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Effects of reducing sedentary behaviour on cardiovascular health, skeletal muscle oxidative capacity and functional exercise capacity in sedentary adults: a randomised controlled trial

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ABSTRACT

Purpose This study aimed to investigate the effectiveness of a 12-week intervention using self-monitoring alone and in combination with motivational interviewing to reduce sedentary behaviour (SB) and improve cardiovascular health, as reflected by cardiac autonomic function, endothelial function, skeletal muscle oxidative capacity and functional exercise capacity in sedentary adults.

Methods In a three-armed randomised controlled trial, 59 (36% male; age: 53.3±8.7 years) sedentary adults were randomly allocated to a control group, a self-monitoring (consumer wearable activity tracker, CWAT) group or the self-monitoring+motivational (CWAT+) group for 12 weeks. SB and physical activity were assessed using activPAL3 accelerometer. Endothelial function was assessed using non-invasive peripheral arterial tonometry with the EndoPAT2000 device and fasting blood samples. Muscle oxidative capacity was evaluated using a submaximal cardiopulmonary exercise test, functional exercise capacity via a 6 min walk test, and cardiac autonomic function through heart-rate variability analysis.

Results The CWAT+group significantly reduced time spent in SB, which resulted in improvements in muscle oxidative capacity (time constant τ: −4.9 s±10.9 s; p=0.010), functional exercise capacity (6 min walking distance: +53 m±36 m; p=0.014) and measurements of heart rate variability (HRV) reflected by the root mean square of successive differences between normal adjacent R-R intervals (112 23 ms; p=0.014), low-frequency component (1178 (11, 2344) ms^2; p=0.039) and high-frequency component (471 (18, 960) ms^2; p=0.035), compared with controls.

Conclusion A reduction in SB results in improvements of HRV, skeletal muscle oxidative capacity and functional exercise capacity in sedentary adults, mainly driven by an increase in moderate-to-vigorous physical activity.

Trial registration number NCT03853018.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Prolonged sedentary behaviour is strongly associated with an increased risk of cardiovascular disease. It negatively affects key physiological systems by contributing to endothelial dysfunction, autonomic imbalance, impaired glucose metabolism and reduced muscle oxidative capacity, which are all early markers of poor cardiovascular health.

WHAT THIS STUDY ADDS

⇒ Combining self-monitoring and motivational interviewing is associated with small improvements in cardiac autonomic function, skeletal muscle oxidative capacity and functional exercise capacity in healthy adults. The observed benefits were largely driven by increases in moderate-to-vigorous physical activity (MVPA) rather than reductions in sedentary behaviour alone. This suggests that reducing sedentary time must be accompanied by increased MVPA to elicit measurable cardiovascular health-related benefits.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This may facilitate the integration of a behaviour change intervention at reducing sedentary behaviour and improving cardiovascular health into healthcare and community programmes.

INTRODUCTION

Cardiovascular diseases (CVDs) are the major cause of death worldwide, leading to an estimated 32% of all deaths each year.[1] The risk of developing CVD could considerably be reduced by addressing behavioural risk factors such as tobacco use, unhealthy diet, physical inactivity and sedentary behaviour (SB). With respect to the latter two, the health benefits of daily moderate-to-vigorous physical activity (MVPA) are well established due to the positive effects on blood pressure (BP), serum lipids, endothelial function, cardiac autonomic function and skeletal muscle oxidative capacity, which are all independently associated with increased CVD risk.[2–4] In contrast,

there is emerging evidence that prolonged SB, defined as 'any waking behaviour characterised by ≤1.5 metabolic equivalents of task, while being in a sitting, reclining or lying posture',[5] is associated with several negative consequences on cardiovascular health[6–8] and an increased risk for developing CVD.[9] Despite evidence suggesting a negative association between SB and cardiovascular health outcomes, adults in westernised societies still spend an average of approximately 9 hours per day being sedentary.[10] Furthermore, emerging evidence in middle-aged adults indicates that substituting SB with LPA and MVPA is associated with a lower risk of CVD.[11 12] This association appears even stronger in older adults,[13] where studies suggest that each additional 30 min per day of light-intensity physical activity (LPA) or MVPA is associated with approximately 11% and 36% reductions in CVD mortality risk, respectively.[11] These findings underscore the importance of reducing SB as a public health priority.

