activity breaks (e.g. walking or resistance exercise). With these strategies, both frequency and duration of breaks are important factors to consider when determining feasibility and health impact.

2.4.1 Active work stations

Some interventions have attempted to modify sedentary behavior by installing treadmill desks, cycle desks or sit-stand desks at the workstation. One study introduced sit-stand desks to a call center, where workers are not able to leave their desks, and found that sedentary behavior was reduced by 5.3% of their total time while at work (78.5% vs 83.8%; p=0.01).[127] Another study using sit-stand desks found that work and all day (work and leisure) sedentary time were reduced by 143 minutes per week and 97 minutes per week, respectfully.[16] This effect was maintained over 3 months with follow-up testing, finding a reduction in sedentary time of 137 minutes per week at work and 78 minutes per week overall. These data, and other studies,[17,128] suggest that sit-stand desks can be effective to decrease sedentary time at work, though partial compensation occurs after work. Studies using treadmill[129] or cycle desks[130] have also been shown to reduce sedentary behavior during work.

Though it seems clear that active workstations can reduce sedentary behavior, no large trials have demonstrated that reducing sitting time by standing or using an active desk improves cardiovascular outcomes in the long term and only limited, small studies have demonstrated improved metabolic outcomes.[131] A meta-analysis of studies using sit-stand desks and active desks found that using either device produces modest benefits to traditional risk factors for CVD and metabolic disease. Specifically, standing desks improved HDL cholesterol and more active desks improved total, HDL and LDL cholesterol, glucose and insulin.[132] However, most of these studies were small and short-term, limiting the strength of their conclusions. Another benefit of sit-stand desks is the beneficial impact on fatigue and physical discomfort. A study by Thorp et al., demonstrated that transitioning from sitting to standing every 30 minutes had a significant benefit on total fatigue score (mean 67.8 for sitting vs 52.7 for sit-stand; $p<0.001$) and lower back discomfort (31% reduction; $p=0.03$).[47]

In addition to potentially limited health benefits, limitations to active work stations for reducing sedentary behavior include space, office aesthetics and cost. If a workplace has limited space, then such devices may not be practical. Additional barriers to utilization are that these devices are expensive and typically require professional installation. Furthermore, a barrier to these workstations is wardrobe considerations with proper footwear required along with appropriate dress that might not be acceptable for every work environment or the employer. Considering these barriers to using active work stations, the use of activity breaks to reduce sedentary behavior may be a more feasible and cost friendly approach.

2.4.2 Activity breaks

Another method for reducing sedentary behavior, and the method proposed in this study, is the use of activity breaks. These breaks typically require an individual to cease work to perform exercises.

Walking breaks range from walking for short bouts to more prolonged breaks of 10 minutes or more. Walking breaks can also be introduced into the workplace as step counts, instructing individuals to take the "long" way to the bathroom or printer, or walking to a co-worker's desk instead of calling or emailing. Strengths of walking breaks are that they are inexpensive and easy to implement and they can be tailored to the individual's availability and ability. Limitations of walking breaks include the need for space to walk and the need to leave the workstation for the duration of the break. Another strategy, implemented by Bond et al., used a mobile app to prompt individuals to take activity breaks.[133] This method compared 3-min breaks every 30 minutes, 6-min breaks every 60 minutes and 12-min breaks every 120 minutes. Significant reductions in sedentary time of 47, 45 and 26 minutes, respectfully, were observed (all $p<0.05$). Another phone intervention that used messaging to prompt activity breaks reduced sedentary time by 22 minutes per day ($p=0.045$).

Walking breaks have yielded modest reductions in sedentary behavior in the workplace.[134] Both route walking and incidental walking can improve physical activity in the workplace in the short term, but longer studies are needed.[135] Walking breaks induced meaningful benefits in area under the curve for insulin, glucose and triglycerides and were more effective than an equivalent volume of continuous physical activity in a single bout for decreasing insulin and glucose.[19] Walking breaks have also been beneficial for blood pressure.[22] There are no studies of the impact of walking breaks on arterial stiffness, but a meta-analysis determined that aerobic exercise in general reduces arterial stiffness immediately following an acute bout of exercise.[136] A study by Perdomo et al., also determined a beneficial reduction in arterial stiffness 24 hours following a bout of exercise.

As for resistance-style exercises, limited research has been done to investigate the health benefits of such sedentary behavior breaks. Resistance exercise breaks can be defined as performing exercises (e.g. squats, leg lifts, bicep curls) for a pre-determined set and repetition range to break up time spent sitting. These exercises can utilize body weight as the method for resistance or use added resistance (e.g. elastic bands or free weights). Strengths of these types of breaks are that an individual can perform these without leaving the workstation and limited equipment is required. One limitation may be the perceived acceptability in the workplace by other co-workers or supervisors. Another limitation is that, if individuals are not provided proper instruction on movements, they might perform exercises improperly which can increase their risk for injury.

Only one study to our knowledge has used resistance exercise breaks to break up sedentary behavior. This study, by Dempsey et al., examined the influence that simple resistance exercise breaks could have on cardio-metabolic outcomes in 24 subjects with diabetes. In a randomized crossover study and using simulated workdays, this study demonstrated that breaking up sedentary time every 30 minutes with 3 minutes of lower body resistance exercises can elicit benefits for glucose and triglycerides disposal represented by area under the curve as well as improvements in blood pressure.[21,22] The effect of the resistance exercise intervention was found to be similar to that of walking breaks. Figure 2 and Figure 3 show the beneficial effect resistance exercise breaks has on blood pressure for both systolic blood pressure and diastolic blood pressure. The vertical lines indicate feeding times. The black circles represents the sitting condition, white circles with dashed lines represents the light walking condition and grey circles represents the resistance exercise condition. The resistance exercise breaks improved means for blood pressure −16±1 mmHg for systolic blood pressure and −10±1 mmHg for diastolic blood pressure.[22] Importantly for the current study, the blood pressure trajectories have separated during the first four hours, which is the proposed duration of this protocol.

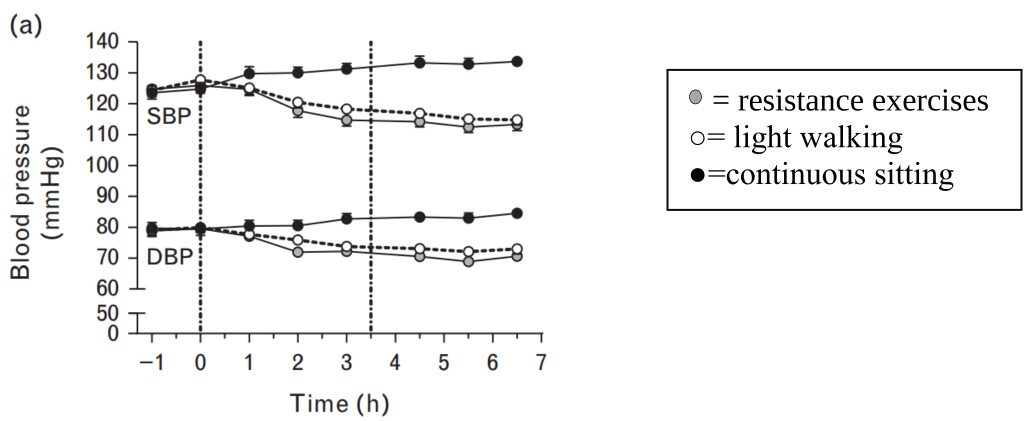


Figure 2. Blood Pressure Response to Resistance Exercise Breaks

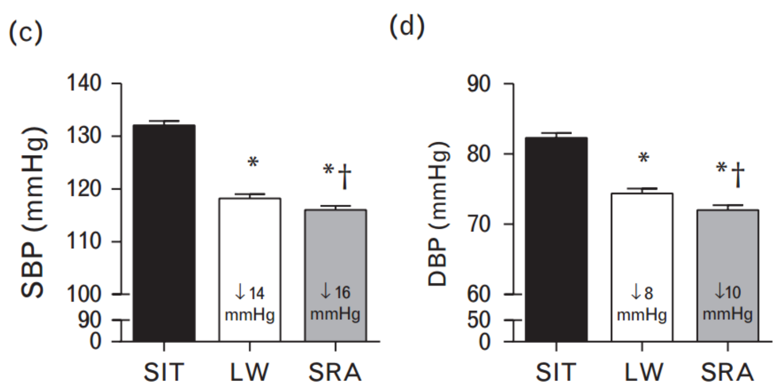


Figure 3. Mean Blood Pressure Response to Resistance Exercise Breaks

Figure 4 and Figure 5 show the beneficial effect resistance exercise breaks have on glucose and triglyceride disposal. Again, the vertical lines indicate feeding times. The black circles represent the resistance exercise condition, the white circles represent the sitting condition and white squares with dashed lines represent the light walking condition. Resistance exercise breaks reduced area under the curve (glucose disposal) for glucose (14.7 vs 24.2 mmol · h · L−1), and triglycerides (2.9 vs 4.8 mmol · h · L−1) compared to the sitting control ($p<0.001$) [21]. Importantly for the current study, the glucose and triglyceride disposal trajectories have separated during the first four hours, which is the proposed duration of this protocol.

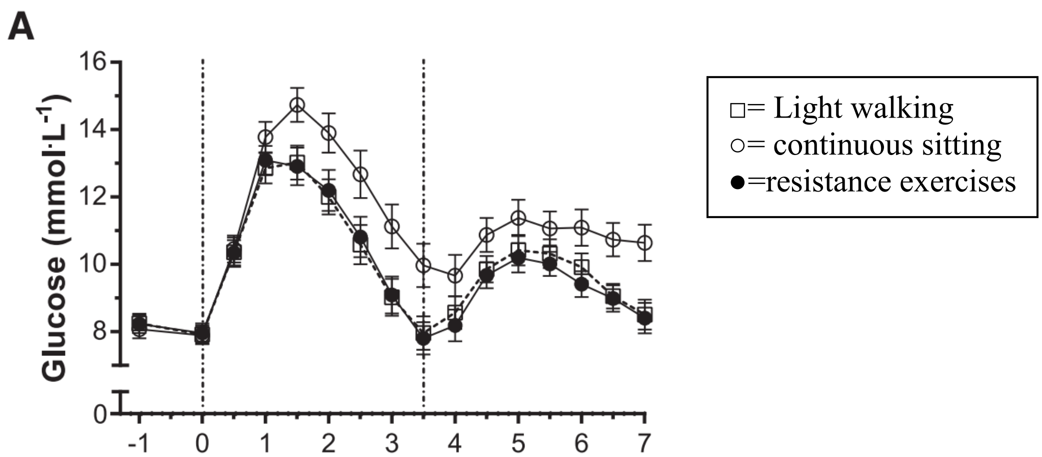


Figure 4. Glucose Response to Resistance Exercise Breaks

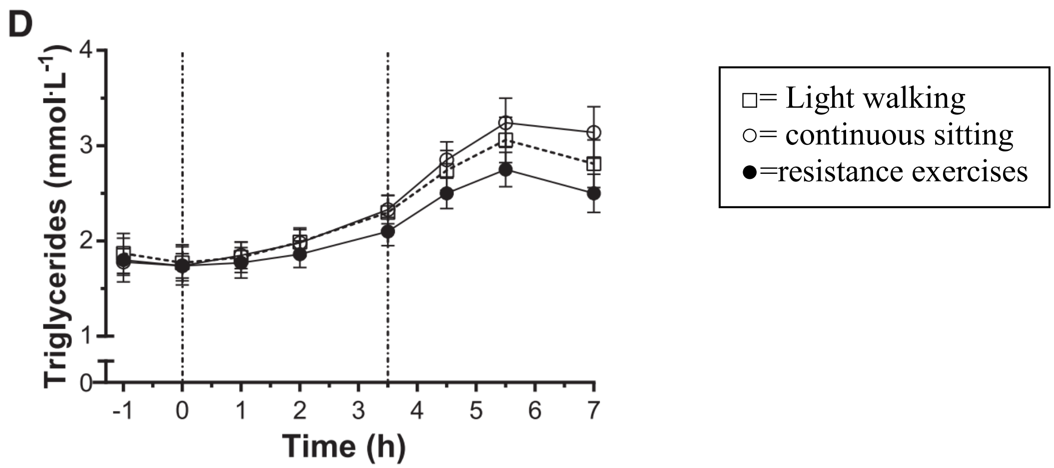


Figure 5. Triglyceride Response to Resistance Exercise Breaks

Also of interest is the lack of research for the role resistance exercise breaks can have on arterial stiffness and rating of physical discomfort, sleepiness, and mental and physical fatigue. This proposed study plans to investigate these outcomes when using resistance exercise breaks to interrupt prolonged sedentary behavior.

3.0 METHODS AND EXPERIMENTAL DESIGN

3.1 SUBJECTS

Fourteen adults with ≥2 of 3 pre-determined CVD and metabolic risk factors were enrolled and completed the research study at the University of Pittsburgh Physical Activity and Weight Management Research Center**.** Table 3 contains a complete list of eligibility criteria.

