Research Protocol

Study title: Sedentary Intervention Trial in Cardiac Rehabilitation (SIT-CR): A randomized controlled trial using the *activ*PAL3™ and *activ*PAL3™ VT to quantify free-living movement patterns and reducing sedentary time in cardiac rehabilitation patients

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LIST OF ABBREVIATIONS

BMI	Body mass index
C	Control group
CABG	Coronary artery bypass graft (bypass surgery)
CAD	Coronary artery disease
CI	Confidence interval
CR	Cardiac rehabilitation
I	Intervention group
MVPA	Moderate-to-vigorous intensity physical activity
PA	Physical activity
PCI	Percutaneous coronary intervention
RCT	Randomized controlled trial
SD	Standard deviation
SIT-CR	Sedentary Intervention Trial in Cardiac Rehabilitation
UOHI	University of Ottawa Heart Institute
VTAP	*activ*PAL3™ VT

1. INTRODUCTION

Exercise-based cardiac rehabilitation (CR) has been shown to consistently reduce the rates of total and cardiovascular-related mortality and morbidity [1, 2]. Cardiac rehabilitation is often prescribed for those who have experienced a cardiac event and follows Canadian guidelines to achieve a minimum of 30 minutes of moderate-to-vigorous intensity physical activity (MVPA) on at least five days per week [3]. Although current CR guidelines focus on MVPA, sedentary behaviours have gained recent attention as strong and modifiable risk factors for heart disease. Specifically, they have an effect on cardio-metabolic functioning and are strongly associated with several markers of cardio-metabolic risk [4]. Recent data from the University of Ottawa Heart Institute (UOHI) shows that CR graduates spend the majority of their wakeful time sedentary and this time is negatively associated with body mass index (BMI) and measured cardiorespiratory fitness [5].

UOHI offers a supervised on-site 8-week CR program. The program consists of twice-weekly sessions (1 hour each) with a focus on aerobic and resistance exercise. There is currently no intervention component or outcome measure focusing on sedentary behaviours. This is unfavorable given the knowledge of the impact of sedentary behaviours on cardio-metabolic health. It is important to assess sedentary behaviours in this population to assess whether current programming affects sedentary behaviours or if more is needed to target these behaviours. This is important to note given that physical activity (PA)-focused interventions do not generally result in clinically meaningful reductions in sedentary behaviours [6]. Therefore, it is important to also investigate the feasibility of adding sedentary behaviour interventions to CR programming and whether these interventions can consequently further improve cardio-metabolic health. Using cues and prompting from wearable technology may provide a feasible way to reduce sedentary behaviours. A recent systematic review noted that interventions using education and prompts/cues were promising for reducing sedentary behaviours [7]. To date, most research using direct measures of PA and sedentary time have used research-grade accelerometers (e.g. ActiGraph®, Actical®, etc.). Research has shown that these monitors are not as valid for measuring sedentary time and postural changes as the *activ*PAL3™ monitor which is more precise and sensitive to changes in sedentary time [8].

The *activ*PAL3™ monitors have the capability to discern between standing and sitting which can increase our knowledge of movement patterns among CR participants. Additionally, the development of the *activ*PAL3™ VT (VTAP) with vibrotactile feedback (VT), offers direct feedback to the wearer regarding time spent being sedentary. The prompts provided by these monitors have the capacity to reduce sedentary time and increase breaks from prolonged sitting by promoting individual awareness around movement patterns.

2.0 PURPOSE

This research is timely given recent interest in the role of sedentary behaviours in both the primary and secondary prevention of cardiovascular disease. Sedentary behaviours have been shown to be high in patients with cardiovascular disease [5] and it is not yet known if current CR programming results in significant reductions of these behaviours, or whether a targeted component is warranted. It is also unclear if self-reported sedentary time measures can provide valid and reliable information for monitoring these behaviours in a CR setting, or whether more objective measures such as the *activ*PAL3™ are needed. This study has multiple purposes:

1. To inform the development of a larger randomize controlled trial;
2. to assess the feasibility and usability of the *activ*PAL3™ devices for measuring sedentary time in a CR setting and identify how it compares to self-report methods.
3. to describe changes in sedentary time that occur over standard CR with the use of prompting cues from the VTAP; and
4. to assess whether the addition of prompting cues can result in further decreases in sedentary behaviour and improvements in clinical outcomes, health-related quality of life (HRQoL), symptoms of anxiety and depression, self-efficacy, aortic stiffness, and aerobic capacity.

Results from this study will inform current gaps in the literature and help to generate recommendations for whether targeting sedentary behaviours in the CR setting is warranted.

3.0 KEY TERMS AND DEFINITIONS

3.1 Sedentary time

Sedentary time refers to the amount of time spent engaged in sedentary behaviours. Sedentary behaviour refers to an energy expenditure of 1.5 metabolic equivalents (METS; measure of energy expenditure) or less while in a sitting or reclining posture during waking hours and not simply the absence of PA [4]. This study will collect both self-reported and objectively measured sedentary time.

3.2 Physical activity (PA)

PA refers to "any bodily movement produced by the skeletal muscle that results in energy expenditure" [9]. This study will employ the use of both self-reported and objectively measured PA, specifically of moderate-to-vigorous intensity (MVPA).

4.0 OBJECTIVES

4.1 Primary objective

The primary objective of this study is to evaluate the feasibility and usability of the VTAP to reduce sedentary time and the *activ*PAL3™ monitors to quantify changes in free-living time spent sitting, standing and lying in CR patients in the UOHI on-site cardiac rehabilitation program (SIT-CR Study).