Various behaviour change strategies, including environmental modifications, education, motivational counselling and consumer wearable activity trackers (CWATs), have been applied to reduce SB in adults.[14–18] However, existing interventions remain limited, and most focus on workplace settings rather than leisure-time SB, which constitutes the largest proportion of daily sedentary time.[14 17] Behaviour change techniques (BCTs) such as self-monitoring with CWATs show promise by increasing awareness of habitual behaviours and providing feedback to help disrupt undesired patterns.[16 19] Nevertheless, most studies have implemented multicomponent interventions, making it difficult to isolate the specific effect of self-monitoring. Motivational interviewing is another promising BCT, known for enhancing motivation and recommended by the American Heart Association for promoting physical activity and dietary change,[20 21] although evidence of its effectiveness in reducing SB specifically remains limited.[22] Overall, while both CWATs and motivational interviewing appear promising, further research is needed to identify the most effective strategies for reducing SB in free-living adults.

Both endothelial and autonomic dysfunctions are early, sensitive and often subclinical markers of cardiac events. Investigating these markers provides insight into the underlying mechanisms that precede overt disease and highlights opportunities for early intervention and prevention. Specifically, endothelial dysfunction and autonomic imbalance, particularly reduced parasympathetic (vagal) activity and increased sympathetic drive, are associated with elevated CVD risk.[23–25] In addition, prolonged SB has been shown to reduce muscle oxidative capacity, potentially due to lower oxidative enzyme activity,[26] diminished mitochondrial respiration and impaired muscle perfusion.[27] This decline in muscle oxidative capacity is associated with an increased risk of CVD.[28 29] In contrast, MVPA appears to play a key role in maintaining and enhancing muscle oxidative capacity, whereas the effects of LPA are less pronounced.[30]

Laboratory-based and short-term studies have demonstrated that interrupting prolonged periods of SB with bouts of physical activity can significantly improve these early markers of cardiovascular health.[7 31 32] In contrast, evidence from interventions conducted in free-living conditions remains limited, particularly regarding their impact on cardiovascular health and muscle oxidative capacity.[33 34] Reported effects on cardiovascular outcomes are inconsistent, and most studies have focused primarily on BP.[14 32 34 35] A few randomised controlled trials have examined the impact of reducing SB through standing interruptions.[32 35] However, these interventions generally did not produce significant improvements in BP. These findings suggest that replacing sedentary time with physical activity, rather than standing alone, may be more effective for improving cardiovascular health.

Therefore, this study aims to investigate the effects of reducing SB on key markers of cardiovascular health, including autonomic nervous system regulation, endothelial function, muscle oxidative capacity and functional exercise capacity. In addition, the second aim is to investigate to what extent standing, LPA and MVPA affect these early markers of cardiovascular function.

MATERIALS AND METHODS

This study consists of secondary outcomes related to cardiovascular and skeletal muscle oxidative capacity and was registered at ClinicalTrials.gov (NCT03853018).[36] In addition, this study was reported in accordance with the Consolidated Standards of Reporting Trials guidelines.

Subjects

59 sedentary adults (sitting time of ≥9 hours/day, 40–75 years of age) were recruited via online and paper advertisements, as described previously.[36] Participants were excluded when systolic BP was >140 mm Hg, diastolic BP >90 mm Hg, body mass index: > 35 kg/m^2, HbA1c>6.5%, when they were pregnant or physically active (>150 min per week during the last 4 months), any cardiometabolic disease, any known contra-indication for physical activity, frequent alcohol use (> 14 alcohol consumptions per week), or planning a weight reduction programme (energy restriction or increase in physical activity). These criteria were assessed during a screening visit involving a medical examination, including their medical history, general health and medication use by means of a general health questionnaire. In addition, HbA1c was measured and the cardiovascular status was screened using a resting 12-lead electrocardiogram (Mortara ELI150c, Welch Allyn, Chicago, Illinois, USA) and resting BP measurement (Omron M2, Omron Healthcare, Lake Forest, Illinois, USA). Potential participants were screened for current use of CWATs, and none reported any usage. Throughout the study trial, participants were instructed to consume and maintain their habitual diet. To assess whether participants were sedentary, physical activity (secondary outcomes) and SB (primary outcome) were assessed using the activPAL3 accelerometer (PAL