Table 3. Study Eligibility Requirements

Inclusion Criteria

- ***Aged 30-65 years old***
- ***≥2 of 3 metabolic and CVD risk factors as follows:***
  - ***Pre-to-Stage 1 hypertension (SBP 120-159 or DBP 80-99 mmHg)***
  - ***Elevated abdominal obesity measured by waist circumference (men > 102 cm; women > 88 cm) or BMI classification of obese (≥30.0 kg/m^2)***
  - ***Family history of type 2 diabetes (1st degree relative), or doctor confirmed pre-diabetes (HbA1C between 5.7 and 6.4 or fasting blood glucose level of 100-125 mg/dL or OGTT levels of 140-199 mg/dL) or lifestyle controlled diabetes (no medication; HbA1C ≥6.5 or fasting blood glucose level of ≥126 mg/dL or OGTT levels of ≥200 mg/dL)***
- ***Ability to attend sessions, perform job-related work and perform resistance exercises***

Exclusion Criteria

- ***Taking medication for high blood pressure, hypercholesterolemia, diabetes or medication that would influence heart rate***
- ***>90 minutes per week of moderate-to-vigorous aerobic activity over the past month***
- ***Resistance training activity ≥ 2 days per week over the past month***
- ***Presence of contraindications to physical activity as identified on a physical activity readiness questionnaire (PAR-Q)***
- ***History of myocardial infarction, coronary bypass surgery, angioplasty, or other cardiovascular-related surgeries***
- ***For women, those currently pregnant, pregnant during the previous 6 months or plan on becoming pregnant during the study duration.***
- ***Any musculoskeletal problem that would limit ability to participate in resistance exercise breaks (bone or joint problem) including:***
  - ***Severe arthritis***
  - ***Limited range of motion***
  - ***"Frozen" joint***
  - ***Severe pain with movement***
  - ***Severe balance issues***
- ***Regular smoker (defined as smoking on most days of the week)***
- ***Current enrollment in weight loss program***

3.2 RECRUITMENT AND SCREENING PROCEDURES

Subjects were recruited from the University of Pittsburgh Clinical and Transitional Science Institute research registry and through the use of flyers posted around the University of Pittsburgh Oakland campus. Interested subjects were instructed to call the University of

Pittsburgh Physical Activity and Weight Management Research Center (PAWMRC) where trained staff conducted an initial telephone screening to determine eligibility. The telephone screening included a detailed description of the study and its potential risks and benefits. Following the potential subject's verbal consent, an initial telephone screening containing questions about medical history and other questions related to eligibility criteria was conducted. As per the ACSM recommendations,[121] all questions from the PAR-Q[137] were asked at this time to limit burden of participant and staff for the need of an in-person visit if the participant if found to be ineligible. A copy of the proposed telephone screening form is attached in Appendix A. If a potential subject became ineligible based upon a telephone screening question, the telephone screening process was stopped immediately and no further questions were asked pertaining to the subject's eligibility. If the phone screening was completed and the individual appeared to be eligible, the study staff obtained the potential subjects' contact information. The principal investigator reviewed all telephone screening forms before inviting anyone to a screening visit.

3.2.1 In-person screening visit

All eligible participants from the phone screening process were invited to the laboratory to undergo further screening. Before any in-person screening procedures occurred, subjects completed the informed consent process where they were given a complete description of the study, including risk, benefits and their rights as a research participant, and were allowed to ask questions to a study investigator. If individuals needed more time to decide if they wanted to participate, they were allowed to complete the rest of the in-person screening session at a later time. After all questions had been answered, interested and eligible subjects signed a written informed consent.

Consented participants then underwent further screening procedures to determine their eligibility. Screening measures and procedures included height, weight, waist circumference and resting blood pressure. Participants were also asked to complete a demographics questionnaire. Once all screening assessments were complete, the eligible participant underwent a familiarization protocol with the resistance exercises prior to completion of the screening visit. Participants were instructed to complete each exercise (4 in total) for 2 sets of 15 repetitions each with 1 to 2 minutes rest in between sets. A standardized video was used to give instructions, demonstrate the proper movement pattern, and give appropriate cues for timing. Research staff also provided non-standardized verbal cues during each repetition to encourage proper movement and to correct any irregular or unsafe movements. If a participant was unable to perform the exercises with proper technique even with modifications, then they were determined to ineligible at that time. Successful completion of exercises was considered within the range of 12-15 repetitions. Following the screening visit, eligible participants were randomized to either of the study condition orders, as shown in Figure 6. All procedures were approved by the University of Pittsburgh Institutional Review Board prior to beginning the study.

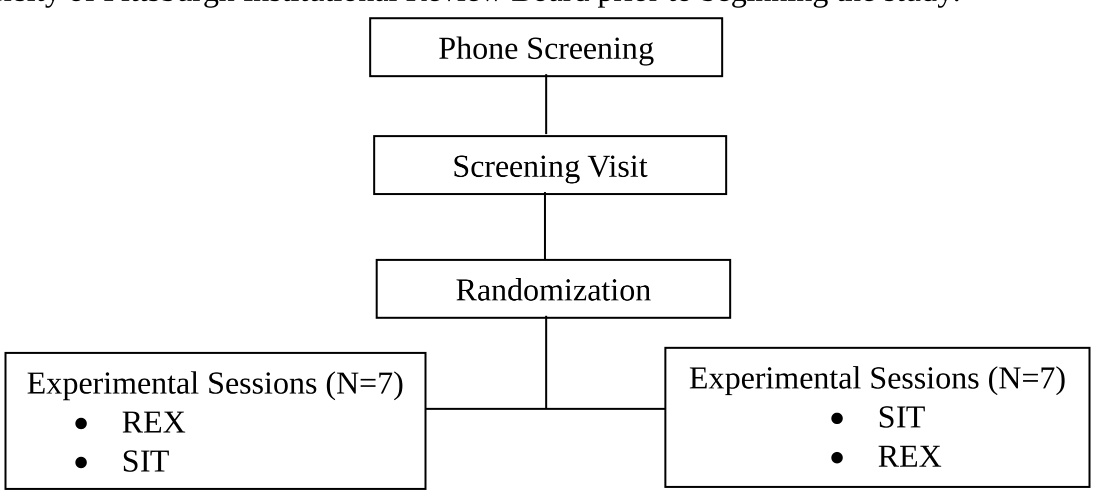


Figure 6. Study Flow Chart

3.3 SCREENING ASSESSMENT PROCEDURES

Complete screening assessments were conducted prior to any experimental procedures and occurred at the University of Pittsburgh Physical Activity and Weight Management Research Center. Subjects reported to the lab after abstaining for at least 4 hours from food, caffeine, nicotine and any drink (except water) and for at least 12 hours from alcohol and moderate-to-vigorous intensity exercise. Order of screening was as follows: blood pressure, height, weight, BMI, and waist circumference. All measures required duplicate measurements and were repeated for a third time if first two measures differed by a pre-determined range (described below) with the closest two measurements being used. If all three measures were equally separated, measurements were continued until two measures fell within an acceptable range. For female participants, questions regarding the timing of their menstrual cycle were asked to determine window of follicular and ovulation phases for scheduling purposes. Metabolic processes, such as insulin sensitivity, are altered during the luteal phase of the cycle which could influence the study outcomes.[138] Standardizing the phase when subjects participated removed the influence menstrual cycle changes on our metabolic outcomes. Thus, all women participated between days 1-14 of their menstrual cycle.

3.3.1 Blood pressure and heart rate

Initially, the appropriate cuff size for blood pressure measurements was determined. First, the arm circumference was measured halfway between the olecranon process and the acromion process on both the left and right arm and using a Gulick tape measure to standardize tension between measurements. A third measurement was taken if the first two measurements differed by more than 0.5 cm. See Table 4 for the selection of the appropriate cuff sizes.

Table 4. Blood Pressure Cuff Size Based on Arm Circumference

Arm Circumference	***Cuff Size***
24.0 to <33.0 cm	*Adult*
33.0 to <41.0 cm	*Large Adult*
≥41 cm	*Thigh*

Following a 10-minute rest period in a comfortable, seated position with feet flat, legs uncrossed, and arms supported at chest level, blood pressure was obtained using an automated blood pressure machine once on both arms in successive order. A second measurement was repeated on the arm will the initial higher blood pressure after an additional 1-minute rest. The two measurements taken on the same arm were recorded and averaged. A third measurement was taken if the first two differed by more than 10 mmHg for systolic blood pressure or 6 mmHg for diastolic blood pressure. Heart rate was measured at the same time as blood pressure and was averaged across measurements. All blood pressure and heart rate measures were obtained using the Omron HEM-705 automated blood pressure machine that has been validated for use in clinical settings and variety of populations.[73,139]

3.3.2 Height, weight and body mass index

Height was measured using a wall-mounted stadiometer (Perspective Enterprises, Portage, MI) with no shoes on and to the nearest 0.1 cm. Two measurements were taken and averaged. If the first two measurements of height differed by more than 0.5 cm, a third measurement was taken or until two measures were within an acceptable range.

Body weight was measured using a calibrated Tanita WB-110A digital scale (Tanita Corporation, Arlington Heights, IL) while the subject was in lightweight clothing and without shoes. Measurements were taken to the nearest 0.1 kg and measured twice and averaged. A third measurement was taken if the first two differed by more than 0.2 kg or until two measures were within an acceptable range. Body mass index (BMI) was calculated as the body weight in kilograms divided by height in meters squared (kg/m^2) with both the averages of height and weight used in the analysis.

3.3.3 Waist circumference

Waist circumference was measured using a Gulick measuring tape and the method used in National Health And Nutrition Examination Survey (NHANES) data collection.[140] Measurements were taken on the right side of the body immediately above the most superior segment of the iliac crest. Measurements were taken to the nearest 0.1 cm twice and averaged. A third measurement was obtained if the first two were not within 1.0 cm or until 2 measures were within an acceptable range.

3.4 EXPERIMENTAL DESIGN

This study used a randomized crossover design. Eligible subjects reported to the lab for two experimental sessions following the initial screening visit. Experimental visits took place at least two days apart, but no greater than 14 days apart, and were approximately five hours long. For female participants, information collected during the screening visit regarding their menstrual cycle was used to determine the appropriate window (follicle phase; days 1-14) to schedule both experimental visits.

3.4.1 Experimental sessions

3.4.1.1 Prolonged sitting condition (SIT)

Subjects reported to the lab after abstaining from food, nicotine and caffeine for 12 hours and alcohol and exercise for 24 hours. Adherence to these instructions was verbally confirmed. Following a 10-minute rest, individuals underwent testing of blood pressure, PWV, triglycerides, and glucose. Subjects were then given a standardized breakfast (for macronutrient and calorie content) consisting of approximately 30% of their daily caloric need (55% carb 35% fat 10% protein) using the Harris-Benedict equation.[141] An identical meal was provided for both conditions. Water and necessary bathroom breaks were allowed ad libitum, but measured and tracked for comparison between conditions. Prior to starting a 4-hour work period, participants completed measures of physical discomfort, mental and physical fatigue, and sleepiness. During the uninterrupted 4-hour work condition, participants were provided access to an internet-connected computer to complete their own work in a seated position. During the work session, subjects were tested hourly for each of the following outcomes: blood pressure, triglycerides, glucose, physical discomfort, fatigue, and sleepiness. Ten minutes prior to hourly outcome measurements, activity was standardized to only reading to remove any influence that could be introduced by subjects engaging in different tasks (typing vs phone call vs reading). Subjects were asked to bring their own reading materials or were provided reading materials such as a magazine. PWV measures were obtained again at the end of the condition.

3.4.1.2 Resistance exercise breaks condition (REX)

The REX condition followed a similar protocol to the SIT condition. Subjects reported to the lab after abstaining from food, nicotine and caffeine for 12 hours and alcohol and exercise for 24 hours. Adherence to these instructions was verbally confirmed. Following a 10-minute rest, individuals underwent testing of blood pressure, PWV, triglycerides, and glucose. The subjects were then given the standardized breakfast as in the SIT condition. Water and necessary bathroom breaks were allowed ad libitum and were recorded. The subject then began with measures of physical discomfort, mental and physical fatigue, and sleepiness followed by the 4-hour session where they had access to a computer with internet access to complete their own work. Ten minutes prior to hourly outcome measurements, activity was standardized to only reading to remove potential influence. Subjects were asked to bring their own reading material or were provided reading material such as a magazine. End of day PWV was also obtained.

The REX condition differed from the SIT condition by having subjects perform one resistance exercise break every hour (halfway between measurements of outcomes) starting 30 minutes into the session. Subjects were prompted to perform a standardized resistance exercise set during each break. Based on endurance resistance exercise guidelines, subjects performed 2 sets with 15 repetitions, with a rest period of 1 to 2 minutes between sets.[8] Resistance exercises included 1) chair stands with calf raises, 2) desk push-ups, 3) lunges with high knees, and 4) resistance band bicep curls with a high pulls. All breaks were timed and subjects were asked to rate their exertion using the 15 category Borg Scale of Perceived Exertion.[142] A standardized video was used during each exercise break that demonstrated the movement along with appropriate cues. The video also prompted the individuals to begin and end each rep using cues such as “down”, “up” and “rise” to standardize the time under tension for each muscle group. All videos followed a similar pattern with the beginning 1-1.25 minutes providing step-by-step instructions for each exercises with visual demonstrations and safety cues. Next, a metronome set at 45 beats per minute began to help participants maintain a steady pace throughout each repetition while still limiting rest time between repetitions. For each exercise video, time spent exercising (not including the minute rest) is as follows: 1) chair stands with calf raises (2.9 minutes), 2) desk push-ups (2.5 minutes), 3) lunges with high knees (2.9 minutes), and 4) resistance band curls with high pulls (2.9 minutes).