4.2 Secondary objectives

Secondary objectives include:

1. quantifying sedentary time (including time spent sitting, standing and lying) in CR patients (control arm);
2. assessing the possible effect of an on-site CR program on reducing time spent being sedentary (control arm);
3. evaluating whether the addition of sedentary prompts (Intervention group [I]) leads to further reductions in sedentary time, beyond those achieved through regular CR (Control group [C]);

4. validating a CR-specific PA and sedentary time log; and
5. evaluating the impact of the Intervention on: clinical outcomes (e.g., blood pressure, resting heart rate, blood lipids, blood sugar, body weight, body mass index [BMI], waist circumference, aortic stiffness); health-related quality of life [HRQoL]; self-efficacy; symptoms of anxiety and depression); MVPA; and maximal aerobic power (VO_2max).

4.3 Hypotheses

In adults with a diagnosis of coronary artery disease (CAD) (including heart attack, angina (chest pain), stent, percutaneous coronary intervention (PCI), and/or bypass surgery (CABG), providing sedentary prompts using a thigh-worn activity monitor (VTAP) will be superior to standard 8-week on-site CR programming in:

1. decreasing sedentary time;
2. increasing breaks from sedentary time;
3. increasing MVPA;
4. improving clinical outcomes (e.g. blood pressure, resting heart rate, blood lipids, HbA1c, body weight, BMI, waist circumference)
5. improving HRQoL, self-efficacy, symptoms of anxiety and depression;
6. improving measures of aortic stiffness; and
7. increasing maximal aerobic power (VO_2max).

5.0 METHODS

5.1 Study design

This is a single-centre, two-armed randomized controlled trial (RCT) to evaluate the feasibility and usability of the *activ*PAL3™ in measuring sedentary time and the VTAP in providing sedentary prompts to reduce sedentary time in a CR setting (SIT-CR Study). The RCT (see **Figure 1** for study flow) will randomly allocate 32 individuals (16 males and 16 females) in a 1:1 ratio entering the CR program to either the Control Group (CR program) or to the Intervention Group (CR program + sedentary prompts from VTAP).

A week prior to their first class, participants will be asked to come to the UOHI to complete informed consent, a short questionnaire to assess employment patterns, self-efficacy to reduce sedentary behaviour and increase light and moderate PA, and HRQoL (see SIT-CR Study Baseline and Follow-up Questionnaires). Participants will also have their aortic stiffness, blood pressure and resting heart rate measured. In order to test for aortic stiffness participants will be asked to fast if possible, the study will provide a package of nuts and a glass of water at this first meeting. After the measurements, participants will then be asked to wear an *activ*PAL3™ during waking time for 7 days to collect baseline measures of sedentary time over one week prior to their first CR class.

On the day of their first CR class, participants will be asked to come in 30 minutes early to complete a Modified Bruce Ramp Treadmill Test to estimate maximal aerobic power. Once the test is complete, participants will be randomized in a 1:1 ratio (stratified by sex) to the Intervention or Control Groups. At this visit, participants in the Intervention Group will receive a wear time log sheet and a VTAP

monitor that will provide sedentary prompts to break up prolonged periods of sedentary time (prompts after 30 minutes of sedentary time). Participants in the Intervention Group receive a full-charged VTAP monitor each week when they attend their on-site CR class. Participants in the Control Group will continue with their regular CR class schedule.

Follow-up sedentary time measures will be taken at the end of CR (during Week 8 of CR/Week 9 of the RCT), participants will be asked to once again wear an *activ*PAL3™ during waking time for 7 days. Participants will be asked once again to complete a short questionnaire to assess employment patterns, self-efficacy to reduce sedentary behaviour and increase light and moderate PA, and HRQoL (see SIT-CR Study Follow-up Questionnaires). They will also have their arterial stiffness, blood pressure and resting heart rate measured and will once again be asked to complete a Modified Bruce Ramp Treadmill Test during this last week.

As part of the regular CR program standard of care, clinical measures will be taken (e.g. blood lipids, HbA1c, body weight, BMI, waist circumference) and depression and anxiety will be self-reported (see CR Questionnaire) at both baseline and follow-up.

The 8 week intervention time period was chosen to align with current CR programming to allow for comparisons between the intervention and standard CR programming (control group). As sedentary behaviour intervention research is currently in its infancy, it is unknown how long an intervention is required; therefore, this investigation will provide pilot-level information to inform whether 7 weeks of intervention is adequate and whether it is feasible to add to the pre-existing CR programming. Previous studies have shown significant reductions in sedentary time following 4 to 24 weeks of intervention [10-14].