Technologies, Glasgow, Scotland) for seven consecutive days.

Study design

The study was performed under free-living conditions using a non-stratified, non-blinded, randomised controlled design, as described previously.[36] Eligible participants were included for baseline measurements and instructed to refrain from strenuous physical exercise (3 days prior to the test day), consuming alcohol (1 day prior to the test day) and consuming food (1 day prior to the test day; from 20:00). During the testing day, the following secondary measurements were performed in sequential order: (1) anthropometry and body composition, (2) BP measurement, (3) heart rate variability (HRV), (4) vascular endothelial function, (5) venous blood samples were collected for measurements of systemic low-grade inflammation and markers of microvascular endothelial function, (6) submaximal exercise test and (7) a 6 min walking test. Prior to the submaximal exercise test and the 6 min walking test, a standardised meal was provided. After 12 weeks all baseline measurements were repeated. In addition, at the beginning and at the end of the intervention period, dietary intake was assessed for seven consecutive days.

Control and intervention conditions

Study participants were randomly allocated to (1) the control group (CON) without any intervention, (2) the CWAT-only (CWAT) group receiving only a CWAT or (3) the CWAT+ group where participants got a CWAT in combination with additional motivational techniques via the ELCIES (ELCIES, Gent, Belgium) lifestyle data platform. Blocked randomisation was performed by an independent researcher using a random block size of two, three or four with the aid of sealed envelopes and eligible participants were randomly assigned using an established allocation ratio of 1:1:1. As described by Franssen *et al*,[36] the CON group continued their habitual daily physical activity behaviours. The CWAT group received real-time feedback from a CWAT device (Polar M200, Polar Electro, Kempele, Finland) in the form of step count and inactivity alerts after 1 hour of inactivity, prompting them to break up sitting time and avoid prolonged SB. During the interruptions, they were asked to walk or stand for at least several minutes. Participants were instructed to increase their step count to 10 000 steps per day, distributed throughout the day during the interruptions of SB. Step count thus served as a practical tool to prompt movement and interrupt sedentary periods.

Participants from the CWAT+group were motivated by both the Polar M200 device and motivational techniques such as an information session to increase participants' awareness of the negative independent impact of SB on the risk of chronic disease development and motivational interviewing via weekly chat conversations under the guidance of a psychologist.[37] All communication and visualisation of physical activity information was supported via a healthy lifestyle data platform (www.elcies.com). During the chat conversations, participants set their own goals of daily sedentary time and physical activity levels, the reasons for interrupting sitting time were identified and enforced, participants' concerns with respect to sitting less were identified and solutions were provided and possibilities to reduce and interrupt sedentary time as much as possible were provided. A more detailed description of the intervention groups has been described previously.[36]

Physical activity and SB assessment

Physical activity and body postures were measured 24 hours per day for seven consecutive days (without removing it at any time) using the activPAL3 activity monitor (PAL Technologies, Glasgow, Scotland) with a sampling frequency of 20 Hz. The device was fully waterproofed using nitrile sleeves and attached to the anterior mid-thigh of the participants' right leg using an adhesive dressing (Tegaderm, 3M, Minnesota, USA). The activPAL could accurately discriminate between SB (sitting and lying), standing and walking in free-living conditions.[38] Raw data were processed and analysed using the PALanalysis software (V.8, CREA V.1.3, PAL Technologies). Sleeping and waking hours for each wear day were identified using the built-in algorithm, which automatically detects sleep periods.[39] Data from the activPAL software were also processed using customised scripts written in MATLAB R2013b (MathWorks, Natick, MA, USA) to correct for misclassified sleeping times.[40]

Output variables from the activPAL software included sleeping time and waking time, the latter consisting of sedentary time (sitting or lying), standing time and physical activity. Physical activity variables included step count and step cadence, classified as low-intensity physical activity (<100 steps/min) and MVPA (>100 steps/min).[39 41] In addition, short (<30 min) and prolonged (>60 min) sedentary bouts were derived using the PALanalysis software.