For the chair stands with calf raises, subjects were instructed to stand with feet shoulder width or slightly farther apart and bend at the hip and knees until they were sitting in the chair and then return to standing position. After each chair stand, subjects flowed straight into a calf raise by rising up on the toes and pausing for a moment before returning to the starting position. Study staff instructed subjects to maintain proper positioning throughout the exercise with knees staying behind the toes, back maintaining a straight posture, and heels coming up off the ground at the same height for the calf raises when needed. The only modification allowed for this exercise was to instruct participants to hold on with only 2 fingertips during the calf raise on the desk if balance was an issue with either movement. It was noted if a modification was used. (See Appendix D)

For the desk push-ups, participants were instructed to step 3-4 feet away from the desk and the place both hands firmly on the edge of the desk in line with their shoulders. Subjects bent their elbows until 90 degrees was reached while using the feet as the pivot point for the movement and then return to the starting position. The angle at the shoulder was roughly 45 degrees from the body which kept their elbows from being too close to the body or flared too far out. Subjects were also cued to maintain proper posture during the movement without letting the hips fall out of alignment. Modifications for this exercise were to have the participant step closer to the desk if the movement was too difficult. It was noted if modifications were used. (See Appendix D)

For the lunges with high knees, subjects were instructed to stand with feet shoulder width apart and to step back with one foot at a time and bend at the knee until the thigh of the standing leg was parallel with the ground. Subjects then raised their knee from the ground and stepped forward with the same leg to return to standing position. Once in standing position, subjects used the same leg they stepped back with during the lunge to raise their knee up until their thigh was parallel with the ground and then returned to the starting position to finish the movement. The first set was done on the right leg, with the second set being completed on the left leg. All participants were instructed to hold onto the back of a chair with 2 fingertips for balance but to not grip tightly so to not inadvertently increase upper body muscle activation. Modification for this exercise was to not go down as far in the lunge if the participant was unable to return to a standing position. It was noted if modifications were used (See Appendix D)

For the bicep curl with high pull, subjects were instructed to stand with feet shoulder with apart and to hold the resistance band in both hands while the middle of the band was under their feet. Subjects were instructed to curl both arms at the same time with elbows anchored to their sides and starting with arms fully extended until the arms were bent as much as possible, and then returned to the starting position. For the high pull, subjects started in the same position and raised their hands, palms down, toward their chins, bending at the elbow, and until their upper arms were parallel with the ground. Modification for this exercise was to use a less resistive band. It was noted if modifications were used. (See Appendix D)

Table 5 outlines each of the study conditions with timing of measurements and resistance breaks. Outside of instructing the participants to partake in resistance exercise breaks or to complete measurements of study outcomes, participants were allowed to engage in any activity that was work related, as long as they remained in a seated position.

Table 5. Study Procedures

	Procedures	***Baseline***	***.5hr***	***1 hr***	***1.5 hr***	***2 hr***	***2.5 hr***	***3 hr***	***3.5 hr***	***4 hr***
SIT	***Outcome measures***	■		■		■		■		■
	Exercise									
REX	***Outcome measures***	■		■		■		■		■
	Exercise		■		■		■		■	

3.5 EXPERIMENTAL ASSESSMENT PROCEDURES

Experimental measurements were obtained for both visits at baseline and at the end of each hour totaling five assessments per session. All assessments were done at the University of Pittsburgh Physical Activity and Weight Management Research Center. At baseline, measurements of blood pressure and heart rate, blood glucose, blood triglycerides, and ratings of physical discomfort, sleepiness and mental and physical fatigue were taken following a 10-minute seated rest and arterial stiffness via PWV following a ten minute supine rest. These measurements were repeated after the 1st, 2nd, 3rd and 4th hour of each experimental visit with the exception of arterial stiffness, which was measured only at baseline and following the 4th hour (Table 5).

3.5.1 Blood pressure and heart rate

Blood pressure was assessed using the Omron HEM-705 automated blood pressure machine. The participants were seated (sitting upright, feet flat on the floor) for at least 10 minutes prior to each blood pressure measurement. Cuff size and the arm used for all measurements were determined during the baseline screening visit and were used during all experimental visits. Two measurements were taken one minute apart at each time point. Heart rate was obtained at the same time as each blood pressure measurement.

3.5.2 Arterial stiffness

Arterial stiffness was assessed as PWV by tonometry. Wave forms were analyzed using the Complior Analyze system (Colson, Les Lilas, France) that calculates PWV using the foot-to-foot method to detect wave speed in arteries. PWV was measured in a supine position with legs uncrossed on an exam table following a ten minute rest. Sensors were placed on the right side of the body for all measurements. Placements of sensors were at the carotid artery, femoral artery, radial artery and posterior tibialis by the medial malleolus to measure arterial stiffness. Intra- and inter-rater reliability of PWV in our laboratory exceeds 90%.

3.5.3 Glucose and triglyceride disposal

Serum glucose and triglycerides were measured hourly during each condition using the Alere Cholestech Analyzer (Cholestech Corporation, Hayward, California). Blood was drawn from the capillary arteries in the finger tips. Site for abstraction was cleaned using alcohol wipes and dried, and then a lancet was used to draw blood. Initial blood was wiped away to allow for a sample to be drawn that does not contain tissue. The blood sample was applied to the machine-specific cartridges that provide values of glucose and triglycerides. This method is widely used for glucose measures and has been tested for reliability for triglycerides with percent bias below 5%.[143] Fingers in use were rotated to ensure safety and limit the possibility of bruising for the participant.

3.5.4 Questionnaires

Subjective ratings of sleepiness, physical discomfort, mental fatigue and physical fatigue were measured at baseline and at the end of the 1st, 2nd, 3rd and 4th hours. Samples of these questionnaires can be seen in Appendices B and C.

Self-reported sleepiness was measured by the Karolinska Sleepiness Scale, which is a 9-point scale ranging from a rating of 1 (very alert) to a rating of 9 (very sleepy, great effort to keep awake, fighting sleep).[144] The study staff displayed the scales to the participant, asked them to rate their sleepiness over the last 5 minutes, and recorded the number the participant reports.

Physical discomfort, mental fatigue and physical fatigue were measured using 100-point visual analog scales from the Physical Discomfort and Fatigue Questionnaire.[145] Physical discomfort was measured for 15 sites on the body from “no discomfort” to “extreme discomfort”. Mental and physical fatigues were measured using a similar 100-point visual analog scale with the anchors of “no physical/mental fatigue” at one end and “extreme physical/mental fatigue” at the other.

A final questionnaire was administered following the REX condition to analyze the acceptability of such programming in a real office setting. This included 6 questions asking about the acceptability of the resistance exercise breaks using 5-point Likert scales as well as an open-ended question (Appendix E). Question about the subject's type of office setting was asked to better characterize the population.

3.6 SAFETY PROCEDURES

Participant safety was monitored throughout both visits. The participant was instructed to report any adverse outcomes during visits that might influence their participation with the study. Furthermore, each resistance exercise break was monitored by study staff to ensure correct form and provide any feedback as required. If participants had any major issues that kept that from being able to complete each resistance exercise, even with slight modifications that did not change the targeted muscles of the exercise, then the study was terminated and the participant was not be asked to perform any more exercise.

3.7 REMUNERATION FOR PARTICIPATION

Participants were compensated $100 dollars for completing the entire study protocol (both visits). If a participant did not complete the study, they were compensated in part for the percentage of participation met. For example, if the participant completed one visit but decided to drop out before the second visit, then they completed 50% of the study, which earned the equivalent of $50, and so forth. One participant was removed following their first visit due to noncompliance to study procedures, so was paid a total of $50.

3.8 STATISTICAL ANALYSIS

Statistical analyses were performed using Stata 14 software (StataCorp LP, College Station, Texas). Statistical significance was accepted at $p \leq 0.05$. Analyses were performed to check for normality of data. If data were not normal, non-parametric tests were performed or the data was logged transformed as appropriate.

Descriptive statistics were calculated to describe characteristics of the sample including demographics, height, weight, BMI, waist circumference, and vascular and metabolic risk factors at rest. RPE across exercises were compared using repeated measures ANOVA to evaluate the presence of any difference. Total area under the curve (AUC) (trapezoidal method) was calculated to describe the postprandial glucose and triglyceride response in each condition. As a sensitivity analysis, net (nAUC) beyond the baseline starting value was calculated by subtracting the product of the baseline value and the time interval from the total AUC. Generalized linear mixed models were used to evaluate the effects of condition (SIT vs. REX) on outcomes. First, if appropriate, a time-by-condition interaction effect was evaluated. If no interaction was present, mixed models evaluated the effect of condition controlling for time, baseline value, sex, age, and condition order. Cohen’s d was calculated to display the magnitude of effect for each variable. A post hoc analysis was completed to evaluate differences between conditions at individual time points using similar linear mixed models restricted to single time points. P values reported from the post hoc analyses are Bonferroni-adjusted to protect against type 1 error.

3.9 POWER ANALYSIS

Sample size was determined using Stata 14 software and with the first outcome of glucose uptake (area under the curve). Based upon the results of a similar study,[21] the standard deviation was 9.5 mmol·h·L-1 and the difference between the continuous sitting and resistance exercise conditions was 9.5 mmol·h·L-1, corresponding to an effect size of 1. To be conservative, and due to the less intense exercise protocol in this study, an effect size of 0.5 was chosen as the minimal detectable difference. Using the effect size of 0.5, with power set at 0.8, a two-sided alpha of 0.05, and a modest correlation within subject of 0.75, it was determined that 14 subjects was needed. We will recruit up to 30 subjects to account for potential stoppage of participation after screening, but will stop recruitment once complete data on 14 subjects is obtained.

4.0 RESULTS

The first aim of this study was to compare the effects of a prolonged sitting condition (SIT) to a resistance exercise break condition (REX) on area under the curve (AUC) of metabolic outcomes (glucose and triglycerides) in working aged adults with increased risk of cardiovascular and metabolic diseases. This was a randomized crossover trial with an acute, 4-hour experimental session in each condition. All study related procedures were conducted at the University of Pittsburgh Physical Activity and Weight Management Research Center (PAWMRC). The results are presented below.

4.1 STUDY PARTICIPANTS

Fourteen (N=14) adults with a mean age of 53.4±9.5 years and a mean BMI of 30.9±4.8 kg/m^2 completed the study protocol. Study participants were 14.3% male and 35.7% non-white. All baseline characteristics are reported in Table 6.

Table 6. Participant Characteristics

CHARACTERISTIC	***MEAN (SD) N=14***
Age (years)	*53.4 (9.5)*
Height (cm)	*165.5 (6.2)*
Weight (kg)	*85.2 (16.6)*
BMI (kg/m^2)	*30.9 (4.8)*
Sex (N, %)	
Male	*2, 14.3%*
Female	*12, 85.7%*
Race	
White	*9, 64.3%*
Black or African American	*4, 28.6%*
Asian	*1, 7.1%*
Waist Circumference (cm)	*97.9 (11.6)*
Occupation (N, %)	
Full-time	*8, 57.2%*
Part-time	*4, 28.6%*
Homemaker	*1, 7.1%*
Unemployed	*1, 7.1%*
Education (N, %)	
Vocational/Training beyond High School	*1, 7.1%*
Some College or Associates Degree	*7, 50%*
College Graduate or Baccalaureate	*4,28.6%*
Masters or Doctoral Degree	*2, 14.3%*
Systolic Blood Pressure (mmHg)	*126.6 (12.3)*
Diastolic Blood Pressure (mmHg)	*79.1 (8.3)*
Resting Heart Rate (beats per minute)	*65.3 (13.4)*

4.2 STUDY RECRUITMENT

A CONSORT diagram is presented in Figure 7. A total of 59 potential subjects responded to the study advertisements with 96.6% consenting to be screened. Of the 57 individuals screened, 25 (43.8%) were initially eligible based upon telephone screening procedures. The two main reasons for ineligibility were not meeting at least 2 of the 3 criteria for elevated cardiovascular or metabolic risk (N=12) and participation in greater than 90 minutes per week of moderate-to-vigorous physical activity (N=12). Eight of the 25 eligible individuals did not schedule in-person screening visits due to lack of interest. Seventeen individuals consented and underwent in-person screening sessions. One person was ineligible due to their blood pressure being above the acceptable range. One individual did not attend their scheduled experimental visits and did not reschedule. The remaining individuals were enrolled in the study. One individual was removed due to noncompliance to study procedures during the first experimental session, resulting in a final sample size for analysis of 14.

