PENNINGTON BIOMEDICAL RESEARCH CENTER LSU

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Approval Includes: **Study and Investigator(s) for an additional continuing review period. This approval expires on the date noted above.**

Clinicaltrials.gov responsibility: **Principal Investigator**

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Investigators and study staff must comply with the Human Research Protection Program policies and procedures that apply to IRB members and staff, which can be found at **www.pbrc.edu/HRPP**

Signed Monday, November 11, 2019 3:36:17 PM ET by Rhode, Paula Ph.D.

# WorkACTIVE-P:
# Multi-component workplace energy balance intervention

# Protocol

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## I. Summary

The purpose of the WorkACTIVE-P study is to assess the outcome of an innovative multi-component intervention focused on increasing energy expenditure and re-balancing the disrupted energy balance equation of sedentary workplaces with an ultimate target of reducing workers' abdominal obesity. The energy expenditure intervention includes replacing workplace sedentary time with access to a dedicated pedal desk and increasing steps/day with wearable monitors. Both components are incorporated into an electronically-delivered behavior monitoring and support infrastructure, thus enabling continuous management. We will utilize pedal desks manufactured and owned by Pennington Biomedical Research Center to conduct this study at Blue Cross Blue Shield of Louisiana, Louisiana State University, Louisiana Office of Technology, Louisiana Healthcare Connections, and Pennington Biomedical Research Center offices in Baton Rouge, LA. 41 individuals will be recruited and randomized to either a control arm or combined Walk More Pedal Desk (WMPD) intervention. Primary (MRI-determined visceral adipose tissue) and secondary (changes in body weight, total adipose tissue, subcutaneous adipose tissue, blood pressure, blood lipids, fasting glucose and insulin, HbA1-c, free-living accelerometer-determined walking, time spent in sedentary behavior, exercise, and dietary intake) outcomes will be assessed at baseline and month 3.

## II. Background and Significance

Low Energy Expenditure/Sedentary Behavior/Weight Gain: Energy balance is a tentative equilibrium between energy intake and energy expenditure.[13] Sedentary behaviors, pervasive in contemporary office-based workplaces,[14] result in lowered energy expenditure, thus disrupting energy balance and contributing to weight gain and attendant chronic diseases (e.g., cardiovascular disease and Type 2 diabetes).[3] Hu and colleagues[15] estimated that the risk in obesity and Type 2 diabetes increases 5-7% for each 2-hour increase in occupational sitting time. As further evidence of the deleterious effects of low energy expenditure occupations on obesity, there has been a trend toward Service Industry occupations that are largely composed of desk-based sedentary behavior over the past 50 years in the U.S., and with it an associated population-level weight gain.[16] The direct[17] and indirect (non-medical)[18] costs of obesity are high. For workers, the overall estimated impact of obesity on lifetime earnings of U.S. men and women born between 1982 and 1993 was close to $1 trillion.[9] The increasing obesity rate was found to be the most important contributor to employers' increased health care spending between 2005 and 2010 (based on data from over 340,000 tracked employees).[19] Further, compared to normal weight employees, overweight and obese workers are estimated to cost employers $201 and $644 more per employee per year, respectively.[20]

Within office-based Service Industry workplaces, the predominant ergonomic theory has promulgated office furniture and environmental design deliberately intended to reduce even token workload demands, resulting in occupational energy expenditures that are near basal requirements.[7] These transitions have also logically shifted the need to obtain adequate amounts of energy expenditure to maintain body weight to a decreasing amount of personal time. Traditional workplace wellness approaches to providing access to fitness facilities and otherwise promoting increased participation in structured exercise outside of work hours have produced modest effects, largely due to "lack of time."

Abdominal Obesity: Workers employed in low energy expenditure occupations (e.g., typists) are 63% more likely to be abdominally obese (>102 cm in men and >88 cm in women) compared to workers in high energy expenditure occupations (e.g., construction trades).[6] Abdominal obesity is considered a driving force behind the metabolic syndrome.[21] A meta-analysis of exercise therapy for abdominal obesity[22] concluded that aerobic exercise is central to intervention, but that even light intensity aerobic exercise, that is below current public health recommendations, may be sufficient for beneficial modification of abdominal obesity. Case in point, John et al.[10] reported an average 5.5 cm waist circumference reduction in 12 sedentary office workers provided dedicated access to treadmill desks (walking at self-selected speeds and durations) for 9 months. Dr. Tudor-Locke, Co-Investigator of **WorkACTIVE-P** has also been an investigator on pedometer-based interventions that have

elicited significant improvements in waist circumference.[1,2] This trial is therefore focused on evaluating changes in the primary outcome of abdominal obesity in sedentary, overweight/obese Service Industry workers exposed to a multi-component energy expenditure intervention that combines dedicated pedal desk use with a step-counting intervention.

Workstation Alternatives: Incipient reports support the feasibility of elevating net energy expenditure by replacing occupational sedentary behavior with low-intensity non-exercise physical activity via "workstation alternatives" to the traditional seated computer-and-desk-based combinations. For example, Edelson and Danoff [23] introduced the feasibility of performing computer-based work while walking on a treadmill in 1989, and Levine and Miller popularized the concept with a publication in 2007 demonstrating its ability to elevate energy expenditure over the seated condition.[8] Dr. Tudor-Locke recently published a systematic review[5] reporting the comparative potential for workstation alternatives (including stability balls, sit-to-stand desks, treadmill desks, and pedal desks) to elevate occupational energy expenditure. Active workstations (i.e., specifically treadmill desks and pedal desks) offer the greatest promise (approximately 2-4 kcal/min compared to 1.2 kcal/min in the traditional seated working condition), but only to the extent that workers find them acceptable, tolerable, and congruent with their primary working tasks and therefore frequently use them for extended periods of time. Dr. Tudor-Locke has recently completed a randomized controlled trial implementing treadmill desks in a real world workplace and have documented a number of challenges to widespread adoption and thus scalability of treadmill desks (recently published[11]). In response to these challenges, we have developed a much more affordable, convenient, integrated and tolerable pedal desk: a semi-recumbent (upright) portable pedal station with a maneuverable and adaptable desktop. Workers are able to complete their tasks comfortably in a more traditional seated position. The cost and size of the device makes it feasible for workers to have their own dedicated pedal desk rather than sharing access (as we have learned, a scheduling and management impediment) to larger and more expensive treadmill workstations.[11] Alternative pedal device designs (notably those that slide under conventional desks) have not yet facilitated extended use in workers,[7] in part because workers "bang their knees" against the desk. Dr. Tudor-Locke's pilot data collection in 10 workers to date indicate that pedal desk use can more than double the energy expenditure of seated computer based work.