Anthropometry, body composition and BP assessment

Body height and weight were measured with participants barefoot. Waist and hip circumferences were measured in triplicate to the nearest 0.1 cm and the mean value of the triplicate measurements was used in the analysis. Whole body composition (fat mass and lean tissue mass) was measured with the aid of Dual Energy X-ray Absorptiometry (Hologic Series Delphi-A Fan Beam X-ray Bone Densitometer, Vilvoorde, Belgium). The mean arterial pressure was calculated from the systolic and diastolic BP using an electronic sphygmomanometer (Omron, Omron Healthcare).

Heart rate variability

The HRV is a non-invasive and easily measured parameter in a time-dominant or frequency-dominant form and reflects cardiac autonomic function.[42] After a 20 min resting period in supine position, continuous beat-to-beat

heart rate signal measurements were obtained at a sampling frequency of 1000 Hz for the duration of ten minutes using the Polar V800 heart rate monitor (Polar Electro, Kempele, Finland) in combination with a Polar H10 chest strap heart rate sensor. During the measurement, participants were instructed to remain lying down and stay as relaxed as possible. Prior to analysis, the R-R intervals were corrected by cubic spline interpolation for ectopic beats and artefacts according to the recommendations of the Task Force of the Society of Cardiology and the North American Society of Pacing and Electrophysiology.[43] Then, time domain analysis of the R-R intervals was performed, including the root mean square of successive differences between normal adjacent R-R intervals (root mean square of the successive difference, RMSSD). Power spectral density of HRV signals was applied using a fast Fourier transformation and was classified as: power of the very low-frequency (VLF; 0.00–0.04 Hz) band, power of the low-frequency (LF; 0.04–0.15 Hz) band, power of the high-frequency (HF; 0.15–0.40 Hz) band and the LF/HF ratio. These variables reflect the autonomic system dynamics (autonomic balance) where the HF band is designated as parasympathetic nervous system activity, the LF band reflects both parasympathetic and sympathetic activity and the LF/HF ratio reflects the autonomic balance.[44]

Vascular endothelial function

Endothelial function was assessed by non-invasive peripheral arterial tonometry (PAT) using the EndoPAT 2000 device (Itamar Medical, Caesarea, Israel), according to manufacturer's instructions. Subjects were tested in a supine position in a quiet room with constant temperature (19°C–21°C). Two flexible pneumatic probes were placed on the right (ischaemic) and left (control) index fingers to measure the PAT, a non-invasive measure to detect pulsatile volume changes in peripheral arterial beds. In addition, a constant inflation pressure (predetermined resting diastolic BP) was applied through these flexible probes to avoid distal venous distention, thereby preventing venous pooling and a subsequent venoarteriolar reflex vasoconstrictor response.[45] The test protocol consisted of a 5 min reference phase, a 5 min occlusion (ischaemic) period and a 5 min reactive hyperaemia (hyperaemic) phase. After the 5 min baseline period, a BP cuff on the right upper arm was inflated to 250 mm Hg for 5 min. Temporary occlusion of the pulsatile arterial flow, causing transitory arm ischaemia, was confirmed by the reduction of the PAT signal to zero. On cuff deflation, changes in PAT signal (increase in PAT signal) were recorded in response to reactive hyperaemia. The reactive hyperaemia response was reflected by the reactive hyperaemia index (RHI) and calculated as the ratio of the average PAT signal in the hyperaemic phase to the baseline PAT signal (post-to-pre-occlusion PAT signal ratio) in the occluded arm, with normalisation to the ratio of the PAT signal in the control arm to account for any systemic haemodynamic changes. A high value (>1.67) of the RHI indicated a normal endothelial function, whereas an RHI of <1.67 was indicated as endothelial dysfunction.