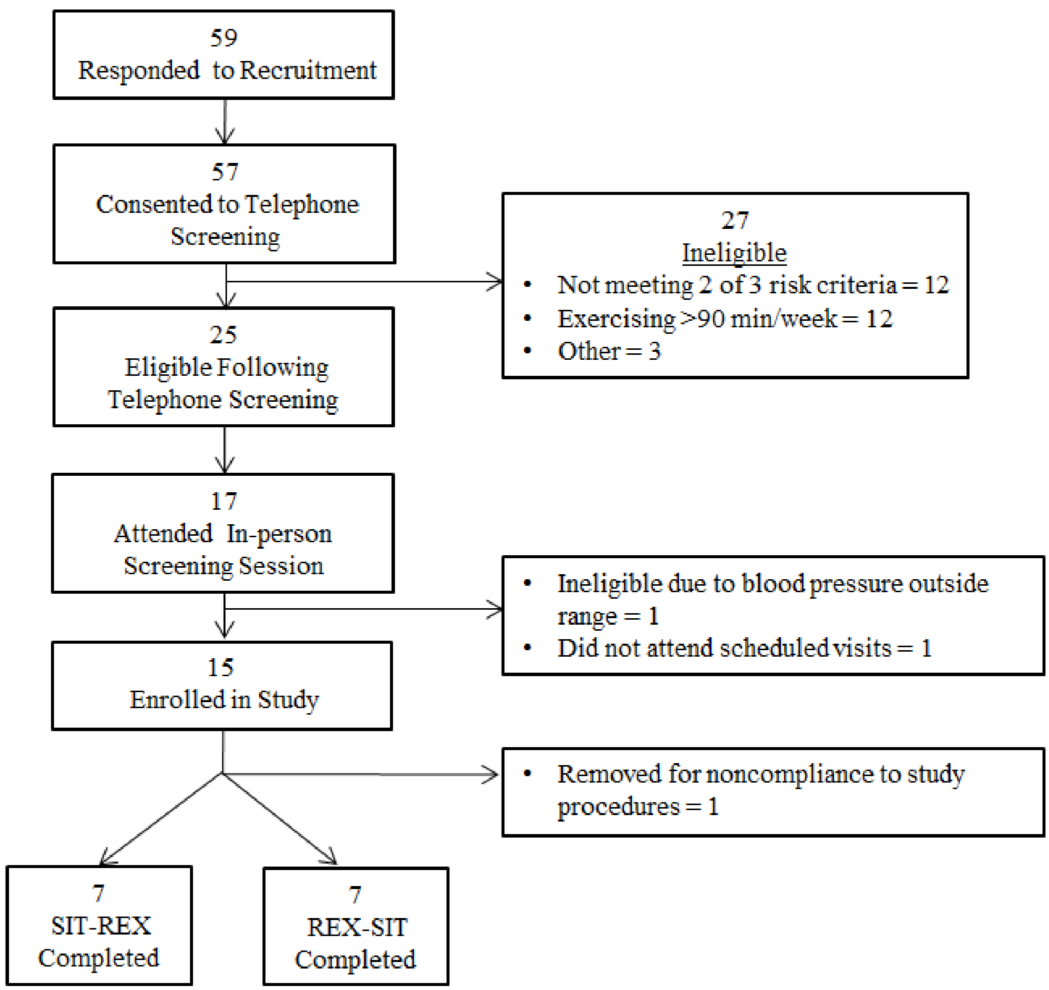


Figure 7. CONSORT Diagram

Water consumption and bathroom breaks were tracked and compared across conditions. There was no statistical difference in either water consumption (14.2 (12.2) oz. in REX vs 16.9 (12.7) oz. in SIT, p=0.571) or bathroom breaks (1.6 (1.2) breaks in REX vs. 1.6 (1.1) breaks in SIT, p=1.000) between conditions. For the REX condition, times to complete exercise breaks as well as rating of perceived exertion (RPE-15 category Borg scale) were tracked. For each break, a timer was started as soon as the exercise break commenced and was stopped as soon as the participant finished the 15th rep of the second set. Averages for each exercise break are reported in Table 7. All participants were able to complete all 15 repetitions for each of the sets during the REX experimental session. Only one modification was taken where one participant performed only a single arm curl paired with a double arm upright row due to wrist pain in one arm. Analysis of RPE using repeated measures ANOVA revealed no statistical difference across exercise breaks (p=0.038.

Table 7. Time to Complete and Perceived Exertion during Breaks

Exercise Break	***Time [minutes, mean(SD)]***	***RPE (6-20)***
Chair Stands with Calf Raise	*5.29 (0.36)*	*10.6 (2.2)*
Desk Push-ups	*3.70 (0.47)*	*12.6 (1.7)*
Lunges with Knee Raise	*5.18 (0.37)*	*11.8 (1.6)*
Banded Arm Curls	*5.20 (0.25)*	*11.4 (2.0)*

4.3 CHANGES IN METABOLIC OUTCOMES

4.3.1 Area under the curve for glucose

Total area under the curve (AUC) was calculated using the trapezoidal method for the 5 time points per condition. Net area under the curve (nAUC) was calculated by subtracting the baseline value multiplied by total time from the total AUC. Figure 8 displays the trajectories for blood glucose levels by condition. At 1 hour following breakfast, postprandial glucose increased in both conditions, with the REX condition's increase being attenuated. Across the subsequent 3 hours, blood glucose returned to baseline and then decreased slightly below baseline levels.

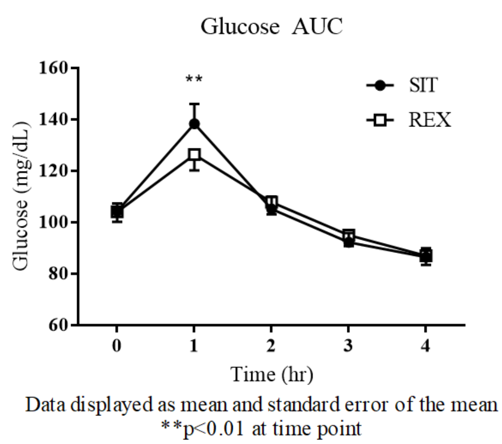


Figure 8. Glucose Response

Linear mixed models demonstrated no statistically significant overall effect of condition on glucose AUC, though the effect size was moderate (β= -6.3 mg/dL, p=0.278, d=0.51). However, post hoc analysis of each time point revealed a significant difference at one hour (β= -12.5 mg/dL, p=0.004, d=1.02) where postprandial glucose was lower in the REX vs. SIT condition by 12.5 mg/dL with a large effect size. A sensitivity analysis of nAUC revealed similar results with no overall effect of condition (β= -5.4 mg/dL, p=0.410, d=.44).

4.3.2 Area under the curve for triglycerides

Triglyceride AUC was also calculated using the trapezoidal method for both total AUC and nAUC. Figure 9 displays the trajectories of triglyceride levels by condition. Triglyceride values were transformed for analysis; Figure 9 displays back transformed means and standard errors of the means for triglycerides to aid in interpretation.

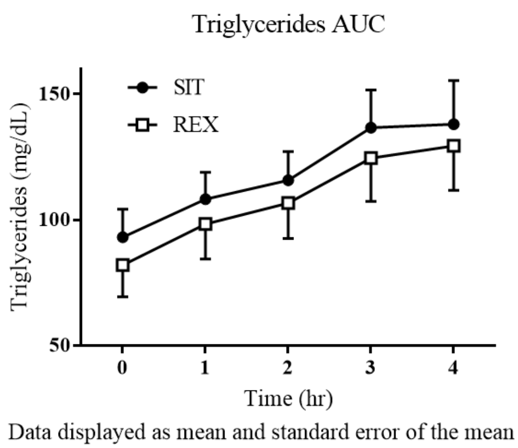


Figure 9. Triglyceride Response

Linear mixed models revealed no overall effect of condition on triglyceride AUC (β= -0.6 log mg/dL, p=0.981, d=0.01). Post hoc analyses of each time point demonstrated no significant difference between conditions. Triglyceride nAUC confirmed similar results to the total AUC with no significant difference between condition (β= -2.3 log mg/dL, p=0.936, d=0.03).

4.4 CHANGES IN CARDIOVASCULAR OUTCOMES

4.4.1 Systolic blood pressure

Blood pressure was measured twice and averaged at each time point. Figure 10 displays systolic blood pressure trajectories by condition. Systolic blood pressure increased from 121 mmHg to 126 mmHg in the SIT condition across the day, while systolic blood pressure increased from 120 mmHg to 122 mmHg across the day.

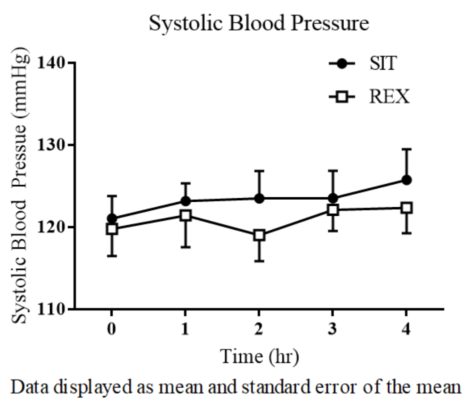


Figure 10. Systolic Blood Pressure Response

For systolic blood pressure, there was no significant overall effect of condition (β= -1.8 mmHg, p=0.102, d=0.13). Even though the effect size was small, systolic blood pressure was reduced in REX by almost 2 mmHg. When analyzed at each time point, no time point was significantly different between conditions.

4.4.2 Diastolic blood pressure

Diastolic blood pressure trajectories are displayed in Figure 11. Diastolic blood pressure decreased then increased across the experimental visits with minimal differences between conditions.

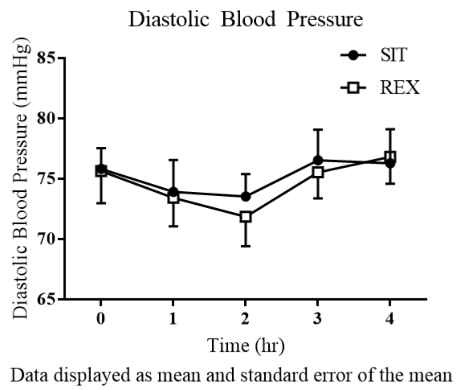


Figure 11. Diastolic Blood Pressure Response

For diastolic blood pressure, there was no significant difference in overall effect by condition (β= -0.6 mmHg, p=0.518, d=0.07). When analyzed at individual time points, no time points were significantly different between conditions.

4.4.3 Heart rate

Heart rate was similarly measured in duplicate each hour and averaged together at each time point for analysis. Figure 12 displays the trajectories of heart rates across each condition. Baseline values were similar, with every hour following higher in the REX condition as compared to the SIT condition. Both REX and SIT conditions followed a similar pattern throughout the conditions with end condition values approaching baseline values.

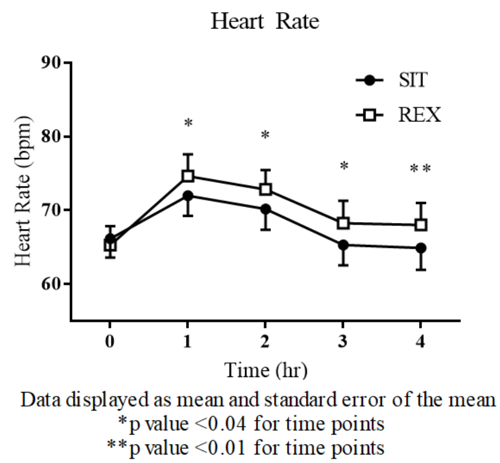


Figure 12. Heart Rate Response

Linear mixed models revealed a significant overall difference between conditions (β= 3.3 bpm, p<0.001, d=0.35). Though highly significant, the difference of increasing heart rate by 3.3 beats per minute had only a small-to-moderate effect size. When further analyzed for each time point, hour 1 (β= 3.2 bpm, p=0.044, d=0.34), hour 2 (β= 3.4 bpm, p=0.032, d=0.36), hour 3 (β= 3.5 bpm, p=0.024, d=0.37), and hour 4 (β= 4.2 bpm, p=0.008, d=0.45) were all significantly different with small-to-moderate effect sizes.

4.4.4 Pulse wave velocity

PWV was measured at baseline and at hour 4 for each condition. At both baseline and end of the day, multiple scans were taken and averaged for analysis.

4.4.4.1 Carotid-femoral pulse wave velocity

Figure 13 displays the cfPWV response in each condition. For both conditions, cfPWV remained fairly consistent. Linear mixed modeling revealed that there was no statistically significant overall effect by condition (β= 0.14 m/s, p=0.497, d=0.09). The effect size was small with a slight, nonsignificant increase in REX by the end of the day as compared to SIT.