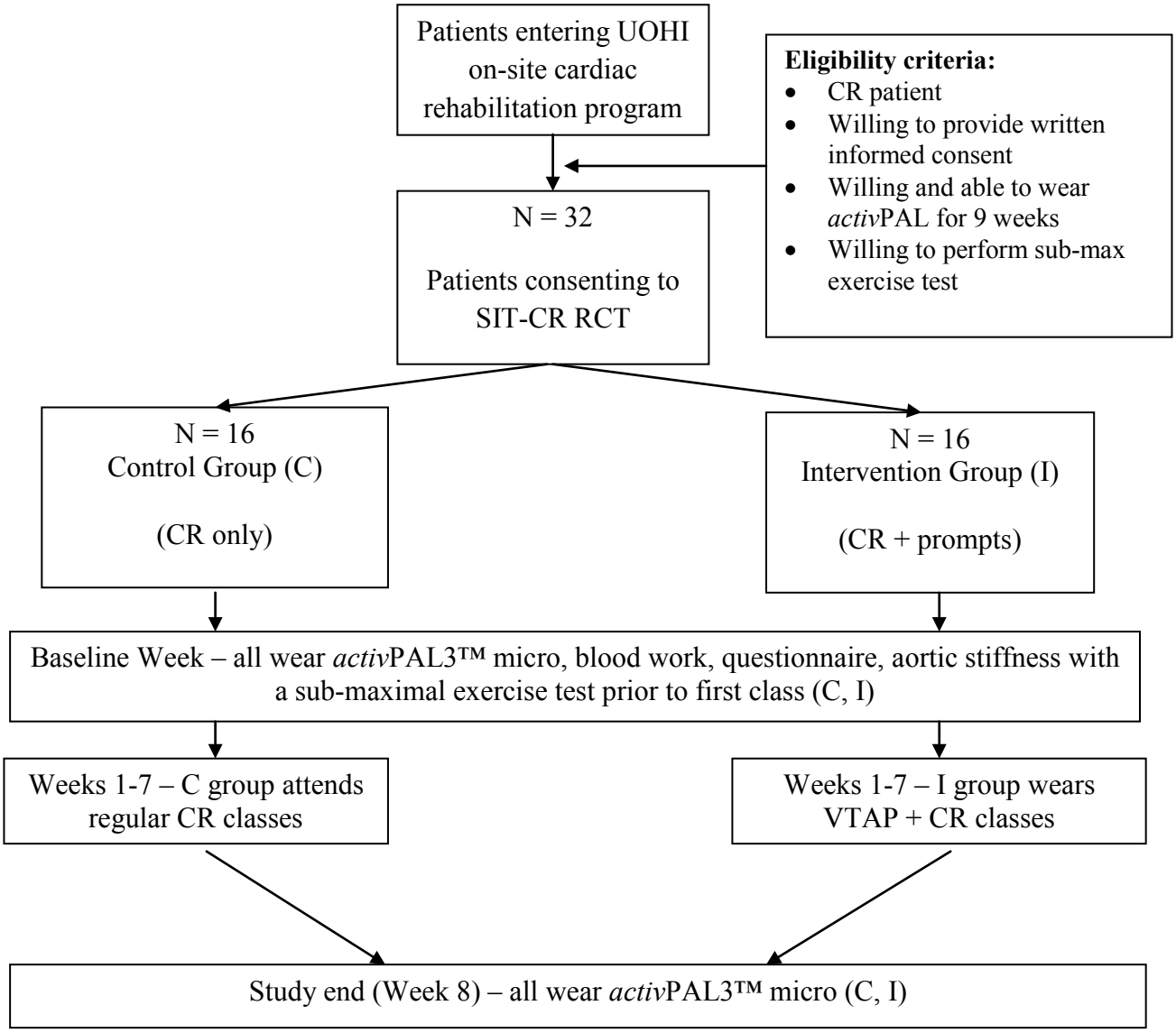

Figure 1. Study schema

5.2 Study setting

This trial will be conducted at the UOHI in the Minto Prevention and Rehabilitation Centre. Specifically, all intake sessions and appointments with participants will be on the Cardiac Rehabilitation Track on the 2nd floor of the UOHI.

5.3 Study population

A total of 32 participants will be included in this study. The study population will be drawn from patients currently enrolled in on-site CR at the UOHI. The sample size calculation is provided in Section 5.6.1. Eligibility criteria are outlined below.

5.3.1 Inclusion and exclusion criteria

Inclusion criteria include:

1. Patient is attending on-site (2 x weekly for 8 weeks) CR at the Minto Prevention and Rehabilitation Centre at the UOHI;
2. Patient is ≥18 years;
3. Patient has confirmed diagnosis of coronary artery disease (CAD);
4. Patient understands English or French;
5. Patient is willing and able to provide informed consent.

Exclusion criteria include:

1. Patient is unwilling to wear activity monitors;
2. Patient is already using a commercial activity monitor with sedentary prompts (e.g., Jump Up, Garmin);
3. Patient is unable to attend follow-up visits;
4. Patient is not participating in a CR program at the UOHI;
5. Patient has cognitive impairment (unable to comprehend or participate in the intervention);
6. Patient has a history of postural hypotension;
7. Patient is unable, in the opinion of the Medical Director, to participate in the study.

5.4 Data collection procedures

If a patient expresses interest in participating in research to a heath care professional within their circle of care, this will be acknowledged as permission to contact the prospective participant, in order to provide them with study information and determine interest and eligibility. The PI and/or RC and/or study staff may also screen incoming cardiac rehabilitation patients using vOACIS for eligibility in the study. The PI and/or RC and/or study staff will only contact patients who have given permission to be contacted by research to provide them with information about the study and determine if they are interested in participating. Interested individuals will be contacted by the PI and/or RC and/or study staff who will prescreen patients for eligibility and arrange a visit to confirm eligibility and obtain written, informed consent.

Each participant will be asked to complete the following study-related visits: 1) baseline (1 week prior to first CR class), 2) exercise test prior to the first class of CR, 3) 8 weeks of a UOHI CR on-site program, and 4) an 8-week follow-up with post measures. The duration of participation will be 9 weeks. Each component of the study is described in more detail below.