Systemic low-grade inflammation and markers of microvascular endothelial function

After antecubital catheter placement, fasting blood samples were obtained for the measurement of cardiovascular risk markers. EDTA-containing BD vacutainer tubes (Becton, Dickinson and Company, Franklin Lakes, New York, USA) were collected. To obtain plasma, EDTA tubes were immediately centrifuged at 1300 x g for 15 min. All centrifugation steps were performed at room temperature (21°C). Supernatants were immediately portioned into aliquots and frozen at −20°C and subsequently moved to a − 80°C freezer until analysis at the end of the trial. Sodium heparinised 18 µL capillary tubes (Marienfeld, Lauda-Königshofen, Germany) were used to collect capillary blood from the middle finger. Blood glycated haemoglobin A1c (HbA1c) concentration was assessed using ion exchange chromatography (Menarini HA-8180 HbA1c auto-analyser, Menarini Diagnostics, Diegem, Belgium). Plasma from EDTA tubes was used for measurements of markers of low-grade systemic inflammation (C reactive protein (CRP) and serum amyloid A (SAA)) and markers of microvascular endothelial function (soluble vascular cell adhesion molecule (sVCAM)-1, soluble intercellular adhesion molecule (sICAM)-1 and soluble endothelial selectin (sE-selectin)) using a Meso Scale Discovery single or multiplex sandwich immunoassay detection system based on electro-chemiluminescence technology (SECTOR Imager 2400; Meso Scale Discovery, Rockville, Maryland, USA), according to the manufacturer's instructions. All measurements were performed in duplicate. The intra-assay and interassay coefficients of variation were 4.7% and 4.1% for CRP, 5.2% and 4.9% for SAA, 4.3% and 4.7% for sVCAM-1, 5.5% and 4.5% for sICAM-1 and 6.1% and 6.6% for sE-selectin, respectively.

Exercise-onset oxygen uptake kinetics

Skeletal muscle oxidative capacity was assessed by exercise-onset oxygen uptake ($\dot{V}O_2$) kinetics, which is a sensitive tool for specific evaluation of skeletal muscle oxidative capacity.[46] Participants performed a submaximal cardiopulmonary exercise test on an electronically braked cycle ergometer (eBike BasicR, General Electric, Bitz, Germany). With the aid of continuous pulmonary gas exchange analysis $\dot{V}O_2$ was collected breath-by-breath (Metalyzer IIR 3B Cortex, Leipzig, Germany). The exercise test protocol included a 3 min pre-exercise resting period, a 6 min exercise period and a 6 min resting period and was repeated twice. During an exercise bout, participants were instructed to cycle against a resistance corresponding to 25% of the predicted maximal cycling power output and to maintain a cycling frequency of 70 revolutions per minute. Predicted maximal cycling power output was calculated as previously described and based on sex, age, body weight and height.[47] The analysis was performed as previously described by Koppo *et al*.[48].

Briefly, raw breath-by-breath $\dot{V}O_2$ data from each test were initially examined to exclude aberrant breaths caused by coughing and swallowing. $\dot{V}O_2$ data with more than 4 SD from the local mean were deleted. Subsequently, the breath-by-breath $\dot{V}O_2$ data were linearly interpolated to give 1 s values. For each subject and each intervention regimen, the two repetitions of each work rate were time-aligned to the start of exercise, superimposed and ensemble averaged to reduce the breath-to-breath noise and enhance the underlying physiological response characteristics. The baseline $\dot{V}O_2$ was defined as the average $\dot{V}O_2$ measured between 150 and 30 s before the start of the exercise bout. The initial cardiodynamic component was ignored by eliminating the first 20 s of data after the onset of exercise. As none of the transitions evidenced a slow component, each averaged response was described using a single exponential model with the following equation:

$$\dot{V}O_2\ (t) = \dot{V}O_{2\ baseline} + A\left(1 - e^{-(t-Td)/\tau}\right) \quad (1)$$

This model includes an amplitude (A), a time constant (τ) and a delay time (Td), which were determined using a non-linear least-square algorithm. The O_2 deficit was determined by integrating the difference between the $\dot{V}O_2$ requirement for the exercise and the actual measured $\dot{V}O_2$ from t=0 s to t=360 s.