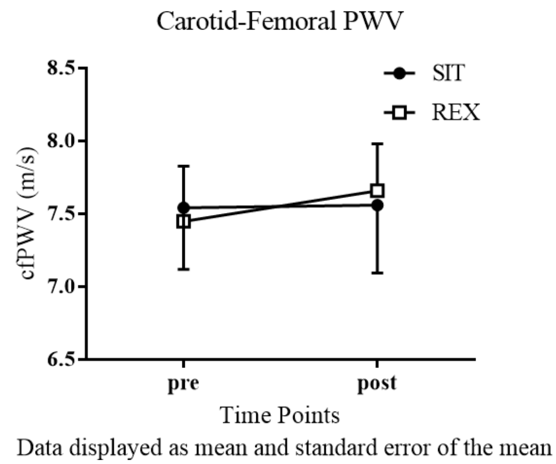


Figure 13. Carotid-Femoral PWV Response

4.4.4.2 Carotid-radial pulse wave velocity

Figure 14 displays the crPWV response to each condition. For both conditions, crPWV remain fairly consistent. Linear mixed modeling revealed no statistically significant overall difference between the REX and SIT conditions (β= 0.05 m/s, p=0.888, d=0.04).

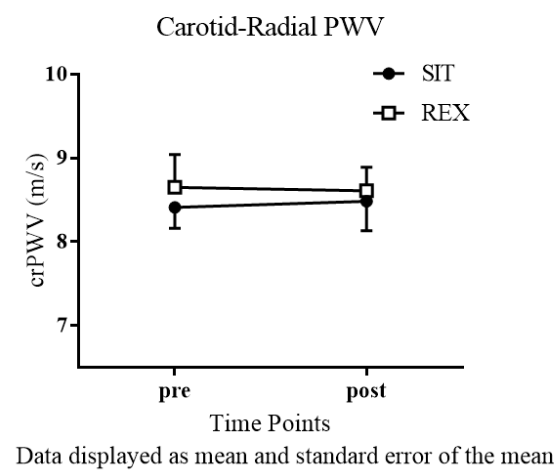


Figure 14. Carotid-Radial PWV Response

4.4.4.3 Carotid-Ankle pulse wave velocity

Figure 15 displays the caPWV response to each condition. For both conditions, caPWV remained fairly consistent. Linear mixed modeling revealed no statistically significant overall difference between conditions (β=0.25 m/s, p=0.271, d=0.21). The magnitude of change was small with slightly lower caPWV in SIT, but not statistically significant.

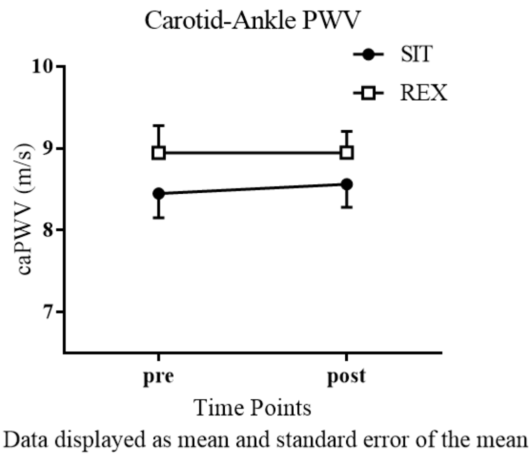


Figure 15. Carotid-Ankle PWV Response

4.5 RATINGS OF DISCOMFORT, FATIGUE, AND SLEEPINESS

4.5.1 Physical discomfort

Overall discomfort was analyzed by averaging the 15 sites across the body for each of the time points. Figure 16 displays the response for overall discomfort (log transformed) by condition. Though there were no significant differences across conditions at baseline, discomfort was higher at the beginning of SIT and increased throughout the experimental visit. Discomfort in the REX condition increased slightly, then returned back to near baseline value.

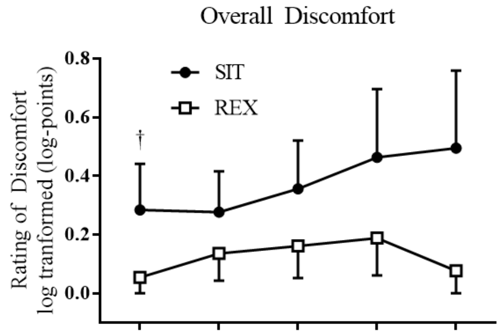


Figure 16. Discomfort Response

Linear mixed modeling revealed no overall statistically significant difference by condition; however, the difference approached significance in favor of the REX condition (β=-0.15 log-points, p=0.074, d=0.34). The effect size was small-to-moderate. When analyzed further by individual time points, baseline differences in REX vs. SIT approached significance (β= -0.22 log-points, p=0.096, d=0.49), but all other time points were not significantly different.

4.5.2 Mental fatigue and physical fatigue

Mental and physical fatigue were measured by single item visual analog scales at each of the 5 time points and compared across conditions. Figures 17 and 18 display the response for both mental and physical fatigue (both log transformed), respectfully, by condition. Mental fatigue for the SIT condition started slightly higher than the REX condition (not statistically significant) and both conditions remained fairly stable throughout the experimental visits. For physical fatigue, baseline values were similar with the SIT condition increasing throughout the visit and the REX condition remaining similar to the baseline value.

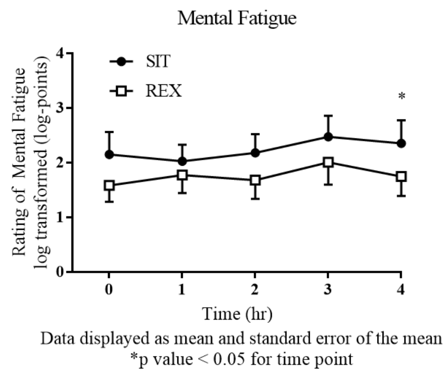


Figure 17. Mental Fatigue Response

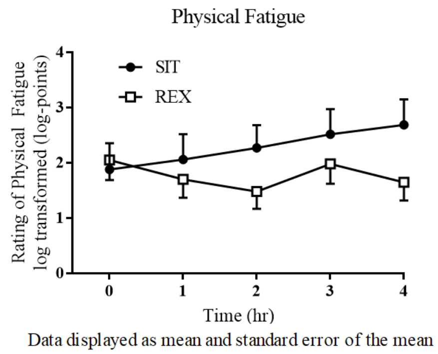


Figure 18. Physical Fatigue Response

Linear mixed modeling revealed that there was no statistically significant overall effect by condition on mental fatigue (β= -0.23 log-points, p=0.116, d=0.18). This is a small effect size in favor of mental fatigue being lower in the REX condition but not statistically significant. However, when analyzed by individual time point, hour 4 revealed a statistically significant difference in favor of the REX condition on mental fatigue (β= -0.48 log-points, p=0.020, d=0.37) with a small-to-moderate effect size.

For physical fatigue, linear mixed modeling demonstrated no statistically significant difference in overall physical fatigue by condition, but the effect was approaching statistical significance in favor of the REX condition being lower (β= -0.30 p=0.056, d=0.2). This was a small overall effect size by condition. When analyzed further by time points, no statistical significance was observed for all time points.

4.5.3 Sleepiness

Sleepiness was obtained using a scale from 1 to 9 (with lower numbers being associated with lower sleepiness) at each of the 5 time points. Figure 19 displays the ratings of sleepiness across the experimental visits for both conditions. Ratings start at a similar level and increases slightly across the experimental visit, more so in SIT.

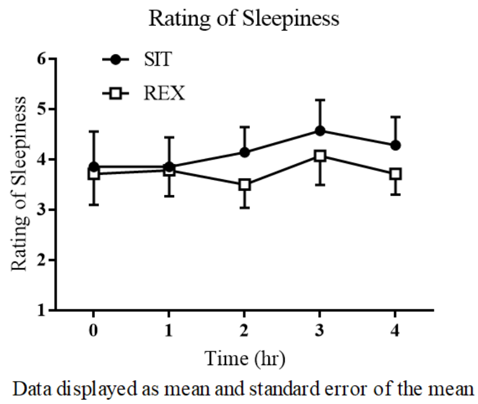


Figure 19. Sleepiness Response

Linear mixed modeling revealed no statistically significant difference between conditions for sleepiness with a small effect size but in favor of the REX condition being lower (β= -0.33 points, p=0.106, d=0.14). Post hoc analysis reveals that no time points were statistically significant between conditions.

4.6 ACCEPTABILITY OF PROGRAM

Participants completed an acceptability questionnaire at the end of the REX condition that consisted of 5 Likert scale-based questions designed to determine the feasibility of the program in the participants' office settings. Table 8 displays the responses to each of the questions as well as participant work environments. Full questions are available in Appendix E. All 5 questions were rated as “high” and “very high” by 55% or more of participants, indicating that the programming would be feasible to implement in a real-world setting. Furthermore, an open ended question asking for potential barriers revealed that 7 out of the 14 individuals reported concerns with being able to adhere to the strict once per hour protocol and would need more flexibility in timing of breaks. Four out of 14 individuals reported space as a potential barrier for implementing such a strategy in their work environment. Other information collected from our participants about their work environment included that 7 out of 14 had salary jobs and 7 out of 14 had hourly pay jobs. Only 2 of the 14 participants billed for their services.

Table 8. Acceptability Responses

Acceptability Questionnaire	*Frequency*	*Percentage*
Question 1: Willingness to Use Program		
Very low	*0*	*0%*
low	*0*	*0%*
Nether low or high	*2*	*14.2%*
High	*6*	*42.9%*
Very high	*6*	*42.9%*
Question 2: Confidence to Perform Exercises Unsupervised		
Very low	*0*	*0%*
low	*0*	*0%*
Nether low or high	*0*	*0%*
High	*7*	*50%*
Very high	*7*	*50%*
Question 3: Willingness to Perform in Front of Coworkers		
Very low	*0*	*0%*
low	*1*	*7.2%*
Nether low or high	*3*	*21.4%*
High	*7*	*50%*
Very high	*5*	*35.7%*
Question 4: Willingness to Perform in Front of Supervisor		
Very low	*0*	*0%*
low	*1*	*7.2%*
Nether low or high	*5*	*35.7%*
High	*5*	*35.7%*
Very high	*3*	*21.4%*
Question 5: Is Frequency and Amount Feasible		
Very low	*0*	*0%*
low	*3*	*21.4%*
Nether low or high	*2*	*14.3%*
High	*7*	*50%*
Very high	*2*	*14.3%*
Office Type		
Private office with door	*4*	*28.5%*
Private office with no door	*1*	*7.2%*
Shared private office with door	*2*	*14.3%*
Shared large room with desk	*4*	*28.5%*
Shared large room with cubicle	*1*	*7.2%*
Classroom	*1*	*7.2%*
Other (field/traveling)	*1*	*7.2%*
Job Type (*1 participant refrained from reporting,% out of N=13)*		
Patient advocate	*1*	*7.7%*
Video analyzer	*1*	*7.7%*
Environmental inspector	*1*	*7.7%*
Administrator	*2*	*15.4%*
Field interviewer	*1*	*7.7%*
Research coordinator	*1*	*7.7%*
Manager	*3*	*23.0%*
Office assistant	*1*	*7.7%*
Therapeutic staff support	*1*	*7.7%*
Consultant	*1*	*7.7%*

5.0 DISCUSSION

This study was conducted to compare the effectiveness of resistance exercise activity breaks to prolonged sitting to improve acute cardiometabolic parameters in a workplace setting in adults who were at increased cardiometabolic risk. Previous studies have demonstrated acute benefits of breaking up prolonged sitting with various activity breaks, but only one previous study has used resistance exercises as the mode of exercise. However, this previous study only included lower body exercises, used a frequency of breaks and intensity of exercise that would be difficult to translate to a general population, and only included individuals with type II diabetes.[21] Our investigation aimed to use guidelines-based resistance exercises that targeted the entire body, a more feasible frequency (once per hour), and a more general population at increased cardiometabolic risk, but without overt disease.

This study used a unique, guidelines-based approach for prescribing resistance exercise breaks to prolonged sitting. Our approach as a whole can be considered more feasible than the previous protocol implemented by Dempsey and colleagues that used 3-minute breaks that cycled through 4 lower body exercises (every 20 seconds with no rest) every 30 minutes.[21] The American College of Sports Medicine (ACSM) guidelines state that individuals should engage in resistance exercises that target 8 to 10 major muscle groups for 2-3 sets of 12-15 repetitions each for muscular endurance training.[8] Because the population that was targeted in our study was required to be previously inactive, we used a conservative approach with an endurance training prescription appropriate for beginners. For each exercise, we had a standardized video that prompted 15 repetitions for 2 sets, with a 1-minute rest between sets, to control intensity and the total stimulus of each break. This resulted in an average Borg 15 category RPE scale rating of 11 or "light", which could lend to easy translation to a workplace setting. Furthermore, we only interrupted the deskwork period once per hour in an attempt to improve the feasibility of our protocol for a real-world setting by limiting disruption to work productivity.

5.1 CHANGES IN METABOLIC OUTCOMES

The first aim was to compare changes in glucose and triglyceride AUC between the SIT and REX conditions. We demonstrated that the REX condition was successful at attenuating the postprandial glucose spike 1 hour following a meal compared to SIT (Figure 8, section 4.3.1) but there was no difference in triglycerides between conditions (Figure 9, section 4.3.2). It was hypothesized that the REX condition would have a beneficial influence on both glucose and triglyceride AUC based upon the previous literature using resistance exercises to break up prolonged sitting.[21] Thus, our data adds to literature for a beneficial glucose response but not for triglyceride metabolism.