5.4.1 Baseline assessment

Participants will be asked to meet with the research staff 1-week prior to their first CR session. Prior to data collection, written informed consent will be obtained. The research staff will then measure aortic stiffness, blood pressure and resting heart rate using a Mobil-O-Graph device. Participants will be provided with a brief study questionnaire to assess self-efficacy to reduce sedentary behaviour and increase light and moderate PA and HRQoL (SF-36). Participants will be provided with a parking pass for this visit. During the baseline phase, participants will also self-report demographics (e.g., age, sex,

income), exercise (using the modified Godin Leisure-Time Exercise Questionnaire [15]), as well as symptoms of anxiety and depression (Hospital Anxiety and Depression Scale [16]) as part of the CR intake questionnaire which is the usual standard of care. In addition, the study staff will extract several cardiovascular risk factor measurements obtained by CR staff at the participant's Intake Session, including: measured height (cm) and weight (kg) to compute BMI (kg/m^2), waist circumference (cm), total cholesterol, high density lipoprotein (HDL), low density lipoprotein (HDL), triglycerides, and fasting HbA1c. Participants will then be provided with an *activ*PAL3™ activity monitor, to be worn for seven days on the right thigh under clothing (see product description of the *activ*PAL3™ device). The *activ*PAL3™ is worn directly on the skin using a hypoallergenic, hair-friendly adhesive sticker. Participants will also be provided with Hypafix tape to use if they feel more support is needed to secure the device. Participants will also complete a daily log (FITS log) over this period of time to assist with the verification of the data collected while the monitor was worn and for validation of self-reported sedentary time. The research assistant will demonstrate how to properly wear the monitors and answer any questions and the participants will be provided with written instructions (see SIT-CR Baseline Questionnaire).

One week following the baseline measures, participants will be asked to meet approximately 30 minutes before their first session begins to complete the sub-maximal exercise test (Modified Bruce Ramp Treadmill Test) to estimate maximal aerobic power (VO_2max) [17].

5.4.2 Intervention

Following the baseline phase and the sub-maximal exercise test, participants will be randomized in a 1:1 ratio to: 1) usual care (C), 2) usual care + sedentary prompts from the VTAP monitor (I) using a computer-generated, stratified by sex, random sequence. Treatment assignments will be generated and placed in sealed, numbered envelopes to ensure concealment until baseline data is collected.

Both groups will complete a combination of supervised and home-based exercise sessions over an 8-week period (as per standard CR programming). Supervised exercise sessions will take place at the Minto Prevention and Rehabilitation Centre at the UOHI.

Intervention Group participants will also be provided with a VTAP monitor to wear directly on the skin of the front of their right thigh during waking hours for weeks 1 through 7. The monitor will provide participants with real-time feedback on their sedentary behaviour. The VTAP is the world's first commercially available device for free-living sedentary behaviour modification. The VTAP alerts wearers to the fact they have been sitting for a period of time and ought to move. The alerts are delivered by way of gentle vibrotactile feedback (buzzing). The monitors will be programmed to provide feedback once the wearer has been sedentary for 30 consecutive minutes. The monitors will also be able to log the duration and intensity of the primary movements including: sedentary, upright and ambulatory activities of the intervention participants. Due to the battery life of the monitors, each week participants will be provided with a newly charged VTAP and sticker applications at the first CR session of the week. See the product information sheet for the activPAL3™ VTAP Specifications.

5.4.3 Intervention assessments

Participants in the Intervention Group will be asked to return their weekly wear time journals each week by dropping off into a study mail box on the Track in the Minto Prevention and Rehabilitation

Centre at the UOHI. They will also exchange their VTAP for a newly charged device and be provided with a new wear time log.

5.4.3 Follow-up assessments

After 8 weeks of the study (end-of-intervention), participants will return to the UOHI for their last week of CR and all participants will once again be ask to wear an *activ*PAL3™ to monitor movement patterns. A research staff member who will be blinded to the participants' allocation will once again collect measures of aortic stiffness, blood pressure and resting heart rate and conduct a Modified Bruce Ramp Treadmill Test to estimate maximal aerobic power (VO_2max). Participants will be provided with a parking pass for aortic stiffness measurement visit.

Once again clinical measures (collected as part of standard of CR care) will be abstracted from the participant's chart (e.g. measured height (cm) and weight (kg) to compute BMI (kg/m^2), waist circumference (cm), total cholesterol, high density lipoprotein (HDL), low density lipoprotein (HDL), triglycerides, and fasting HbA1c) and participant responses from the CR questionnaire will also be abstracted (e.g. self-reported exercise, HADS).

Participants in both groups will also be asked to complete a brief intervention satisfaction survey to assess satisfaction associated with wearing both the *activ*PAL3™ and VTAP monitors (see Evaluation Surveys).

Upon completion of the study, both groups will receive a fact sheet about sedentary behaviours including the hazards associated with sedentary time and 'Tips and Tricks' for reducing sedentary time (see Sedentary Fact Sheet).

5.5 Measures

The primary objective of this study is to assess the feasibility and usability of the *activ*PAL3™ and the VTAP in a CR setting to inform the development of a larger RCT. This will be assessed by examining:

- Recruitment rates;
- acceptability of intervention and wearing the *activ*PAL3™ and the VTAP using an evaluation survey (see Evaluation Surveys);
- completion and drop-out rates; and
- intervention adherence using wear time logs.

The primary outcome of the intervention focuses on changes in sedentary time measured by self-report and the *activ*PAL3™ over the 8-week intervention period. These outcomes will provide standard deviations to estimate an effect size for a future RCT. Secondary outcome measures will include:

- changes in MVPA (self-reported and objectively measured);
- changes in clinical outcomes (e.g., body weight, BMI, waist circumference, blood pressure, total cholesterol, HDL, LDL, triglycerides, and fasting plasma glucose);
- changes in measures of anxiety and depression (HADS);
- changes in self-efficacy to reduce sedentary time and increase PA;

- changes in HRQoL (SF-36);
- changes in aortic stiffness (PWV); and
- changes in maximal aerobic power (Modified Bruce Ramp Treadmill Test).