Increasing Steps/day with Wearable Step Counters: Steps/day is an increasingly utilized metric for objectively capturing and representing total daily walking.[24,25] Researchers recently reported 5-year changes in body mass index (BMI), waist-to-hip-ratio, and insulin sensitivity related to 1,000 step incremental changes in step-defined physical activity.[26] Meta-analyses indicate that step-counting interventions can expect to realize incremental increases in walking behavior on the order of 2,000-2,500 steps/day. The Co-Investigator of this R21 is a world leader in such interventions.[25,27,28] She developed a self-selected goal approach that elicited up to an extra 4,000 steps/day in individuals with Type 2 diabetes,[2] and was subsequently adapted and delivered as a workplace intervention that elicited a 3,500 steps/day change.[1] As reported in a recent meta-analysis,[29] at least four other controlled workplace studies have incorporated wearable step-counters into multi-component interventions. The inclusion of a pedal desk is novel. No one has previously estimated the relative contributions of independent intervention components to changes in abdominal obesity.

A Combined Approach: Pedaling actions are largely ignored by waist-worn step counters.[30] Therefore, layering a step-counting intervention on top of a pedal desk intervention permits a clear evaluation of their separate and combined dose-response effects. Daily electronic tracking of pedal desk use (duration, rpm, estimated distance and energy expenditure) and steps/day via automatic internet-based software enables continuous tracking of both behaviors for tailored feedback, behavioral shaping, and evaluation purposes. **WorkACTIVE-P** will clearly inform the feasibility of combining these distinct yet compatible components of a workplace multi-component energy expenditure intervention.

Remote Food Photography Method (RFPM) and SmartIntake**:** Use of the Remote Food Photography Method© (RFPM) [1,2] and SmartIntake[SM] smartphone app offers a number of advantages over other methods to estimate food intake. Self-report methods, such as pen-and-paper and dietary recall, rely on the ability of the participant to accurately recall the types and portion sizes of foods consumed, and the accuracy of these methods have been questioned [3,4] [5,6]. Importantly, ~50% of the error in self-report methods is due to participants inability to accurately estimate portion size, a limitation that is avoided when using the RFPM and SmartIntake[SM] app. Additionally, self-report methods result in larger underestimates of food intake for overweight and obese

individuals [5], people tend to selectively underreport dietary fat intake [7], and people tend to under eat during the monitoring period [7,8], which results in data that is not representative of habitual food intake. All of these

limitations are overcome with the RFPM [1], which demonstrates the significance of using this approach in the proposed project.

Research to Practice (r2p): Controlled but simulated environments and artificial constraints are typically implemented in research design to circumvent every conceivable threat to validity. For example, the rate of energy expenditure of active workstations at researcher-set speeds has been previously measured under laboratory conditions using portable metabolic devices.[8,31] However, it is more logical that patterns of use enacted under real world conditions will naturally vary more with user preferences, access, and day-to-day work schedules.[7] Rather than controlling access and use by tight scheduling and enforcement, we agree with others[32,33] that believe that supporting and tracking user-initiated use is a more realistic and effective approach to documenting, evaluating, and ultimately enabling optimal yet flexible use under real world conditions. We have previously established an excellent collaborative relationship with a large office-based Service Industry while we were engaged in evaluating their adoption of treadmill desks.[11] They are supportive of working with us together again on this endeavor (see Appendix 1 for letter of support).

Expected Outputs and Outcomes: **WorkACTIVE-P** will provide clear feasibility and preliminary effectiveness evidence for a combination of practical technology-supported products and programs for Service Industry employers and workers interested in addressing health risk exposures (and related health care costs) associated with occupational sedentary behavior.

**Innovation:**

The innovation of **WorkACTIVE-P** is based on the following tenets:

1) Occupational requirements for extended sedentary behaviors in contemporary workplaces have disrupted the energy balance equation and present a real risk for weight gain, abdominal obesity, and corollary conditions.
2) The health care costs of low energy expenditure occupations are not trivial and are borne by the individual workers, employers, and society.
3) Abdominal obesity is a driving force of the metabolic syndrome but appears amenable to aerobic exercise and even light intensity physical activity interventions.
4) Traditional workplace wellness programs focused on exercise and fitness have reported modest adherence and limit the opportunity to re-balance the occupational energy expenditure deficit to time outside of work.
5) Workplace deliveries of interventions that use wearable step counters to increase lifestyle physical activity have demonstrated some short term success.
6) Further elevating energy expenditure by replacing sedentary working behaviors with tolerable low intensity non-exercise physical activity via scalable active workstations (e.g., pedal desks) is a promising strategy.
7) Uniquely, we have fashioned an affordable, convenient, integrated and user-friendly pedal desk: a semi-recumbent (upright) portable pedaling station with an attached, maneuverable, adaptable desktop capable of supporting a large computer monitor. This is an improvement over “under desk” designs.
8) No study has documented the separate and potentially synergistic effects of a behaviorally supported, multi-component workplace energy expenditure intervention that layers step counting on top of pedal desk use.
9) Moving the study of workstation alternatives out of the laboratory and into real workplaces is necessary to assess scalability and track real patterns of use, ultimately informing their true potential to elevate workplace energy expenditure.

a. Specific Aims:

The objective of WorkACTIVE-P is to conduct a preliminary outcome evaluation of an innovative multi-component intervention focused on raising energy expenditure and re-balancing the disrupted energy balance equation of sedentary workplaces with an ultimate target of reducing workers' abdominal obesity. The energy expenditure intervention includes replacing workplace sedentary time with access to a dedicated pedal desk and increasing steps/day with wearable monitors. Both components are incorporated into an electronically-delivered behavior monitoring and support infrastructure, thus enabling continuous management. This pilot study is a necessary step towards our long term goal to conduct an RO1 investigation to exactly quantify the separate and combined dose-response effects of this multi-component intervention on promoting healthy weight management, and in particular, abdominal obesity in the sedentary workplace.