Breaking up prolonged sitting has been effective at reducing postprandial glucose. Strategies that have been beneficial to glucose disposal include standing breaks,[131,146] walking breaks,[18,146] and resistance exercise breaks.[21] Similar to glucose, triglycerides have also been positively influenced by breaking up prolonged sitting with walking and resistance execises.[19,21] Specific to this study, resistance training is known to be beneficial to the metabolism of both glucose and triglycerides via muscle activation allowing for increased uptake of both fuel sources, thereby reducing levels in the blood.[147,148] Moreover, resistance exercise breaks in a workplace setting have demonstrated an acute beneficial response to triglyceride and glucose outside of a traditional setting for exercise (e.g., a gym) with Dempsey et al., showing a reduction in glucose AUC (147 mg/dL) and triglyceride AUC (34.2 mg/dL).[21] This can be compared to our study demonstrating a nonsignificant overall reduction in glucose AUC (6.3 mg/dL) and almost no difference in triglyceride AUC. However, a significant reduction of 12.5 mg/dL was observed 1 hour following meal consumption in our study, which can be considered clinically meaningful if changing some from diabetic to pre-diabetic or pre-diabetic to normal. Even though this change is small, this slight reduction over time if accumulated day to day can result in less time exposed to higher blood glucose levels and potentially less risk of disease development. Our smaller result for glucose and lack of effect on triglycerides likely reflects our less intense protocol, healthier population free of type II diabetes (though still with increased cardiometabolic risk), and the fact that our protocol was only 4 hours compared to their 8-hour protocol. Our current study suggests that a more feasible approach that is also in line with current recommendations for resistance training by the ACSM[8] is a sufficient stimulus to achieve glucose (1 hour following a meal), though not triglyceride, benefits.

Previous research has shown that resistance exercise increases lipoprotein lipase activity, which is responsible for the breakdown of triglycerides and other lipids in the body.[32] Higher sedentary behavior is associated with higher triglycerides levels,[125] so it is reasonable that breaks in sedentary behavior would reduce triglyceride levels. We hypothesize a few reasons why our intervention did not cause a reduction in triglyceride AUC. First, an insufficient stimulus might be the reason why triglycerides were not reduced with resistance exercise breaks in our study. Another reason we may have not seen a difference is that we did not specifically recruit individuals with elevated triglyceride levels. Our participants had an average fasting triglyceride level of 102 mg/dL, which is well within the normal range (<150 mg/dL). Therefore, it is possible the room for improvement was limited. It is also possible that our small sample size limited our ability to detect a significant difference. Lastly, if we continued the protocol across the entire day (instead of 4 hours), we might have observed an effect of the REX condition on triglycerides compared to prolonged sitting.

Research has demonstrated that exercise can influence blood glucose levels and this effect depends mainly on the intensity and duration of exercise.[149,150] This is due to two defined pathways that stimulate glucose uptake by the muscles: insulin-dependent and insulin-independent.[151] Both pathways cause activation of the GLUT4 pathway, allowing for individuals to maintain appropriate blood glucose levels by muscle contractions that stimulate GLUT4 translocation by activation of the 5'-AMP-activated protein kinase separately from insulin activation.[152,153] This holds true for both aerobic and resistance exercise, even in individuals with impaired insulin sensitivity.[154-157] In our study, we observed a reduction in postprandial glucose level of 12.5 mg/dL one hour after meal consumption compared to the SIT condition and an overall difference in glucose AUC of 6.8 mg/dL across the 4-hour period. Sedentary behavior interventions utilizing standing evaluated the influence on postprandial glucose and have found reductions in glucose AUC of 14.4-32.4 mg/dL.[131,146] These studies used strategies that had individuals stand for 5 minutes every 30 minutes or alternate sitting and standing every 30 minutes. Studies that used light-to-moderate walking to break up sedentary time found differences in glucose AUC ranging from 27.4-30.5 mg/dL.[18,21,146] For the walking breaks, participants were asked to complete 2 minutes of walking every 20 minutes or 5 minutes every 30 minutes. It should be noted that these other studies utilized study protocols at least 1 day in length and up to 5 days compared to our 4-hour protocol, which could partially explain our lower absolute findings.

Another finding of our study was the statistically significant increase in blood glucose at hour 3 for the REX condition. This reflects an extended glucose disposal period postprandial, but still in the context of the attenuated spike 1 hour following the meal. This indicates a more consistent blood glucose level which reflects better metabolic function and would be healthier for the arteries compared to higher fluctuating blood glucose levels found in the SIT condition.[158]

Overall, our guidelines-based resistance exercise breaks attenuated the postprandial glucose response with no influence on triglyceride response. Though both conditions returned to baseline values or lower by the end of the experimental period for blood glucose, the importance of the spike attenuation and less fluctuation in blood glucose levels should be highlighted as important for reducing the risk of complications from elevated blood glucose levels.

5.2 CHANGES IN CARDIOVASCULAR OUTCOMES

5.2.1 Blood pressure and heart rate

Secondary aims of this study were to compare the effects of REX vs. SIT on blood pressure and heart rate. For both systolic blood pressure and diastolic blood pressure, no significant differences were found between conditions. However, systolic blood pressure was approaching significance in favor of REX for an overall difference between conditions as well as for hour 2 in particular. For heart rate, an increase was observed in both conditions with REX increasing significantly higher than the SIT condition across the experimental condition.

Previous research on the impact that reducing sedentary behavior can have on cardiovascular outcomes has found that even standing breaks can be beneficial to workday blood pressure.[159,160] A previous study from our laboratory demonstrated a significant reduction of 1 mmHg in diastolic blood pressure while alternating between sitting and standing every 30 minutes over a simulated workday.[160] Further, several studies have found that using walking or cycling breaks to reduce prolonged sitting results in a reduction in systolic blood pressure of 2-12 mmHg and diastolic blood pressure of 2-16 mmHg.[22,37,159] Related to this study is the impact that resistance exercise breaks can have on blood pressure. Dempsey and colleagues observed a statistically significant reduction in blood pressure during the resistance condition of 12 mmHg for systolic blood pressure and 8 mmHg for diastolic blood pressure compared to a sitting condition in adults with type II diabetes.[22] Our results were not statistically significant and were smaller in magnitude, with reductions in systolic blood pressure of 2 mmHg and diastolic blood pressure of 0.5 mmHg for the REX condition. The discrepancies in results between studies could be due to the lower frequency and intensity of exercise breaks in our study. As mentioned previously, their study was a full day with 3-minute exercise breaks every 30 minutes as opposed to our protocol over 4 hours with hourly breaks. The previous study from our lab using standing to break up sedentary behavior observed similar and more modest results as this study, used a similar population to our study (increased risk of cardiometabolic disease)[160] and did not actually have the presence of disease (type II) as Dempsey et al.'s population had.[22]

We speculate that a lower blood pressure when interrupting prolonged sitting with resistance breaks could be due to an inhibition of physiological mechanisms that increase blood pressure, however other mechanism could be influencing this change. One method we propose is the suggestion that prolonged sitting leads to reduced blood flow in the legs as a result of lack of muscle pump activation and gravity.[161-163] This pooling causes decreased renal profusion pressure,[163] leading to renin secretion,[164] that then could activate the renin-angiotensin-aldosterone (RAAS) system and result in increased blood pressure. Another possible mechanism is that prolonged sitting leads to increased sympathetic activity[22] which also influences the RAAS system.[165] This influence can lead to a prolonged activation of the RAAS system, leading to an extended increase in blood pressure.

Heart rate was significantly higher in the REX condition compared to SIT with all times points following baseline showing a significantly higher heart rate. Our results are consistent with other studies that have broken up prolonged sedentary time finding no difference or a slight increase in heart rate.[22,160] This response to exercise is expected with increases in heart rate likely resulting from the need to meet the demand of the workload (exercise). Possible explanations for the significantly higher heart rate in our study during the REX condition could be lower musculoskeletal and cardiorespiratory fitness levels in our population that was specifically inactive based on our inclusion criteria. Individuals with lower cardiorespiratory fitness typically have a longer heart rate recovery period following exercise to return to resting values.[166] However, it should be noted that other mechanisms could be influencing this response and our proposed mechanism is not in action alone. Future studies should investigate the effect of resistance exercise breaks on heart rate in more fit populations and over time.

5.2.2 Pulse wave velocity

PWV was measured at the beginning and end of each session including cfPWV, crPWV, and caPWV. cfPWV is a measure of central stiffness and crPWV and caPWV are measures of peripheral stiffness. All three measures had no significant differences between conditions.

PWV is a marker of arterial stiffness, which is a slow developing condition that can take years to change.[75] However, changes in PWV in an acute setting could reflect improved endothelial function, another important aspect of vascular health and not necessarily stiffness of the arteries.[167] Endothelial function derives from the bioavailability of vasodilators, such as nitric oxide.[168] Typical response of PWV to increased vasodilators would be to decrease due to decreased stiffness of the arteries. Another possible mechanism of PWV changes is that prolonged sitting is thought to lead to reduced blood flow, creating blood pooling, and lack a of venous return due to skeletal muscle pump.[161-163] Decreased venous return can eventually lead to activation of the RAAS that would subsequently increase vasoconstriction and result in increased PWV. However, we did not observe improved PWV in REX compared to SIT, so it is possible that our stimulus was not sufficient to cause an increase in vasodilators or to counteract the effects of blood pooling. It should be noted however, that other mechanisms could be in play and the ones suggested here are not the only ones with influence on the results.

This is the first study, to our knowledge, that measured the effects of resistance exercise breaks compared to prolonged sitting on PWV. However, in our laboratory, we evaluated differences in PWV between a prolonged sitting condition vs. a condition that alternated between sit and stand every 30 minutes. We found no significant difference in cfPWV, but did reveal a decrease in peripheral PWV measures in the sit-stand condition with significant decreases in caPWV.[160] Compared to the current study, where we saw no changes in all three PWV measures, differences in results could be due to the frequency and amount of breaks. The previous study involved 30 minutes of standing every half hour over a full workday as compared to our study that only engaged in exercises that lasted 4-5 minutes and only over a 4-hour period. It is possible our stimulus was not enough to induce significant changes in our population.

In conclusion, breaking up sedentary behavior every hour for 4 hours with resistance exercises did not reduce central or peripheral PWV. More research is needed to establish whether interrupting sedentary behavior with resistance exercise can chronically improve PWV.

5.3 CHANGES IN RATING OF DISCOMFORT, FATIGUE, AND SLEEPINESS

5.3.1 Discomfort

Overall ratings of discomfort were not significantly different between conditions. However, when controlling for baseline values, a benefit to discomfort with lower values in REX compared to the SIT conditions was approaching significance (p=0.074). It should be noted, though, that the baseline discomfort level in REX was slightly lower than SIT and this difference was also approaching significance (p=0.096). Though we statistically controlled for baseline values, this could have influenced the results.

Prolonged sitting is associated with several negative health outcomes including increased musculoskeletal discomfort.[169] In the United States, the total cost of discomfort, including the loss of productivity, is estimated to be between $560 and $635 billion per year.[170] Roughly 100 million people suffer from back discomfort in the United States.[171] Since a large proportion of waking time can be spent at work, the occupational environment is an important area to target.

Previous research has demonstrated that exercise can have a beneficial impact on discomfort, especially lower back discomfort.[172] In a work setting among desk-based employees, some studies have found that using sit-stand desks as the intervention for reducing prolonged sitting can reduce musculoskeletal discomfort.[17,47] There are also a few studies that have evaluated the effects of more active breaks on musculoskeletal discomfort with modest beneficial impact; however, these breaks were typically stretching[173] and did not include resistance exercise training. To our knowledge, our study is the first to analyze the impact of resistance exercise breaks on acute musculoskeletal discomfort at multiple time points across the entire body using a visual analog scale.

Potential mechanisms for the observed trend in favor of the REX condition reducing overall discomfort are that REX could counteract poor posture that occurs with higher frequency of prolonged sitting. Desk workers who remain seated for prolonged periods of time are avoiding beneficial postural changes that could alleviate pain. This avoidance of postural change can lead tight, inactive musculature, resulting in increased discomfort.[174] Furthermore, performing hourly resistance exercises could lead to variability in postural alignment, allowing for relaxation in spinal compression[175] as well as changing the joint angles in other areas of the body. It should be noted that exercise can also increase endorphin production, and could lead to a better mood and a decrease in pain.[176] However, other mechanisms could be influencing this result.

Overall, using resistance exercises to break up prolonged sitting may be a novel method to reduce acute overall discomfort, but more research is needed to determine the true impact of such an intervention.

5.3.2 Mental and physical fatigue

Both mental and physical fatigue demonstrated no overall statistically significant difference between conditions, but both were approaching significance in favor of the REX condition. For mental fatigue, analysis of specific time points revealed a reduction at hour 2 that was approaching significance (p=0.074) and a significant difference at hour 4 (p=0.005), both in favor of the REX condition. For physical fatigue, analysis of specific time points revealed significantly lower fatigue in REX at hour 4 (p=0.041).