Measures and study time-line are provided in **Table 1**.

5.5.1 Sedentary time

The primary objective of this study is to evaluate the feasibility and usability of the *activ*PAL3™ in collecting time spent sitting, standing and lying in an on-site CR program. From this, the primary outcome of the RCT will be changes in sedentary time as measured both by self-report (sitting time from the International Physical Activity Questionnaire [see SIT-CR Baseline and Follow-up Questionnaires], sitting time from a FITS log [see SIT-CR Baseline and Follow-up Questionnaires], a sitting time question from the CR intake questionnaire), and objectively measured by the *activ*PAL3™ over 7-days. See the provided PAL Technologies Ltd. End User Licence Agreement.

5.5.2 Moderate-to-vigorous intensity physical activity (MVPA)

MVPA will be measured by both self-report (using the modified Godin Leisure-Time Exercise Questionnaire [15] [see the CR Questionnaire] and FITS log [see the SIT-CR Baseline and Follow-up Questionnaires]) and objectively measured using the *activ*PAL3™ over 7-days. Minutes of MVPA per week will be summed and used to assess goals and meeting guidelines. The device will also provide time spent in sedentary and light movement, as well as steps/day.

5.5.3 Body composition

Height (in cm), weight (in kg) and waist circumference (in cm) are measured as part of the regularly scheduled CR intake and final sessions by a nurse or physiotherapist using a standardized procedure. BMI will be computed from measured height and weight (kg/m^2). For the purpose of this study BMI will analyzed both continuously and using adult categories of underweight ($<18.5\ kg/m^2$), normal weight ($18.50\text{-}24.99\ kg/m^2$), overweight ($25.0\text{-}29.99\ kg/m^2$) and obese ($\geq 30.0\ kg/m^2$) [18]. Waist circumference will be analyzed both continuously and using adult cut-offs of ≥ 102 cm (40 in.) for men and ≥88 cm (35 in.) for women at increased risk of diabetes, heart disease and high blood pressure [19].

5.5.4 Lipid profile

Total cholesterol, HDL, LDL, and trigylcerides will be extracted from the participant's CR file. These will be measured as part of CR evaluation practice at intake and upon completion.

5.5.5 Fasting HbA1c

Fasting HbA1c will also be extracted from the participant's CR file. This is also measured as part of CR evaluation practice at intake and upon completion.

5.5.6 Aortic stiffness

Aortic stiffness will be measured using the Mobil-O-Graph device (see Case Report Form). This device uses an algorithm based on blood pressure measurement taken at the upper arm to estimate the participants' aortic pulse wave velocity (PWV). The Mobil-O-Graph is a valid and reliable tool to measure PWV in clinical populations. Our lab has successfully used this device before in individuals with CVD. Participants are asked to sit at rest for five minutes prior to the measurement being obtained. A blood pressure cuff is placed on the individuals arm and four readings are taken. The test should take 5 to 10 minutes to complete. While measures are being taken the participant is asked to sit in a comfortable seated position, not to talk, to stay still and to keep their legs uncrossed. The Mobil-O-Graph will also supply resting heart rate and blood pressure values. These are both secondary outcome measures. Participants will be asked to follow the pretesting guidelines for PWV:

- No eating or drinking within 4 hours of the test
- No moderate or vigorous exercise within 12 hours of the test
- Void urine completely within 30 minutes of the test
- Abstain from alcohol consumption within 48 hours of the test
- Do not ingest diuretics, including caffeine before the assessment unless they are prescribed by a physician
- If you are in a stage of your menstrual cycle during which you perceive you are retaining water, postpone testing (female participants only)

5.5.7 Blood pressure

Resting blood pressure will be measured by the research coordinator or assistant using a. Blood pressure will be measured in a seated position after a five-minute rest period using a Mobil-O-Graph device (see aortic stiffness for further detail) that performs three measurements. An average of three measurements will be used for statistical analyses (see Case Report Form).

5.5.8 Resting heart rate

Resting heart rate will be measured by the research coordinator or assistant using a. Blood pressure will be measured in a seated position after a five-minute rest period using a Mobil-O-Graph device (see aortic stiffness for further detail) that performs three measurements. An average of the three measurements will be used for statistical analyses (see Case Report Form).

5.5.9 Anxiety and depression

Screening for anxiety and depression is carried out at baseline and follow-up CR visits using the Hospital Anxiety and Depression Scale (HADS) [16]. The HADS is a 14-item scale; seven of the items relate to anxiety and seven relate to depression. Each item on the questionnaire is scored from 0-3 with a final score between 0 and 21 for either anxiety or depression, with higher scores indicating greater anxiety and depression symptoms. See the CR intake questionnaire for the HADS.

5.5.10 Self-efficacy

Self-efficacy to reduce sedentary behaviour and increase light and moderate PA will be measured using a reliable questionnaire developed and validated by Adams [20]. The questionnaire includes twelve confidence scales (4 for each measure). Each item is a likert-type scale, ranging from 1 to 5.

Participants are asked to rate their level of confidence (not at all confident to completely confident) for specific sitting and PA behaviors. The average of the four items will produce the score for each particular sub-scale. See the SIT-CR Baseline and Follow-up Questionnaires for the self-efficacy questions.

5.5.11 Health-related quality of life (HRQoL)

Health-related quality of life (HRQoL) will be measured using the Medical Outcomes Study short form (SF-36) [21]. The SF-36 is a multi-purpose, short-form health survey with 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index. See the SIT-CR Baseline and Follow-up Questionnaires for the SF-36.