Recent evidence suggests that contemporary sedentary behaviors may contribute to the obesity epidemic and trigger the development of cardiovascular disease and Type 2 diabetes.[3] Because occupational sitting is the single largest contributor (52%) to total weekday sitting time,[4] employment in a sedentary occupation may represent a risk factor for weight gain, especially among those who are physically inactive during leisure-time.[3,5] Workers employed in such low energy expenditure occupations (e.g., typists) are 63% more likely to be abdominally obese (>102 cm in men and >88 cm in women) compared to workers in high energy expenditure occupations (e.g., construction trades).[6]

In response to these challenges, researchers have begun to consider[7] how modern occupational practices and environments could be enriched to facilitate, rather than discourage, increased energy expenditure by replacing sedentary behaviors with opportunities for non-exercise physical activity without competing with time committed to work tasks. For example, in 2007 Levine and Miller described a "walk-and-work desk," a treadmill and desk combination.[8] Since that time, Thompson et al.[9] reported a positive treadmill desk feasibility study with nurses, clinical assistants, and secretaries and John et al.[10] published the pre-post impact of a 9-month treadmill desk intervention in 12 sedentary office workers. Between baseline and 9 months, median steps/day increased from 4352 to 7080 and average waist circumference decreased 5.5 cm. Despite these initial positive reports, Dr. Tudor-Locke's pilot randomized controlled study of treadmill desks in a local workplace (recently published[11]) suggest that there are many behavioral and logistical challenges, including financial (treadmills desks are $4000-6000) challenges, that make widespread adoption formidable. In direct response to these identified challenges, we have fashioned a much more affordable (approximately $800), convenient, integrated and user-friendly pedal desk: a semi-recumbent (upright) pedal station with an attached, maneuverable and adaptable desktop capable of supporting a large computer monitor. Workers are able to complete their tasks comfortably in a more traditional seated position. The cost and size of the device makes it feasible for workers to have their own dedicated pedal desk rather than sharing access to larger and more expensive treadmill workstations. We believe that the combination of using a pedal desk while also increasing steps/day will provide workers with flexible and compatible strategies for effectively combating the low energy expenditure of a sedentary working lifestyle.

## b. Primary Aims and Hypotheses:

Primary Aim: The primary outcome is the change in abdominal obesity operationalized as MRI-determined visceral adipose tissue (VAT). Over the course of a 2-year period and working collaboratively with a real workplace, **WorkACTIVE-P** will randomly assign 41 low active (< 7,500 steps/day), overweight/obese sedentary full-time workers (reporting "mostly sitting" during the work day), 18-64 years of age, with abdominal obesity defined by waist circumference and at least one additional component of the metabolic syndrome (dyslipidemia, elevated blood pressure, and/or impaired fasting glucose[12]), to a 3-month-long controlled trial. The trial will include baseline and 3 month assessments and two intervention arms: 1) a combined electronic behavior support program of "walk more and pedal desk" (WMPD, n=20), which, in addition to provision of a dedicated pedal desk in individual worker's office space, participants are supported to increase daily walking by at least 3000 steps/day; and 2) a no-intervention control condition (CON, n=20). This design allows us to test the hypothesis that*:* this innovative multi-component workplace energy expenditure intervention will elicit measureable improvements in abdominal obesity superior to the control condition. Relative contributions of the two intervention components (walk more and pedal desk) will be determined by regression analyses predicting VAT changes.

Additional Aims: Secondary outcomes include changes in body weight, total adipose tissue, subcutaneous adipose tissue, blood pressure, blood lipids, fasting glucose and insulin, [HbA1c], free-living accelerometer-determined walking (steps/day and cadence), time spent in sedentary behavior, exercise (time spent at moderate-to-vigorous physical activity), and dietary intake. We will electronically track daily steps data for WMPD participants and also duration of use and cadence (revolutions per minute, or RPM) of dedicated pedal desks. After completion of this pilot study, a subsequent R01 will be proposed to perform a full-scale RCT to quantify the separate and combined effects of the intervention components on change in the study endpoints.

## III. Overview of Research Design

The purpose of the WorkACTIVE-P study is to assess the outcome of an innovative multi-component intervention focused on increasing energy expenditure and re-balancing the disrupted energy balance equation of sedentary workplaces with an ultimate target of reducing workers' abdominal obesity. The primary outcome is MRI-determined visceral adipose tissue (VAT), which is an indicator of abdominal obesity. Secondary outcomes include changes in body weight, total adipose tissue, subcutaneous adipose tissue, blood pressure, blood lipids, fasting glucose and insulin, HbA1-c, free-living accelerometer-determined walking, time spent in sedentary behavior, exercise, and dietary intake.

Table 1 describes the timeline of activities during the 2 year trial period for **WorkACTIVE-P.**

**Table 1. Timeline**

| **Activity** | **Year 1** | | | | **Year 2** | | | |
|---|---|---|---|---|---|---|---|---|
| | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** |
| MOP development, procedures training | | | | | | | | |
| Recruitment & screening | | | | | | | | |
| Writing design & methods paper | | | | | | | | |
| Baseline testing & randomization | | | | | | | | |
| 3-month testing | | | | | | | | |
| Data cleaning & management | | | | | | | | |
| Data analysis & interpretation | | | | | | | | |
| Paper writing & submission | | | | | | | | |

## IV. Study Population

The target study group will be up to 41 sedentary men and women aged 18 to 64 years. Because potential participants will be overweight and obese individuals, the study sample will be at risk for negative health conditions associated with excess adiposity, including cardiovascular disease (CVD). Consequently, the same will be representative of individuals who have a sedentary job and are likely to be prescribed exercise regimens.