Fatigue is hard to measure as well as compare across studies due to the variety of definitions and methods of measurement.[177] Several studies have reported that sedentary breaks result in reduced fatigue with the use of sit-stand desks to break up prolonged sitting.[17,47] Another study using more active breaks (i.e. walking) also found a beneficial impact on fatigue.[178] Our findings add to these studies with the separation of mental and physical fatigue, allows for a better understanding of how these interventions impact the components of fatigue. Furthermore, other studies have not assessed multiple time points across a simulated work period and our study uniquely describes the time course of fatigue with and without sedentary breaks. Our novel approach allows for a better understanding of the impact that resistance exercise breaks can have on both mental and physical fatigue across a 4-hour work period.

A possible mechanism for decreased fatigue when engaging in resistance exercise breaks is increased blood flow. Engaging in activity breaks allows for musculoskeletal pump of blood throughout the body, helping to circulate blood flow and reduce blood pooling.[179] This could lead to potential increased cerebral blood flow. Furthermore, Exercise has been shown to increase catecholamine and endorphin production, specifically with resistance training.[180] Endorphins play a key role in pain and fatigue management as well as controlling mood and could result in decreased levels of both mental and physical fatigue.[176] This increased endorphin production and increased cerebral blood flow could be associated with reduced physical and mental fatigue, respectfully. Furthermore, physical fatigue can be associated with unchanged body position, such as standing, sitting or repetitive tasks for prolonged periods.[181,182]

5.3.3 Sleepiness

Ratings of overall sleepiness were not different between conditions. Importantly, it can be observed in Figure 19 that the REX condition was not significantly lower throughout the visit ($p=0.106$). Level of sleepiness in the context of a workday has been previously researched, with one study showing that every 60-minute increase in objectively measured sedentary behavior results in a 16% greater chance of feeling unrested during the day and a 22% greater chance of feeling overly sleepy during the day.[183] Furthermore, studies with interventions to break up sedentary time have demonstrated that using sit-stand desks does not negatively affect productivity, a surrogate for sleepiness.[184,185] However, unlike our study that differentiates between sleepiness and fatigue, it should be noted that fatigue and sleepiness are often used interchangeably in previous literature. To our knowledge, this is the first study to evaluate sleepiness in response to resistance exercise breaks.

A possible mechanism for decreased sleepiness could be the attenuation of the glucose spike following the meal. Following any glucose surge, there is compensatory insulin increase to reduce blood glucose levels. In some situations (e.g. metabolic dysfunction) the insulin response can overcompensate and cause a hypoglycemic event. This surge in insulin has been related to increased drowsiness and an inability to concentrate.[186] The attenuation of the glucose spike and subsequent slightly higher glucose 3 hours after the meal that we observed in the REX condition could reflect improved glucose disposal, a decreased insulin response, and reduced subsequent hypoglycemia.[31] Even though this study only observed a 4 hour period, extending the protocol into a full workday could potentially result in an even larger effect as a large increase in sleepiness is known to occur in the afternoon between 1:00-2:00 pm.[187]

In summary, using resistance exercise breaks to reduce periods of prolonged sitting can be potentially beneficial to levels of sleepiness. Further research to determine if this decrease is observed across a full workday, particularly in the afternoon where sleepiness is known to peak, is an area for future research.

5.4 ACCEPTABILITY

Acceptability of our REX program was an exploratory outcome to determine the feasibility of our approach for a more long-term intervention as well to our knowledge the first study to look at the feasibility of resistance exercise breaks. It was hypothesized that, for all Likert scale questions, individuals would report a "4" or "5" indicating a high level of feasibility in a real-world setting. The majority of participants (>50%) indicated a "4" or "5" for all questions, though some lower scores were observed. All 14 participants answered "high" or "very high" when asked to "rate their level of comfort to perform these exercises on your own without direct supervision every hour during your workday" (question 2). The lowest scoring question for "high" or "very high" (57.1%) asked the participants to "rate your willingness to perform these exercises in front of your supervisor" (question 4). This result potentially indicates that similar programs should gain approval and support from supervisors/management before implementation to facilitate employee participation while limiting barriers.

A major challenge in workplace activity interventions is designing programs that are not disruptive to the workday but still allow a meaningful benefit to occur from the intervention. The rise in popularity of sit-stand desks as well as more active treadmill/bike desks helps decrease the disruptiveness of such breaks by allowing the individual to continue work. However, these devices may be difficult to implement in a large company due to space restrictions and associated costs. Another alternative is to take walking breaks, but again, this takes employees away from their workspace, requires space to walk, and may depend on weather. Implementing resistance exercises that can be done at the desk with minimal equipment is an inexpensive intervention that allows for a quick return to work. Furthermore, all exercises done in this intervention were performed in a roughly a 1 by 2 meters space, suggesting this strategy could be implemented even if space is minimal.

Our biggest interest with this protocol was the feasibility of the program and if the participants perceived the frequency and intensity to be acceptable for individuals to carry out over a longer duration. In regards to the previous study done by Dempsey et al., a 3-minute break every 30 minutes is likely too disruptive to the workday and could therefore create a barrier to long-term adherence. Although we did not measure long-term adherence, it is reasonable to hypothesize that a program such as ours that uses breaks only once per hour would be more feasible to implement. 64.3% of participants in our study reported “high” or “very high” for “do you feel the frequency and amount of resistant exercise breaks is feasible for you to complete on a day to day basis.” This demonstrates that about 35% of the subjects thought this protocol was not as feasible, so steps should be taken to design a strategy that can be manipulated to fit the schedules of more individuals. However, adherence in a long-term study using hourly resistance breaks to interrupt prolonged workplace sitting needs to be further studied.

The RPE values in this study ranged from 10.6 to 12.6, which indicates a “light” intensity for the activity. This is lower than the typical intensity of resistance training, which is normally done at higher intensities that correspond to ratings of 13 or “somewhat hard” to 17 or “very hard” intensity categories.[188] Higher intensity resistance training may have led to different results and would be more in line with the intensity than is recommended by ACSM.[8] However, this lower intensity may be more desirable to participants that perform exercises during the work day(i.e. eliminating need to change clothes or shower due to higher intensity exercise). A potential way to increase the intensity of the protocol would be to increase the speed of each exercise or increasing the resistance of the band or adding weight to the exercises to create more of a stimulus. This study used 45 beats per minute to pace each exercise, but all exercises could be done at a faster pace. This, however, may pose potential barriers for performing the exercises during the work day.

5.5 STRENGTHS AND LIMITATIONS

The primary strength of this study is the investigation of a more feasible, recommendations-based program that could reduce prolonged sitting and contribute to meeting recommendations for resistance exercise. Other strengths include the crossover design, multiple time points of measures establishing a time course for several outcomes, use of a standardized protocol including meals and videos for exercises, and increased external validity by allowing participants to engage in their own desk work. The crossover designed allowed for each participant to act as their own control, allowing for high internal validity between conditions and isolation of the intervention effect. Having multiple measures across the experimental visit allows for analysis at each individual time point to better understand the response for each outcome, however, this analysis was post hoc and not specified before the study was initiated. Furthermore, the measures of discomfort, sleepiness, and fatigue are novel outcomes when using resistance exercise breaks. Using standardized videos allowed for better control of the stimulus from the exercise breaks to ensure all subject were consistent in their tempo and time under tension for muscle contractions. While participants had to come into the lab facility and were not in their own work environment, participants were allowed to bring their own work while having access to a computer with internet access. This allowed participants to be able to do the work that they typically do, which increases the generalizability of subjective outcomes (e.g., discomfort and fatigue) and the acceptability questionnaire.

This study also has limitations. First, we had a small sample size which could have resulted in type II errors for several outcomes that were approaching statistical significance. Another limitation is the use of a point-of-care system to measure the metabolic outcomes. Though not as reliable as a continuous blood draw or newly available continuous glucose monitoring devices, the device we used has been shown to be reliable for these outcomes and is used clinically and for health wellness programs. This method was chosen because it was less invasive than a blood draw, only needing a small sample of blood taken from a finger prick, and this benefit to participant burden outweighed the slightly reduced accuracy. This could have potentially influenced the metabolism results. A third limitation is the length of each visit. Typical workdays last 8-9 hours and cover a lunch period that would likely have a further influence on metabolic outcomes. Also, a full workday would have allowed for 4 more hourly exercise breaks that would line up with the ACSM recommendation of 8 to 10 exercises and possibly impact our outcomes measures on a greater level. A final limitation of this study is the recruited sample. We specifically recruited individuals of higher cardiometabolic risk due to the fact that they have the most room for improvement in the specific outcomes we measured. Though risk factors such as obesity, elevated blood pressure, and prediabetes are common among working adults, these results cannot be generalized to healthier individuals. Finally, it should be noted that these results are acute and would not necessarily translate to long-term health benefits. However, this program is promising and should be investigated in such a scenario.

5.6 FUTURE DIRECTIONS

Though this study adds to the literature of sedentary behavior breaks and their benefits, more research is needed in several areas. First, a replication of this study with a larger sample size and over a full workday would be beneficial to determine if the outcomes that are trending towards significance reflect true effects. Another direction would be to implement this protocol in an intervention over weeks or months to determine if prolonged engagement in this program can result in chronic benefits to these outcomes. Along with this, determining the feasibility and adherence to such programming would be of interest for implementation in a real-world setting. Finally, extending this type of programing into various populations would be beneficial to determine if similar benefits would be observed. This population was specifically recruited due to their increased risk of cardiometabolic risk; however, similar programs in other populations (elderly, children, apparently healthy) have the potential to act as a proactive strategy against the development of increased cardiometabolic risk. Moreover, applying this intervention as a treatment strategy in certain related disease states (diabetes, hyperlipidemia, hypertension, or chronic low back pain) is another future direction.

It should also be noted that if this if hourly breaks are not feasible during the work, it would seem most feasible to implement a protocol that at least implements an exercise break following a meal where we saw a response in our primary outcome of glucose. Future studies should compare an hourly break protocol to one that implements a resistance exercise break following meals to examine differences in outcomes. Furthermore, this strategy should be combined with other intervention strategies to break up sedentary time to maximize feasibility and the benefit to health outcomes. ACSM recommends resting 48 hours between working the same muscle groups for resistance exercises, so using this strategy in combination with other strategies during resting days, might be the most effective intervention. This is an area for future research.

5.7 SUMMARY

In summary, this study demonstrated that guidelines-based resistance exercises to break up prolonged sitting once an hour can be effective at reducing postprandial glucose over a 4-hour work period. Furthermore, this protocol demonstrated potential for also reducing acute systolic blood pressure, discomfort, mental and physical fatigue, and sleepiness. Promising ratings of acceptability for this strategy open up the possibility of this program being used long-term and warrant further investigation. These findings inform workplace wellness programs striving to improve employee health and other outcomes such as employee presenteeism. Furthermore, resistance exercise breaks as a strategy to reduce sitting has a potential to impact public health as a translatable intervention with minimal equipment necessary that can be implemented in a variety of settings. Future research on long-term effects and acceptability is needed to better understand the full impact of resistance exercise breaks on health and wellness.

Clinical implications for this study have a potential to be impactful for several health outcomes. Although this acute setting demonstrated changes that have small-to-moderate effect sizes, if this protocol was followed daily and these small changes were accumulated, then the potential impact on these outcomes could result in a more meaningful change and could potentially prevent further disease development.

APPENDIX A

TELEPHONE SCREENING FORM

SCREENING FORM:

1. *Thank you for your interest in our program. My name is __________ and I would briefly like to tell you about this research program.*

2. ***Procedure for Describing the Study and Obtaining Verbal Consent to Conduct the Phone Screen:** A description of the study will be read to participants, and this description includes important components of the informed consent process (see attached script). Individuals who express an interest in participating in this study will be told the following to obtain verbal consent:*
    - ***Investigators Component of Informed Consent:** The REX at Work Study is being conducted by Robert Kowalsky under the mentorship of Dr. Bethany Barone Gibbs at the University of Pittsburgh.*
    - ***Description Component of Informed Consent**: The purpose of this study is to examine whether breaking up prolonged sitting at work with simple resistance exercises during a typical workday has a beneficial effect on blood pressure, stiffness of the blood vessels, and metabolic function when compared to just sitting**.** If you are initially eligible for the study after this phone screening, we will invite you to the laboratory near the University of Pittsburgh Oakland Campus for an orientation visit where the full details of the study will be described to you and you will undergo further screening procedures. It is possible that after this in-person screening session, you may not be eligible to participate in the study. If you are determined to be eligible after the screening visit, you will be asked to complete two experimental sessions, whose order will be randomly assigned. For each experimental session, you will arrive at the laboratory in the morning at about 7:30 AM and stay until about 1 PM. There are no direct benefits to participating in the study, but potential risks could include discomfort while having your blood pressure taken, muscle fatigue from performing exercises, discomfort from having blood samples taken from your finger tip, or a breach of confidentiality for your questionnaires or other information the study collects. Upon the full completion of all study procedures, you will be given up to $100 for your participation. Participation in this study is voluntary and you are free to discontinue at any time.*

    Do you have any questions? Now that you have a basic understand of the study, do you think you might be interested in participating?