5.5.12 Maximal aerobic power (VO_2max)

Maximal aerobic power (VO_2max) will be estimated using a Modified Bruce Ramp Treadmill Test [22]. The Modified Bruce Ramp Treadmill Test is a sub-maximal multistage test for the prediction of aerobic capacity. Participants will be asked to walk on the treadmill with the incline and speed increasing every 3 minutes. During the test participants' heart rates (HRs) will be measured at the end of each 3 minute stage. The test is stopped once participants reach 85% of their estimated maximum HR (207-(0.7*age)). The test will be instructed by a research assistant and should take 10-15 minutes to complete. The HR values will be extrapolated to measure HRmax, and VO_2max estimated from the highest speed and grade that would have been achieved if the participant had worked to maximum (see SIT-CR Case Report Form).

5.5.13 Covariates

The following are possible confounders that will be used in the analysis.

Age: Each participant's age will be extracted from the CR patient file.

Sex: Participant's sex will be extracted from the CR patient file.

Education: Participant education is self-reported as part of the CR intake questionnaire and is defined as the highest education level attained from Grade 6 or less, up to 4+ years of college/university.

Marital status: Participant marital status is self-reported as part of the CR intake questionnaire, it is categorized as: "single", "married/common law", "divorced/separated", or "widowed".

Occupational status: Participants' current occupational status is self-reported as part of the CR intake questionnaire and is categorized as: "Full time, working for pay (35 hrs or more/wk)", "retired", "part time, working for pay", "unemployed (looking for work)", "not working, but have a job to return to (e.g. sick leave)", "unemployed", "not/never employed outside the home", or "presently on disability leave".

Occupation activity: Participants that are currently working, will be asked to rate their current occupation activity using the following categories: "mostly sedentary (e.g., desk-based job)",

"moderately active (e.g., mix of desk-based job and walking about)", "active and on your feet most of the time (e.g., teacher, nurse)", or "very active and physical (e.g., mail carrier, manual labour)"

Number of people in the household: Participants will be asked for the number of people in their household.

Season: The season/time of year the participant completed the majority of the intervention will be collected.

5.6 Statistical considerations

5.6.1 Sample size calculation

Pilot/feasibility studies are generally not designed with the power to detect intervention effects, which is the intention of future definitive trials. Pilot/feasibility studies are often carried out to be able to estimate an effect size for a larger trial. However, to provide guidance, we have estimated a sample size based on previous study effect sizes to detect differences in sedentary time. G*Power Version 3.1.9.2 power analysis and sample size software was used to calculate the sample size [23]. A minimal clinically important difference (MCID) for reductions in sedentary time (i.e. substituting sedentary time for light or moderate+ intensity PA) associated with improvements in cardiometabolic health, health-related quality of life and reduced mortality, has been estimated to be 30-60 minutes/day [24-26], with a cumulative effect (i.e. more is better). Unfortunately, as this study is a pilot-level RCT, there are not adequate resources to accommodate a large enough sample size to detect differences in 30 minute/day. Rather, there will be adequate power to detect a difference of 91 minutes/day, which was the average reduction in sedentary time from sedentary interventions found by the authors in a recent systematic review [6]. A total sample size of 32 participants, 16 per arm, is needed to detect a 91 minute/day difference in sedentary time at a 0.05 significance level with 80% power, an addition of 10% for those who do not complete the trial, and 5% for data missing at random, assuming a standard deviation of 94 minutes/day as found in a recent evaluation of sedentary time among CR graduates from the UOHI [5]. This sample size is sufficient to test the research hypothesis using t-tests to measure the difference in sedentary time between the intervention and control groups.

When the study is close to completion a sample size recalculation will be undertaken by the Research Methods Centre at the UOHI.

5.6.2 Analysis strategies

Baseline clinical and socio-demographic characteristics will be compared between groups to identify any chance differences that may have occurred despite random assignment. Outcome variables will be screened to determine whether they meet assumptions of normally distributed random variables with equal variances, and a descriptive examination will be performed, including plotting of relationships by condition. Retention rate will be computed by condition.

For the primary analyses, group differences in objectively measured and self-reported sedentary time (using the average of seven days) over the two time points (baseline and 8 weeks) will be examined using independent t-tests for parametric variables and Wilcoxon Mann Whitney test for nonparametric

variables. Similar analysis techniques will be used for secondary outcomes of interest (i.e., *activ*PAL-measured and self-reported weekly MVPA; BMI, waist circumference, total cholesterol, HDL, LDL, triglycerides, fasting blood glucose, blood pressure, resting heart rate, aortic stiffness, HRQoL scores, self-efficacy scores, HADS scores, and maximum aerobic capacity).

Table 1. Study measurement timeline.

			Cardiac rehabilitation							
Visit	**Screen**	**Baseline week**	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 8/ follow-up**
Length of time needed	30 min	1-2 hours	45 min	30 min	30 min	30 min	30 min	30 min	30 min	1-2 hours
Informed consent	C, I									
Diagnosis	C, I									
Age	C, I									
Sex (male/female)	C, I									
Height		C, I								
Weight		C, I								C, I
Waist circumference		C, I								C, I
Blood pressure (Mobil-O-Graph)		C, I								C, I
Resting heart rate (Mobil-O-Graph)		C, I								C, I
Blood work (cholesterol, HDL, LDL, triglycerides, HbA1c)		C, I								C, I
MVPA (CR questionnaire + *activ*PAL3)		C, I								C, I
Questionnaires (self-efficacy, HRQoL, anxiety/depression)		C, I								C, I
Aortic stiffness (Mobil-O-Graph)		C, I								C, I
Aerobic power (Bruce Treadmill Test)			C, I							C, I
Sedentary time (*activ*PAL3™, IPAQ, CR Questionnaire)		C, I								C, I
7-day activity journal (FITS)		C, I								C, I
Wear-time log			I	I	I	I	I	I	I	
Sedentary feedback (VTAP)			I	I	I	I	I	I	I	
Feedback survey										C, I