| **Table 2. Criteria for Study Participation** | |
|---|---|
| **Inclusion Criteria** | |
| Gender | Both men and women. |
| Age | 18-64 years. |
| BMI | BMI ≥ 25 kg/m$^2$ |
| Waist circumference alone **OR** two or more of the remaining four risk factors defining metabolic syndrome[12] | • Waist circumference ≥102 cm (men) or ≥88 cm (women)<br>**OR**<br>• Triglycerides ≥ 150 mg/dL or currently prescribed and taking anti-hyperlipidemic medications<br>• HDL cholesterol < 40 mg/dL (men) or < 50 mg/dL (women) or currently prescribed and taking anti-hyperlipidemic medications<br>• Resting systolic blood pressure ≥ 130 mm Hg or diastolic ≥ 85 mm Hg or currently prescribed and taking anti-hypertensive medications<br>• Fasting glucose ≥ 100 mg/dL[34] |
| Sedentary worker | Affirmative response to "I mostly sit during the day at work and do not walk about very much" |
| Objectively determined low active | Averaging < 7,500 steps/day at Run-In as confirmed by step counter |
| Other | • Willing to accept randomization into either Walk More Pedal Desk (WMPD) group or Usual Working Condition (UWC) group and follow the intervention procedures associated with that group.<br>• Plan to remain employed full-time at the workplace participating in the study for the duration of the study (4 months)<br>• Willing to wear activity monitor devices during the study<br>• Willing and able to have a partially closed MRI |
| **Exclusion Criteria** | |
| Weight | Weigh more than 275lbs |
| Resting blood pressure | Systolic blood pressure > 179 mmHg and/or diastolic blood pressure > 99 mmHg |
| Diabetes | Self-reported Type 1 or Type 2 diabetes, or use of diabetes-related medications |
| Significant CVD or disorders | Including but not limited to serious arrhythmias, cardiomyopathy, congestive heart failure, stroke or transient ischemic cerebral attacks, peripheral vascular disease with intermittent claudication, uncontrolled angina. Any cardiovascular event in the past 6 months will be exclusionary. |
| Other significant medical conditions | Including but not limited to implants that may interfere with MRI, chronic respiratory, gastrointestinal, neuromuscular, or psychiatric conditions, malignancies in the past 5 years, with the exception of skin cancer therapeutically controlled, endocrine (including diabetes), any other medical conditions or disease (including arthritis) that is life threatening or that can interfere with or be aggravated by exercise. |
| Poor compliance to activity monitors | Failing to wear the step counter or accelerometer for at least 4 days or failing to return the device to clinic. |
| Females Only | Pregnant, has been pregnant in the past 6 months, is currently nursing, or planning to become pregnant over the next 4 months. |
| Other | • Currently enrolled or planning to enroll in a diet/nutrition, exercise, or smoking cessation program.<br>• Plan to be out of town for longer than 2 total weeks over the next 4 months<br>• Currently taking any weight loss medications |

Rationale for inclusion/exclusion criteria: Since this is a real world implementation the gender breakdown will reflect the makeup and preferences of the targeted office-based workplace. Ages 18-64 were chosen since these are the ages that increase our likelihood of targeting metabolic syndrome. This will reduce the costs of screen fails in this pilot study. We anticipate that we will expand the age range to include younger people with metabolic syndrome in a future R01 study.

## V. Recruitment

Since we are primarily targeting workers from a local, large corporation (Blue Cross Blue Shield, Baton Rouge, LA) that Pennington Biomedical has previously worked with to conduct a randomized controlled trial of a treadmill desk intervention, we will be using specially tailored recruitment strategies based on this earlier direct experience. During the study startup phase, members of our research team will attend face-to-face meetings with key members of the company's staff including facilities directors, human resources representatives, information technologists, department supervisors, and wellness coordinators. If required, we will also attend a supervisors' meeting to present information about the planned study, including who will be eligible, time and space requirements, and other expectations. Email and telephone communication will also prepare the company for the study recruitment and implementation. We will also recruit from Pennington Biomedical Research Center, Louisiana State University, LA Office of Technology, LA Healthcare Connections, Entergy, and LA Community and Technical College System in order to supplement enrollment. All companies will follow similar recruitment strategies and processes if deemed appropriate by the site.

A company-generated email providing a link to an online screening survey (maintained by Pennington Biomedical) will be sent out to full-time company employees using their company intranet. The online screening survey will include a series of eligibility questions for the initial screening process (identified in Table 2). As previously requested by one of the collaborating companies, a list of identified individuals deemed eligible from the online survey will be subsequently reviewed by workplace supervisors to confirm individuals' permission to participate in the study if the site chooses to include this in their recruitment process. Once a full list of approved staff members is generated from the supervisors within the company, recruiters will contact participants to complete a phone screen. A similar "real world" recruiting process was followed for a previous randomized controlled trial of treadmill desk adoption in the same workplace.[11] A verbatim list of reasons for excluding participants will be obtained to inform future implementation in terms of characterizing workers and workplaces/jobs that would be suitable targets for such an intervention.

## VI. Measurements and Procedures

Table 3. Schedule of Procedures

| Measure | **Orientation (at Workplace)** | **Run-in (at Workplace)** | **Screening (in Clinic)** | **Baseline (in Clinic)** | **Intervention (at Workplace)** | **3-month Follow-up (in Clinic)** |
|---|---|---|---|---|---|---|
| Informed consent | X | | | | | |
| Demographics Questionnaire | | X | | | | |
| Physical Activity Questionnaire | | X | | | | X |
| MRI | | | | X | | X |
| Height | | X | X | | | |
| Anthropometrics (BP, weight, HR) | | X | X | | | X |
| Waist circumference | | X | X | | | X |
| Urine Pregnancy Test | | | | X | | X |
| Blood draw (measures) | | | X | | | X |
| Adverse Events | | | | | X | X |
| Step counter distribution | X | | | | | |
| Step counter return | | X | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Accelerometer distribution | | | X | | | |
| Accelerometer return | | | | X | | X |
| FitBit | | | | | *WMPD only | |
| Pedal Desk Installation | | | | | *WMPD only | |
| Dietary intake+ | | | X | | | X |
| Randomization | | | | X | | |
| *WMPD: Walk More Pedal Desk Intervention<br>+Participants will use Remote Food Photography Method for dietary intake for 1 week (7 days) to assess dietary intake patterns. | | | | | | |

Orientation:
Interested participants who are deemed eligible on the online screening survey, received supervisor approval to participate, and complete the phone screen will attend a 1-hr orientation visit conveniently located at their worksite where they will receive detailed information on the purposes, goals, procedures, participant flow, timeline, and randomization. Interested participants will be offered an informed consent form to continue. Participants will sign two copies of the informed consent and will be able to keep one copy. All questions and concerns will be clarified prior to participants signing the form or conducting any procedures. Participants will be scheduled for their run-in visit and provided a step counter (pedometer or Fitbit Zip) which requires 1 week (7 days) of self-monitored step counter-determined physical activity.

Run-In:
A Run-In visit will occur approximately one week after Orientation and will be held at their workplace. At the Run-In visit, initial inclusion/exclusion criteria will be assessed (e.g., BMI, waist circumference, blood pressure). Participants will return the step counter to determine their ability to self-monitor behavior and further confirm baseline eligibility (< 7,500 steps/day) from the step-counters retrieved at their workplace. Participants will complete questionnaires related to physical activity, medical history, and demographic information. Those who continue to remain eligible will be scheduled for an in-clinic screening visit (SV1) held at the Pennington Biomedical Research Center. Participants may be asked to repeat measures based on the PI's discretion.