    Before enrolling you in the study, I will need to ask you a few questions about your demographic background and questions about your physical health and medical history to determine if you appear to be eligible to participate in this study. It will take approximately 5 minutes to ask you all of the questions. If we complete the interview, I will ask you for some specific information (your complete name, date of birth, and mailing address) so that we can contact you regarding your participation in this study. I will then schedule you to attend a session that will explain all of the procedures of this study in greater detail. Your responses to these questions are confidential, and all information related to your health history or current behaviors that you are about to give me will be destroyed after this interview if you are found to be ineligible. The purpose of these questions is to determine whether you may be eligible to participate in the study. Additional screening at a later time may be necessary beyond answering these questions. Remember, your participation is voluntary; you do not have to complete these questions. Please feel free to stop me at any time if you have any questions or concerns.

Staff member will answer any questions or will defer these questions to the Principal Investigator or Co-Investigator when appropriate prior to proceeding. If the individual would like to think about their participation prior to proceeding with the Phone Screen, they will be provided with the telephone number that they can call if they decide to participate in the future.

Voluntary Consent Component of Informed Consent: *Do I have your permission to ask you these questions?*

> *If "YES" indicate the participant's agreement with this statement on the top of the next page, sign your name and date the form, and then complete the Phone Screen. If "NO", thank the individual for calling and <u>do not</u> complete the Phone Screen.*

<u>Phone Screen Interview</u>

The caller gives verbal permission to conduct the Phone Screen:

_____ *YES* ______ *NO*

Verbal Assent was given to:

____

Staff Member Signature

____

Date Verbal Assent was given:

Eligible based on telephone screening: ☐ *Yes* ☐ *No*

If "No", list reason for ineligibility: ______________________________

____

Discontinue Phone Screen if Participant Does NOT Meet Eligibility Criteria for a Question.

1. *Gender:* ☐ *Male* ☐ *Female*

2. *Age:* ☐☐ ***(18-65 years)***

3. *How tall are you?* ☐ *feet* ☐☐ *Inches*

4. *How much do you weight?* ☐☐☐ *lbs.*

BMI = ☐☐.☐ kg/m^2

(eligible if ≥ 30 kg/m^2)

5. *Are you taking medication to control your blood pressure, lipids, heart condition or blood sugar?* ☐ *Yes* ☐ *No*

6. *Do you remember a blood pressure reading that you've had taken in the past 3 months?* ☐ *Yes* ☐ *No*

If yes, what were the numbers? ☐☐☐/☐☐☐ *mmHg*

(Eligible to continue screening if reported SBP is 115 – 165 mmHg or DBP is 75 – 105)

7. *If no, has a healthcare provider recently told you that you have very low blood pressure?* ☐ *Yes* ☐ *No*
Do you have atrial fibrillation? ☐ *Yes* ☐ *No*

8. *Has a healthcare provider recently told you that you have pre-diabetes?* ☐ *Yes* ☐ *No*

9. *Do you have family history of diabetes? (1st degree)* ☐ *Yes* ☐ *No*

10. *Are you currently being treated for heart disease, cancer, end stage renal disease, or any other serious condition?*
☐ *Yes* ☐ *No If "yes", specify:* ______________________________

11. *Have you had a cardiovascular event or procedure in the past 6 months (such as a heart attack, stroke, bypass surgery, or angioplasty?)* ☐ *Yes* ☐ *No If "yes", specify:* ______________________________

12. *Do you use any prescription or over-the-counter medications regularly?*

Medication name:	*Indication:*

13. *In the past 3 months, how many minutes have you spent exercising in a typical week (aerobic)?*

☐☐☐*min/week* *(≥150 is exclusionary)*

14. *In the past 3 months, how many days have you spent resistance training in a typical week?*

☐☐*days/week* *(≥2 is exclusionary)*

15. *Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?* ☐ *Yes* ☐ *No*

16. *Do you feel pain in your chest when you do physical activity?* ☐ *Yes* ☐ *No*

17. *In the past month, have you had chest pain when you were not doing physical activity?* ☐ *Yes* ☐ *No*

18. *Do you know of any other reason why you should not do physical activity?* ☐ *Yes* ☐ *No*
*If yes, explain*____

19. *Do you smoke?* ☐ *Yes* ☐ *No*

If yes, how many days per week do you typically smoke? ☐☐*days/week (≥4 is exclusionary)*

20. *Do you have any bone or joint problem made worse by exercise?* ☐ *Yes* ☐ *No*

21. *Have you had a recent bout of dizziness or loss of consciousness?* ☐ *Yes* ☐ *No*

If yes, describe: ____

22. *Including currently, have you been pregnant in the past 6 months or nursing in the past 3 months?* ☐*Yes* ☐*No*

23. *Are you currently enrolled in a weight loss program?* ☐ *Yes* ☐ *No*

24. *Would you be able to come to our office on two occasions, about 2-14 days apart, from approximately 7:30 AM – 1 PM?* ☐ *Yes* ☐ *No*

25. *Could you perform 4 hours of job-related or school work on two occasions, about 1 week apart, in our laboratory with desk, a computer and internet connection?* ☐ *Yes* ☐ *No*

26. *Would you be able to abstain from alcohol, nicotine caffeine, and any form of exercise for 24 hours prior to an experimental session at our laboratory?* ☐ *Yes* ☐ *No*

Contact Tracking Form

THIS PAGE IS COMPLETED ONLY IF THE RESPONDANT APPEARS TO QUALIFY FOR PARTICIPATION IN THIS STUDY

Date: ____/____/_____ Staff Member Completing Form: ________________________

Name: ____

Street Address: ____

City: _______________________________ State: ___ Zip Code:_________

Home Phone: ____________________ Work Phone: ____________________

OFFICE USE ONLY:

Eligible: ☐ *Yes* ☐ *No*
Invited to Orientation: ☐ *Yes* ☐ *No*
Date of Orientation:____/____/____

APPENDIX B

KAROLINSKA SLEEPINESS SCALE

Karolinska Sleepiness Scale

Please use the following scale to rate your level of sleepiness during the previous 5 minutes. ***Point*** *to the number that best represents you. Be sure to read all responses before choosing the best fit number.*

Number	*Explanation*
1	*Extremely alert*
2	*Very alert*
3	*Alert*
4	*Rather alert*
5	*Neither alert nor sleepy*
6	*Some signs of sleepiness*
7	*Sleepy, but no effort to keep awake*
8	*Sleepy, some effort to keep awake*
9	*Very sleepy, great effort to keep awake, fighting sleep*

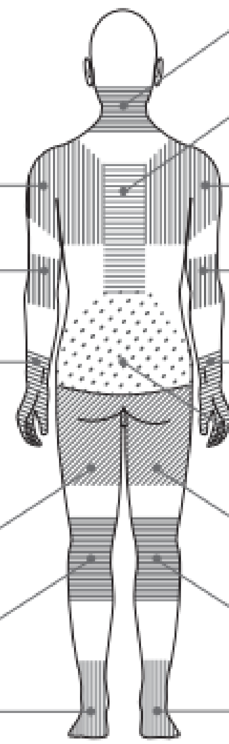
APPENDIX C

PHYSICAL DISCOMFORT AND FATIGUE QUESTIONNAIRE

Discomfort and Fatigue Questionnaire

A **At this point in time, do you have any physical discomfort in your body?** ☐ Yes ☐ No

If **Yes**, please indicate the **amount of discomfort** you feel for each body part by marking on the line corresponding to the body part.



neck	no discomfort ——— extreme discomfort
upper back	no discomfort ——— extreme discomfort
left shoulder	no discomfort ——— extreme discomfort
right shoulder	no discomfort ——— extreme discomfort
left forearm	no discomfort ——— extreme discomfort
right forearm	no discomfort ——— extreme discomfort
left wrist / hand	no discomfort ——— extreme discomfort
right wrist / hand	no discomfort ——— extreme discomfort
lower back	no discomfort ——— extreme discomfort
left hip / thigh	no discomfort ——— extreme discomfort
right hip / thigh	no discomfort ——— extreme discomfort
left knee	no discomfort ——— extreme discomfort
right knee	no discomfort ——— extreme discomfort
left lower leg	no discomfort ——— extreme discomfort
right lower leg	no discomfort ——— extreme discomfort

B **At this point in time, how fatigued do you feel?**

Please mark on the lines below, your level of **physical and mental fatigue.**

How **physically fatigued** do you feel now?

no fatigue ——— extreme fatigue

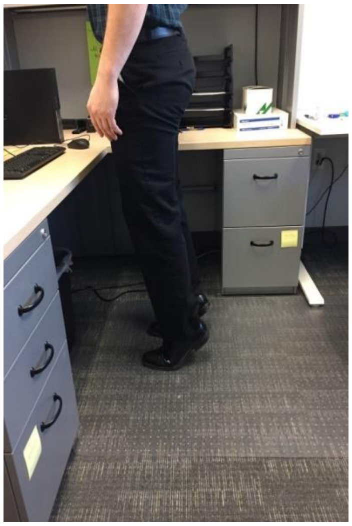
How **mentally fatigued** do you feel now?

no fatigue ——— extreme fatigue

APPENDIX D

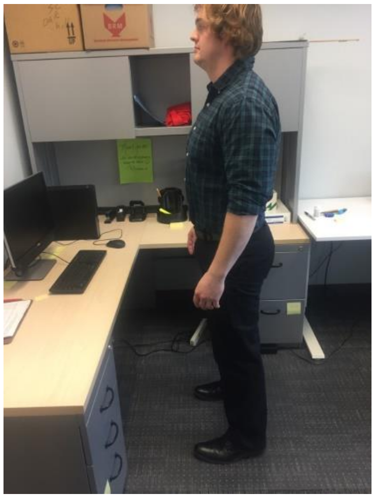
VISUAL DEMONSTRATION OF EXERCISES FOR REX CONDITION

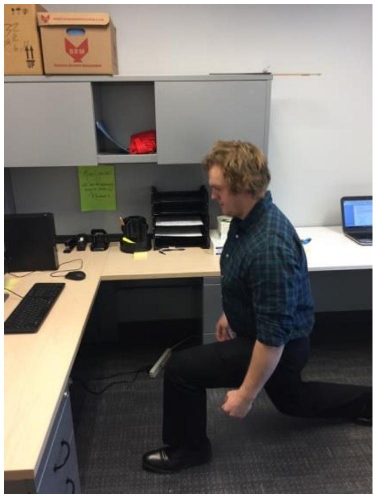
1. Chair stands with Calf Raises

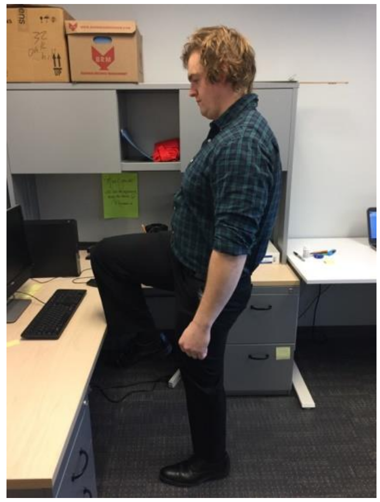


2. Desk Push Ups

3. Lunge with Knee Raise







4. Bicep Curl with High Pull

APPENDIX E

ACCEPTABILITY OF REX AT WORK PROGRAM

Acceptability of REX at Work Program

Please answer the following questions by selecting the number that best represents your ratings of acceptability for the REX at Work program. Each scale ranges from very low all the way to very high.

1. *Please rate your willingness to utilize this program of resistance exercises every hour to break up sedentary time at your own office?*

Very Low	Low	Neither low Or high	High	Very High
○	○	○	○	○

2. *Please rate your level of comfort to perform these exercises on your own without direct supervision every hour during your work day.*

Very Low	Low	Neither low Or high	High	Very High
○	○	○	○	○

3. *Please rate your willingness to perform these exercises in front of your co-workers?*

Very Low	Low	Neither low Or high	High	Very High
○	○	○	○	○

4. *Please rate your willingness to perform these exercises in front of your supervisor?*

Very Low	Low	Neither low Or high	High	Very High
○	○	○	○	○

5. *Do you feel the frequency and amount of resistance exercise breaks is feasible for you to complete on a day to day basis?*

Very Low	Low	Neither low Or high	High	Very High
○	○	○	○	○

6. *What barriers might you face if you tried to perform 1 exercise every hour at work? (Please use the space below to answer)*

Please List the type of job you have (e.g. manager, supervisor, receptionist): ________________

Is your job salary or hourly: ☐ *salary* ☐ *hourly*

Do you bill individuals for your services: ☐ *Yes* ☐ *No*

Please select the description that best applies to your office setting:

_______ *Private office with door*

_______ *Private office with no door*

_______ *Shared private office with door*

_______ *Shared private office with no door*

_______ *Shared large room with desk*

_______ *Shared large room with cubicle*

_______ *Other (please list)* _____________

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