C - Control group, HDL - high-density lipoprotein, HRQoL - health-related quality of life, I - Intervention group, IPAQ - International Physical Activity Questionnaire, LDL - low density lipoprotein, MVPA - moderate-to-vigorous intensity physical activity

6.0 RESEARCH PLAN AND FEASIBILITY

6.1 Clinical relevance

Results from this study will provide important missing information regarding movement patterns and sedentary time in patients undergoing CR. Results of the trial will be useful for the design of a larger intervention trial to reduce sedentary time in CR patients and further improve patient-related clinical and behavioural outcomes. Additionally, results of this study will identify whether using the *activ*PAL3™ as a means of measuring sedentary time in a CR population is feasible, and whether the use of prompting devices are acceptable to patients.

6.2 Risks, benefits and usual standard of care

No changes will occur to the usual standard of care for patients enrolled in CR.

Participation in this study requires that participants wear an *activ*PAL3™ monitor taped (using stickers) to the front of the right thigh during waking hours for a minimum of 7 consecutive days (baseline and follow-up) and the VTAP monitor continuously during waking hours for weeks 1-7 in the intervention group. The PALstickies used to apply the *activ*PAL devices are hypoallergenic and consist of a dual layer hydrogel that does not pull at skin or hair. They are used for waking day recordings and are removed when going to bed, showering or bathing and will therefore, be reapplied each morning. In order to reduce possible skin irritations, participants in the intervention group will be instructed to alternate the location and leg used over weeks 1-7. The monitors are not an intentional emitter or radiator of electric or magnetic fields and poses no risk to a person fitted with a pacemaker. Important to note however that there are some limitations to when the monitor can be worn during scans and testing. The table below outlines when it should be removed and will be provided in the information sheet to participants:

Scan/test	Affects activPAL	activPAL affects scan	Comment/action
MRI scan	YES	YES	Remove from test
CT scan	YES	YES	Remove from test
X-ray	NO	Yes if in imaged area	Remove if in imaged area
EMG	NO	MAYBE if in test area	Remove if thigh is tested
ECG	NO	NO	ECG electrodes are on chest
EEG	NO	NO	EEG electrodes are on chest

Participation in this study requires that participants perform an exercise test (Modified Bruce Treatment Test) and training sessions. The risk of cardiovascular events during exercise testing varies directly with the incidence of cardiovascular disease. The risk of exercise testing is low, with approximately 6 cardiac events per 10,000 tests (0.06%). This is comparable to the usual care that patients in cardiovascular rehabilitation programs would receive. Recent studies have reported a rate of 1 cardiac arrest per 116,906 patient-hours, 1 myocardial infarction per 219,970 patient-hours, 1 fatality per 752,365 patient-hours, and 1 major complication per 81,670 patient-hours in a cardiovascular rehabilitation setting. It should be noted that these rates are low and

likely due to the fact that patients in these studies were screened and exercised in a medically supervised setting equipped to handle emergencies. This is the case of the UOHI, Division of Prevention and Rehabilitation.

The commonly reported side effects that may result from exercise testing and training sessions may include palpitation, chest pain, shortness of breath, headache, nausea and/or fatigue.

Participants may find the questionnaires regarding HRQoL (Short Form 36) and anxiety and depression (HADS) distressing.

Mild discomfort is sometimes associated with blood draws, however, the procedure is quick, completed by a trained professional in a sterile environment and is associated with minimal discomfort.

6.3 Monitoring and reporting of adverse events/serious adverse events

The following definitions have been approved as part of Good Clinical Practice in Research:

Unanticipated problem
An unanticipated problem is defined as any incident, experience, or outcome that meets all of the following criteria:

Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the REB-approved research protocol and informed consent document, or the Investigator Brochure (IB) or product monograph (PM); and (b) the characteristics of the research participant population being studied; and

Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the [investigational product(s)] or procedures involved in the research); and

Suggests that the research places research participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Adverse event
An adverse event is defined as any untoward medical occurrence in a research participant administered an investigational product and which does not necessarily have a causal relationship with this product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of an investigational product, whether or not related to the investigational product.

Serious adverse event
To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe," which are not synonymous, the following note of clarification is provided:

The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache).

This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a patient's life or functioning.

Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

After reviewing the various regulatory and other definitions in use or under discussion elsewhere, the following definition is believed to encompass the spirit and meaning of them all:

A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose:

- results in death;
- is life-threatening;
- requires inpatient hospitalization or prolongation of existing hospitalization;
- results in persistent or significant disability/incapacity; or
- is a congenital anomaly/birth defect.

The term "life-threatening" in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

Medical and scientific judgment should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above. These should also usually be considered serious.

Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization; or development of drug dependency or drug abuse.

All unanticipated problems/adverse events/serious adverse events will be recorded on the case report form (CRF) and in the source documents at the site of testing. A log for all unanticipated problems/adverse events/serious adverse events occurring in the study will be kept. The details of any unanticipated problems/adverse events/serious adverse events at each study visit, using the protocol-defined terminology, will be recorded.

The principal investigator and or study staff will educate the participants about unanticipated problems/adverse events/serious adverse events as well as the importance of reporting them to the study coordinator at study visits.