Screening Visit 1:
At Screening Visit 1, which will occur as early as two working days after the Run-In visit, participants will have a blood draw to measure fasting levels of glucose, insulin, HOMA-IR, HbA1c and blood lipids. Anthropometrics will be taken during SV1 including height, weight, BMI, blood pressure, heart rate, and waist circumference. Food intake data will be captured with the Remote Food Photography Method (RFPM) using participants' personal (or one of our loaned) smartphones to collect energy and nutrient intake data. Participants will be distributed an Actigraph Accelerometer (GT3X+) and will be instructed to wear the device for one week (7 days). After lab results are available, study staff will confirm if the participant is eligible to continue based on the inclusion criteria.

If more than 16 days lapse between SV and Baseline scheduled date, participants may be asked to repeat measures to re-assess eligibility.

Baseline Visit:
Eligible participants after SV1 will return to Pennington Biomedical Research Center approximately one week but up to 16 days after SV1 for a Baseline Visit. Participants will return the accelerometer to further evaluate each participant's ability to comply with the wearing requirement of objectively monitored devices (i.e., at least 4 days with at least 10 hours of wear time recorded), allowing us to exclude participants with poor adherence to study requirements. Accelerometer data (physical activity and sedentary behavior) obtained during this screening process will serve as participants' baseline accelerometry data. An MRI will be completed to collect visceral fat, subcutaneous fat, and muscle compartments. Female participants will have a urine pregnancy test before the MRI. Randomization will occur at the conclusion of the Baseline Visit. Using a computerized pseudo-random number

generator, the study statistician will determine the randomization order in advance. The participants will be enrolled as directed by the next assignment letter contained in a randomized sequence of sealed and numbered envelopes. The project manager or interventionist (i.e., unblinded staff member) will reveal the randomization assignment to the participant. The participant will be provided with a behavioral expectations document informing them of the expectations of their randomized group. Study assessment staff will remain blinded to a participant's study arm allocation.

Month 3 Follow Up:
Randomized participants will return to Pennington Biomedical Research Center for a Follow-Up Visit approximately 3 months after intervention starts. Participants will return an accelerometer that was provided to them 1 week prior at their work place. Participants will complete questionnaires related to physical activity. All measures collected at the Screening and Baseline Visits will be repeated (blood work, body measurements, MRI, and RFPM. Female participants will have a urine pregnancy test prior to the MRI.

**a. Description of Tests and Procedures:**

- Accelerometry (Physical Activity)**:** Participants will be instructed to wear the GT3X+ accelerometer (ActiGraph, LLC, Pensacola, Florida, USA) at their waist for seven consecutive days, approximately 24 hrs/day. We have successfully used this 24-hour protocol in diverse populations including children, adults, and older adults and find it maximizes wear time. This accelerometer has been validated[35,36] and is one of the most widely used accelerometers in research and has the capability of detecting minute-by-minute physical activity intensity and sedentary behavior using previously validated activity count cut points.[36,37] Participants enrolled in the WMPD Intervention Group will be fitted with a FitBit® activity monitor to wear at their waist during the intervention. Participants will be asked to wear the FitBit® for all 12 weeks of the intervention, removing it only for activities involving water, such as baths or swimming, and while sleeping.
- Blood Draws**:** Participants will be asked to fast at least 12 hours prior to blood draw. In addition, participants will be asked to refrain from consuming alcohol or participating in an exercise training session at least 24 hours prior to blood withdrawal. Fasting levels of glucose, insulin, HOMA-IR, HbA1c, and blood lipids will be analyzed. Approximately 12 mL of blood will be collected at SV1 and Month 3 visits, which is a total of 24 mL during the course of the study.
- Blood pressure**:** Blood pressure will be measured at rest. Two measures will be taken with a heart rate in between. The average will be recorded per standard Pennington Biomedical's procedures.
- Dietary Intake**:** Food intake data will be captured with the Remote Food Photography Method (RFPM) using participants' personal (or one of our loaned) smartphones. The RFPM and SmartIntake© app (previously developed and validated by study Principal Investigator, Dr. Corby Martin and colleagues[38,39]) will be used to collect energy and nutrient intake data at baseline and month 3. Participants will use the procedure to photograph and track their dietary intake for 7 consecutive days, with the first 1-2 days being a run-in period to acclimate participants to the procedure, resulting in approximately 4-5 complete days of data per participant. Three days of recorded food intake has been shown in several studies to provide an accurate estimate of average food intake;[40-42] hence, we are collecting ample data to obtain a representative sample of habitual food intake.
- Height and weight**:** Height and weight will be measured to the nearest 0.1 kg using a standard stadiometer and balance beam scale, according to Pennington Biomedical's SOP.
- MRI-determined visceral adipose tissue (VAT; indicator of abdominal obesity)**:** Magnetic resonance imaging (MRI) will be performed using a 3.0 T scanner (General Electric, Discovery 750w System, Milwaukee, WI). Subjects will in a supine position on the scanner table with the arms above the head. Subcutaneous fat, visceral fat, and muscle compartments will be traced on each slice by a trained analyst using Analyze™ software (AnalyzeDirect, Overland Park, KS) and a standardized tracing protocol.
- Step-counter: Participants will be instructed to wear the NL-1000 pedometer or a similar model at their waist for seven consecutive days. Fitbit Zip© devices may be worn in place of the pedometer during the Run-In period as needed.
- Waist circumference**:** Waist circumference will be taken according to Pennington Biomedical's SOP and measured to the nearest 0.1 cm.

## VII. Interventions

Participants will be randomized into 1 of 2 intervention arms: Usual Working Condition Control group (UWC) or a combined intervention of Walk More and Pedal Desk (WMPD).

**a. Usual Working Condition Group (UWC):** The no-intervention control condition will be asked to maintain their usual work and lifestyle throughout the study. Participants may be contacted by Pennington Biomedical staff during the intervention.

**b. Combined Intervention (Walk More and Pedal desk; WMPD):** Participants in the WMPD condition will engage in both step-counting (Walk More, WM) and pedal desk (PD) intervention components. The content of both intervention components will be covered during scheduled phone contacts (or in-person meetings, as needed). The step-counting component of the WMPD intervention will be modeled off the success of The First Step Program (FSP), originally developed by Dr. Tudor-Locke. Briefly, the FSP is a facilitated behavior modification program built on the framework of Social Cognitive Theory (SCT),[43,44] emphasizing the components of self-efficacy and social support.[45] Participants will be given internet-enabled step-counting devices (Fitbits). Participants will be taught how to manage their own stepping behavior by regularly checking the on-board visual display and also by monitoring the accompanying internet reporting software to track their own average steps/day each week. Dr. Tudor-Locke has successfully piloted this technology to also provide interventionists with an opportunity to view participants' data as they accrue. We have implemented this same interventionist-supported behavior change and monitoring approach on numerous occasions.[2,46-49] Using these same techniques to collect pilot data for WorkACTIVE-P, we successfully motivated 98 participants averaging 4973 steps/day during at baseline up to an average of 9692 steps/day (max 13971) during a three month pedometer-based intervention, an average increase of almost 5,000 steps/day. We are thus confident that participants assigned to WMPD condition in WorkACTIVE-P will be easily able to increase their daily ambulatory activity at least 3,000 steps,[50,51] and much likely more as confirmed by our pilot data.

Co-investigator, Dr. Tudor-Locke has developed an integrated pedal desk: a semi-recumbent (upright) pedal station with an attached, maneuverable and adaptable desktop capable of supporting a large computer monitor. She has also fabricated additional units and enabled them with hardware sensors and accompanying software capable of displaying and tracking daily use. Pilot testing with 41 workers demonstrated their acceptability; participants estimated they could use the pedal desk a median 4 hours/day. The user is able to view a pop-up box on the computer monitor with a real-time display of rpm, accumulated revolutions ("rev counting"), and energy expenditure estimates based on the measured rpm. Pilot testing affirmed the validity of this rev counting sensor. They are also able to readily view graphical presentations of their daily, weekly, and monthly accrued data. All data are also transferred via internet to an interventionist's level, permitting programmatic oversight and tracking of use parameters. Pilot testing has affirmed the functioning of this tracking software. This is a powerful tool that is used both for measurement but also for identifying behavioral issues as they emerge, and intervening early if needed. Pilot testing has also affirmed that participants can actually use the pedal desk for multiple hours in a day comfortably.

SCT will be used to guide WMPD participants to monitor their own pedal desk use data and review the previous week's pedal desk use during their weekly meetings with the study interventionist, discuss preferred strategies for success, and set personally-relevant and incremental time-based goals. For example, participants may set a goal of using their pedal desk for 2 accrued hours/day initially but over time work their goals up to 4 or more hours/day, depending in part on their work schedules that may regularly require their attendance at events/meetings outside of their office and away from their desk. Participants will also be taught how to track and manage their own behavior using the real time visual display, monitoring their display graphics, and recognizing and addressing relapse (defined as not achieving their time-based pedal desk use goal on any single week).

Study interventionists will discuss goal achievements and progress with WMPD participants throughout the study intervention. This will be done by periodic (weekly or biweekly) phone contacts or in-person meetings as a group or one-on-one. In-person meetings will be scheduled conveniently at the participants' workplace. WMPD participants will be trained to view and report on their own electronically averaged steps/day and pedal desk data each week, including recognizing when they fulfill their goals. Our experience

indicates that such detailed and accurate self-monitoring requires considerable training and a number of learning trials; therefore, participants will receive extensive training during the first 4 weeks of the intervention. Objective data will be used to identify participants who require more resources to adhere to their condition-specific goals. For the WMPD pedal desk component, interventionists will rely on our proprietary pedal desk tracking software to maintain accurate time-based use records and track adherence. These methods follow the "toolbox" approach used during the Diabetes Prevention Program, [52] Look Ahead, [53] and CALERIE Phase II trials. The toolbox approach provides guidelines to deliver specific intervention strategies for certain problems that participants encounter, and the approach requires that the strategies' effectiveness be evaluated regularly (every two weeks). More intense strategies are used if less intense strategies fail to result in improved adherence.

**c. Adherence:** The importance of completing the expected intervention will be reinforced at every opportunity. A concern is that some participants may fail to complete their time on the pedal desk as well as complete the extra 3,000 steps per day. Prior to randomization, participants will have completed an extensive screening process, including the run-in, which we have found promotes adherence and excludes potential participants who cannot commit to the study. Participants will also be given a study expectations page for their intervention. If a participant misses a day on the pedal desk, his/her interventionist will contact them to check in, encourage attendance, and help problem-solve if a barrier to participation is present. These staff will be trained by Dr. Martin, a licensed Clinical Psychologist, in behavioral strategies to promote adherence, and Dr. Martin will be available for consultation regarding challenging participants. The exercise laboratory will be open 5 days per week for 12.5 hours/day to accommodate a variety of schedules.

We recognize that it is unrealistic to expect 100% adherence to the intervention protocol. Participants may miss work due to illness or family obligations or have vacations planned. Therefore, we are defining acceptable compliance to the study protocol as completing 75% or more of the total amount of sessions prescribed. This will be defined as attended sessions per week on the pedal desk divided by expected sessions per week. In addition, steps per day will be used to calculate total adherence by dividing completed steps per day by expected steps per day. An average of the two compliance and adherence numbers will be used for the participant's total adherence.

**d. Dropouts:** We define dropout as failing to return for the 3-month examination. We believe the run-in and screening visit will exclude many at high risk of dropout. Personalization and problem solving approaches to ensure adherence to exercise also will be helpful in preventing dropout.

**e. Participant incentives:** We will provide $200 per individual as a compensation stipend for participation in the study regardless of group assignment. Enrolled participants (control or WMPD group) will receive $100 for completing baseline and another $100 for completing follow-up clinic visits held at the Pennington Biomedical clinic for a total of $200.

## VIII. Participant Safety and Confidentiality

Below describes the risk to subjects for procedures included in WorkACTIVE-P.

**a. Risks to Subjects:**

- Accelerometry: There is no known risk associated with measuring activity with accelerometers, . Accelerometers fit comfortably on your arm and can easily be adjusted should they become uncomfortable. In rare cases, the device may irritate your skin. If this should happen, the device can easily be repositioned to be more comfortable.
- Blood Draws: There is the possibility of pain and bruising at the vein on your arm where the needle is inserted. Aseptic (sterile) technique and trained personnel minimize these risks.
- Blood Pressure Testing: Participants may experience temporary discomfort during blood pressure recordings due to the pressure of the cuff on their arm.
- Height measurement: There is no risk to participants who record their height.