Anyone within the research team who becomes aware of unanticipated problems/adverse events/serious adverse events will report this to the principal investigator. The principal investigator will assess the unanticipated problems/adverse events/serious adverse event and provide the research participant with appropriate medical care as applicable. The principal investigator will report to the REB within 7 days only the local adverse events/serious adverse events that are deemed to be unanticipated problems.

The monitoring of these unanticipated problems/adverse events/serious adverse will be made in accordance with SOP C3-007.1 Safety Reporting Requirements.

6.4 Benefits of participant participation

Participants may not receive any direct benefit from their participation in this study. Upon completion of the study, participants will receive a summary of their sedentary and health measurements.

6.5 Withdrawal criteria

Participants have the right to withdraw from the study at any point in time. Personnel conducting the study have the right to withdraw participants from this study for any of the following reasons:

- The investigator feels it is in the participant's best interest.
- Participant needs medication/treatment that would interfere with the study.
- Participant does not follow the study staff's instructions.

6.6 Confidentiality/privacy

All Personal Health Information (PHI) and Personal Identifying Information (PII) will be kept confidential, unless release is required by law. Release of PHI/PII information will only be allowed if it is legally required by law. For audit purposes only, representatives of the Ottawa Health Sciences Network Research Ethics Board (OHSN-REB) and the University of Ottawa Heart Institute may review participants' records under the supervision of Dr. Stephanie Prince Ware.

Results of research studies should be shared, to ensure participants are always provided with the best possible care. Therefore, results from this study may be presented at scientific conferences and/or published in journals but participants' will not be identifiable in any publications or presentations.

All participants will be assigned a study ID number once informed consent in obtained. The study ID will serve as the only identifier used on all study related documents. Informed consent will occur at the time of recruitment once verification of eligibility has been completed. The master list will be maintained by study staff and stored in a separate file from the coded study dataset on a password protected computer. The master list will be in a password protected file stored separately from all other study files; the master file will be password protected and only individuals directly involved with the study (e.g., principal investigator or designate) will have

access to this file. The participant identifiers to be stored in the master list include full name and contact information (e.g., phone number, email, address). The UOHI and the Health Sciences Network Research Ethics Board (OHSN-REB) will have access to the records for audit purposes.

A separate database will be kept that contains study ID numbers along with personal identifiers. The database containing descriptive information (e.g., height, weight, etc.) will only have study ID numbers as identifiers. Case Report forms will only have study ID numbers used as identifiers, all other personal information (e.g., name) will not be collected on these forms. Participants will be reminded not to write their name on any forms. Please refer to the Case Report Form (CRF) for personal health information to be collected.

No identifying information will leave the UOHI. All information that leaves the UOHI will be coded with an independent study number that will be used throughout the study on all of the study records. The Master List which links participants' name and the independent study number will only be accessible by Dr. Stephanie Prince Ware and/or her staff. The link and study files will be stored separately and securely.

6.7 Record keeping/document management

Dr. Prince Ware and research assistants will perform all data collection and entry. Data quality will be maintained via validation checks at the time of data entry and will be reviewed and cleaned on an on-going basis by a Research Assistant.

Both paper and electronic records will be kept by Dr. Prince Ware and her staff. All paper records will be stored in a locked filing cabinet and office. All electronic records, including the Master List, will be stored on a secure internal hospital server and password protected, only accessible by Dr. Prince Ware and/or her staff. No identifiable information will be stored on any mobile devices (laptops, USB keys, CDs, DVDs, etc.). Research files will be kept for a period of 10 years after the study has been completed, as required by law. At the end of the retention period, all paper records will be disposed of in confidential waste for shredding and all electronic records will be securely deleted.

6.8 Data handling

All data will only be accessible by the Principal Investigator, Co-Investigators or Research Staff.

6.9 Proposed timeline

Submission to the Ottawa Health Science Network Research Ethics Board – May 2016
Registration with ClinicalTrials.gov – June 2016
Acquire *activ*PAL devices – June 2016
Start date for recruitment and enrollment – July 2016
End of recruitment – December 2016
End of data collection – February 2017
Data analysis – March 2017
Final Report generation – April 2017

Publication of results – June 2017

6.10 Assembled research team

Robert Reid (PhD, MBA), is Deputy Chief of the Division of Prevention and Rehabilitation Centre at UOHI, and a Full Professor in the Faculty of Medicine at the University of Ottawa. He has extensive experience conducting RCTs of rehabilitation interventions in patients with heart disease [27-32]. Dr. Reid will have overall responsibility for the conduct of the trial. **Stephanie Prince Ware (PhD)** is a post-doctoral fellow in the Division of Prevention and Rehabilitation at UOHI. Her post-doctoral work is focuses on sedentary behaviours in cardiac populations and their effects on health. She has expertise in the use of activity monitors in research and clinical settings. Dr. Prince Ware will be responsible for the final analysis of the study results. Dr. Prince Ware will also be overseeing the trial. **Jennifer Reed (PhD, MEd CS)** is an Associate Scientist in the Division of Prevention and Rehabilitation at the UOHI and a Part-Time Professor at the University of Ottawa in the Faculty of Health Sciences. She led a RCT examining the role of feedback from a motion sensor with a web application on nurses' physical activity levels. Dr. Reed will provide guidance on the project and its design and will contribute to the final analysis and interpretation of the study results.

6.11 Funding

This trial is made possible through the provision of an equipment award (PI: Dr. Prince Ware) to provide the *activ*PAL3™ and VTAP devices from PAL Technologies Ltd. Dr. Prince Ware is the recipient of their "Show Us the Numbers" competition which provides up to £12000 in equipment. For further information please see: http://www.paltechnologies.com/blog/university-of-ottawa-heart-institute-submission-wins-pal-competition-prize/

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