- Waist circumference: There is no anticipated risk to participants who record their waist circumference. Measurements will be taken in a secluded area to protect the participants' privacy.
- Body weight: There is no risk to participants who record their body weight. Measurements will be taken in a secluded area to protect the participant's privacy.
- WMPD intervention: The potential risks and discomforts associated with participating in this study are very minimal. You can self-select the pace at which you would like to pedal while working. However, there remains the risk of muscle soreness associated with an increase in activity level and minimal anxiety associated with trialing a novel task. You may also find the seat mildly uncomfortable. Every effort is made to minimize these risks by having study staff closely observe your tracked behavior and by soliciting your comments and concerns throughout the intervention.
- Questionnaires: There are no anticipated risks from completing self-report questionnaires. It is estimated that the questionnaires will take from 15 to 30 minutes to complete. The questions contained in some of the questionnaires may make people feel uncomfortable since they ask about topics such as how they feel about their body size. Responses to the questions will be coded to protect confidentiality, and participants may choose to not answer questions.
- Magnetic resonance imaging (MRI): There are no significant risks associated with MR spectroscopy and imaging. There is a small chance of claustrophobia or muscular discomfort from lying partially in the magnet for up to 30 minutes. During the imaging measurement, the subject may hear loud banging that may be somewhat unpleasant. Earplugs and/or headphones, however, are provided to mute this banging. Although the long-term risk of exposure to a magnetic field is not known, the possibility of any long-term risk is extremely low in view of the information accumulated from this type of testing over the past 10 years.

**b. Data Safety Monitoring Plan**

WorkACTIVE-P is a study with a minimal level of risk to study participants and does not warrant the establishment of an independent Data and Safety Monitoring Board. This plan describes the safety monitoring procedures for the proposed study, including a description of how often and to whom serious and unexpected adverse events will be reported. The plan will help ensure the safety of all participants. The PI will communicate via electronic submission to the IRB all unanticipated problems as defined by the IRB and all serious adverse events (SAEs) to the program officer within 24 hours. All less serious adverse events will be reported to the program officer within 3 days of occurrence.

The study investigators will monitor conduct of WorkACTIVE-P. Study staff will report adverse events or other problems directly to the PI as they occur. The PI will schedule monthly meetings with study staff to review data on adverse events, and recruitment or adherence to regimen problems. Any significant health problems coming to our attention during the study will be referred to the participant's usual source of medical care, with his/her permission. We will cooperate fully with his/her physician by providing relevant medical records. The following criteria, if detected during any part of the study regimen, will lead to referral to the participant's usual source of medical care:

- *1. Clinical symptoms or signs of CVD to include chest pain suggestive of angina pectoris, unusual dyspnea on exertion, severe ankle edema, symptoms suggestive of transient ischemic attacks or intermittent claudication.*
- *2. Musculoskeletal injuries or problems causing severe pain during exercise or interference with daily activities.*

**c. Adverse Events**

Adverse events that occur in WorkACTIVE-P will be classified as a Serious Adverse Event (SAE) or an Adverse Event (AE). Serious adverse events in WorkACTIVE-P are defined to include:

- Death
- A life-threatening event
- Severe illness including worsening of a pre-existing condition, injury or accidents

- An inpatient hospitalization, surgical procedure, or a treatment to prevent an SAE
- A permanent disability or incapacity
- A clinically significant abnormal laboratory or diagnostic test result
- Any other event that, in opinion of the principal investigator or study physician, might have resulted in a serious adverse event if medical intervention had not been initiated

Serious adverse events will be reported to the study PI, Project Manager, and MSO throughout the trial. Serious adverse events will be collected from randomization until the final closeout visit. SAE Data will be analyzed quarterly, but serious or life-threatening adverse events require immediate reporting and follow-up. In the event an adverse event occurs on campus and results in a serious or life threatening situation, the investigator or other project staff present will begin emergency measures, as appropriate, and call 911.

- For minor physical injury, the individual will be encouraged to see a health care practitioner of his or her choice.
- If the study participant experiences psychological or emotional distress, the project staff will cease research activities and attempt to calm and reassure the participant. The participant will be directed to an appropriate health care practitioner for further assessment and treatment as needed.
- The investigator and/or project staff will record detailed narrative notes describing the adverse event they witnessed or that was reported by participant. The MSO will complete the form Notification of a Serious Adverse Event.

Serious adverse Event reporting will follow the requirements of the IRB of the Pennington Biomedical Research Center. Serious adverse events that are unanticipated problems will be reported within 48 hours.

**d. Stopping Rules**

There is minimal risk for participating in this trial. The most likely scenario that would indicate a cessation of the study would be failure to recruit participants or implement the intervention as planned. Nevertheless, in addition to monitoring recruitment and compliance to the intervention, we also will monitor the rates of injury in our participants. The safety officers, in conjunction with the study investigators, will alert the IRB and NIH if a larger than reasonably expected injury rate occurs in the treatment groups. Other issues that are related to the stopping rules include:

- New information – It is unlikely that new information will become available during this study that would result in discontinuing the trial.
- Limits of assumption – It is possible that the value of data analysis will be limited by differences between the intervention groups at baseline or because of study dropouts or missing data. Baseline differences will be analyzed annually and effects on the power to detect differences in the outcome measures will be evaluated and discussed with the PI, safety officer, and the NIH Project Officer. Although an excessive number of dropouts could occur, this has not been our past experience. In our DREW study, the dropout rate was only 8%. If the dropout rate for the proposed study exceeds 15%, the safety officer will initiate a meeting with the PI to discuss strategies to increase retention. If the dropout rate exceeds 25%, the safety officer will meet with the study investigators to determine whether or not the study should continue.
- Limit of rules – We acknowledge that circumstances, other than what are listed, may justify stopping the study.

**e. Confidentiality**

All attempts will be made to maintain a subject's privacy. Safeguards such as password protected computer and networks have been put in place in order to limit access to subject data. Subjects will be given ample time to read over the consent, ask questions, and agree to participate in the research study. Subjects may decline answering questions they are not comfortable with. Each procedure will be explained to the subject before it is performed. We will always ensure the privacy of the subjects. When weighing, it will be done in a private setting.

## IX. Data Management and Quality Control

### a. Sample size and statistical power:

This is a study of an innovative multi-component intervention delivered in a real workplace. The primary outcome is change in VAT. The sample sizes herein were set based on data collected in our Pounds Lost51 study that showed baseline VAT to be approximately 5.43 kg and indicated that a 21% reduction in VAT (equivalent to 1.15 kg, SD=1.20kg) can be achieved with a suitable intervention. The nominal level of significance alpha = 0.05 will be used to compare mean VAT change (e.g., reduction) in WMPD vs CON, A minimum of 18 subjects per intervention who all complete protocol through end of study would conservatively provide at least 80% power for detecting significance where the underlying true differential intervention change in VAT is at least 1.15 kg. We have planned for 20 participants per group (total n = 41) in this study to allow for 10% attrition. As designed, this study will clearly inform the feasibility of combining these components of a workplace multi-component energy expenditure intervention.

### b. Data Management:

The data management will be conducted by the Pennington Biomedical Research Computing Group. There will be limited access to all data including locked cabinets for paper files and password protected computers for electronic data. The PBRC has a fully integrated, campus-wide, automated, data management system. All data are entered into a Central Database using existing methodology that has been fully validated and undergoes continuous quality assurance by the PBRC Research Computing Core and NORC. Most data are automatically uploaded from the instruments that measure the endpoint. All self-report inventories will be scanned and scored automatically using the Psychological Assessment Laboratory's optical scanning system, which automatically uploads the data into the Central Database. Exercise testing data will be downloaded from the Parvo Medics' TrueOne® 2400 cart directly following each test and reviewed for integrity. All data are backed-up daily and the Research Computing Core at the PBRC oversees all data management.

### c. REDCap Database:

REDCap, a web-based application used to build and manage surveys and databases, will be used for questionnaire collection in this study. REDCap (Research Electronic Data Capture) is a secure, web-based application that is flexible enough to be used for a variety of types of research. REDCap provides an intuitive user interface that streamlines project development and improves data entry through real-time validation rules (with automated data type and range checks). REDCap also provides easy data manipulation (with audit trails for reporting, monitoring and querying patient records) and an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus).

In addition to traditional data capture functionality, REDCap's survey capabilities are a powerful tool for building and managing online surveys. The research team can create and design surveys in a web browser and engage potential respondents using a variety of notification methods. All data collection projects rely on a thorough, study-specific data dictionary, defined by all members of the research team in an iterative, self-documenting process. This iterative development and testing process results in a well-planned and individualized data collection strategy. Pennington Biomedical has a license agreement with Vanderbilt and the database and software are installed on our local servers and hosted by Pennington Biomedical, not by Vanderbilt. The Vanderbilt University Office of Research will not be used as a central location for data processing and management. That is all done by Computing Services and RCG staff at PBRC. More information about the consortium is available at http://www.project-redcap.org/.

### d. Data Analysis:

Baseline participant characteristics (e.g., age sex, race, weight, BMI, fasting glucose insulin, and HOMA-IR) will be summarized by intervention group as counts and percentages for categorical variables, and means and 95% confidence intervals for continuous variables. Adherence to protocol assessments (e.g., daily steps, minutes accrued on the pedal desk, rpm on the pedal desk) will be summarized similarly by week for each intervention.

On study change in MRI-determined VAT, weight, waist circumference, fasting glucose and insulin, HOMA-IR will be summarized by intervention group as means and 95% confidence intervals in an intention-to-treat analysis of (1) all participants and (2) the subset of participants who achieve the highest tertile of adherence to the intervention. Linear models will provide the primary framework for significance testing. In the analysis of VAT (the primary outcome), statistical significance of differential longitudinal changes in response to intervention (WMPD vs CON) will be assessed employing repeated measures mixed effects models with maximum likelihood estimation and Kenward-Rogers adjustment to the degrees of freedom in an intention-to-treat analysis of (1) and (2) for each outcome measure using all available data. Study arm (WMPD. or CON), age, race, sex and interactions will be taken as having fixed effects; participants within groups will be considered as having random effects. Covariates such as age, sex, race and baseline assessment of VAT will be included in preliminary models and retained in final analytic models if warranted. The model residual covariance structure (e.g., unstructured, compound symmetric, auto-regressive) across time will be investigated to enhance efficiency of statistical tests. Secondary outcomes, such as on-study changes in weight, waist circumference, fasting glucose, inssulin, and HOMA_IR will be analyzed using statistical models analogously to the approach described for the primary outcome.] Results for each outcome will be summarized as least squares means and 95% confidence intervals for each intervention across the assessment times. Model residuals will be tested to see if they have distributions that are approximately Gaussian and data transformations will be performed if needed. Group differences in baseline characteristics will be tested and corrective steps, such as post-stratification and adding model covariates will be employed as necessary Null hypotheses will be tested against two-directional alternatives at the nominal 0.05 significance level using Bonferroni adjusted p-values when appropriate. All statistical analyses will be performed using statistical software in SAS version 9.3.

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Appendix 1: Letter of Support

P.O. Box 98029
Baton Rouge, Louisiana 70898-9029
225/295-3307 • FAX 225/295-2054

BlueCross BlueShield of Louisiana
An independent licensee of the Blue Cross and Blue Shield Association.

October 31, 2014

Catrine Tudor-Locke, PhD, FACSM
Associate Professor
Director, Walking Behavior Laboratory
Pennington Biomedical Research Center
6400 Perkins Road
Baton Rouge, LA 70808

Re: "WorkActive-P"

Dear Dr. Tudor-Locke:

As Medical Director of Blue Cross Blue Shield Louisiana, I write this letter to express our support and enthusiasm for your NIH application to conduct a preliminary outcome evaluation of an innovative multi-component sedentary workplace intervention designed to raise energy expenditure and reduce workers' abdominal obesity. This effort fits perfectly within our mission to promote a wellness culture in our workplace.

Your research team already has extensive experience conducting physical activity and other behavioral intervention trials. As you know, we have worked together with you previously to evaluate our pilot distribution of treadmill desks in our workplace. We found you and your Pennington Biomedical staff to be collaborative, accessible, and professional in your approach. We learned a great deal about the potential issues hampering widespread uptake of such workstation alternatives and are excited about the solutions that you have developed. We are committed to ensuring the health and well-being of our workforce into the future, and this study will inform us (and our clients) about the separate and combined effects of a multi-component approach to mitigating the potentially deleterious cardio-metabolic effects of prolonged sitting at work.

We will do our best to ensure the success of the proposed study, however, additional team members, including management level staff will work with us to ensure the success of this study. We have support of our company's management to work collaboratively with you on this project. As we have done successfully in our prior collaboration, we look forward to regular communication with you through email, telephone, and routine face-to-face meetings at our worksite.

On behalf of our workforce at Blue Cross Blue Shield Louisiana, I look forward to working closely with you on what I deem to be a very important, innovative, and practical study.

Yours sincerely,

Andrea Barrack, MD

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