Submaximal functional exercise capacity

The submaximal functional exercise capacity was measured using the 6 min walk test (6MWT) and performed in a 30 m hallway and in accordance with the guidelines from the American Thoracic Society.[49] Participants were instructed to cover the greatest distance (6 min walking distance, 6MWD) possible within a 6 min period at a self-determined walking speed (without jogging or running). Subjects were verbally encouraged to achieve maximal effort. The 6MWT was stopped if the subjects experienced chest pain, intolerable dyspnoea or leg cramps.

Statistical analysis

Statistical analyses were performed by IBM SPSS V.27.0 (IBM SPSS Statistics for Windows). Data were expressed as mean±SD, unless otherwise indicated.

The Shapiro-Wilk test was used to test normality of the data (p<0.05). Because the markers of endothelial function and low-grade inflammation show a marked intraindividual variation, the biological variability of each measure was reduced by calculating a standardised averaged sum score (*z*-score). *Z*-scores were determined according to a predefined cluster of conceptually related biomarkers, as described elsewhere,[50] and calculated as follows: first, for each individual biomarker a *z*-score was calculated as: (individual value–population mean)/population SD. The endothelial function overall *z*-score (zEF) was calculated by averaging the individual *z*-scores of the biomarkers sICAM-1, sVCAM-1 and sE-selectin. The low-grade inflammation overall z-score (zLGF) was calculated by averaging the individual *z*-scores of the biomarkers CRP, SAA and sICAM-1. The sICAM-1 levels were included in both of the overall *z*-scores as it is expressed by both monocytes and the endothelium and is strongly affected by inflammatory stimuli.[51]

Baseline characteristics between the three groups were compared using general linear model analyses (Bonferroni post hoc comparison test). Data were analysed using an intention-to-treat approach. Comparisons between groups were tested using Fisher's exact test for categorical variables. Intervention effects were calculated using linear mixed-effects models for repeated measurements, with physical activity, SB and cardiovascular health-related variables as dependent variables, and group (control, CWAT and CWAT+), time (baseline and post 12-week intervention), and their interaction (group×time) as independent variables. To further examine specific between-group differences, general linear models to the change scores (baseline and post 12-week intervention) were subsequently applied. A pairwise analysis (Bonferroni post hoc comparison test) was performed when a significant interaction effect was found. A p<0.05 (two tailed) was considered statistically significant. Multivariate regression analyses were performed on pooled data including all groups (control, CWAT and CWAT+) to examine associations between the change scores (baseline to post–12-week intervention) for SB, physical activity, cardiovascular health, skeletal muscle oxidative capacity and functional exercise capacity outcomes that showed significant improvements after the intervention.

Cardiac autonomic function (RMSSD, LF and HF), skeletal muscle oxidative capacity (τ) and functional exercise capacity (6MWD) variables were used as dependent variables and standing time, LPA and MVPA as independent variables. Model 1 was the unadjusted model, model 2 corrected for potential confounders sex and age, and model 3 also corrected for all other variables (standing, LPA and/or MVPA). The sample size calculation was performed using GPower V.3.1 (Düsseldorf, Germany). Prince *et al* showed in a systematic review and meta-analysis a significant reduction in SB (effect size d: 1.08) in adults.[18] Based on a statistical power >0.8 and a two-sided alpha of 0.017 (0.05/3 groups), it was calculated that a sample size of 16 individuals per group had to be included in the present study. Taking into account a drop-out rate of 10%, the number of participants to include in this study was at least 18 participants per group.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

Subject characteristics

A total of 137 persons showed interest to participate in the study, of which 79 were invited to be screened for

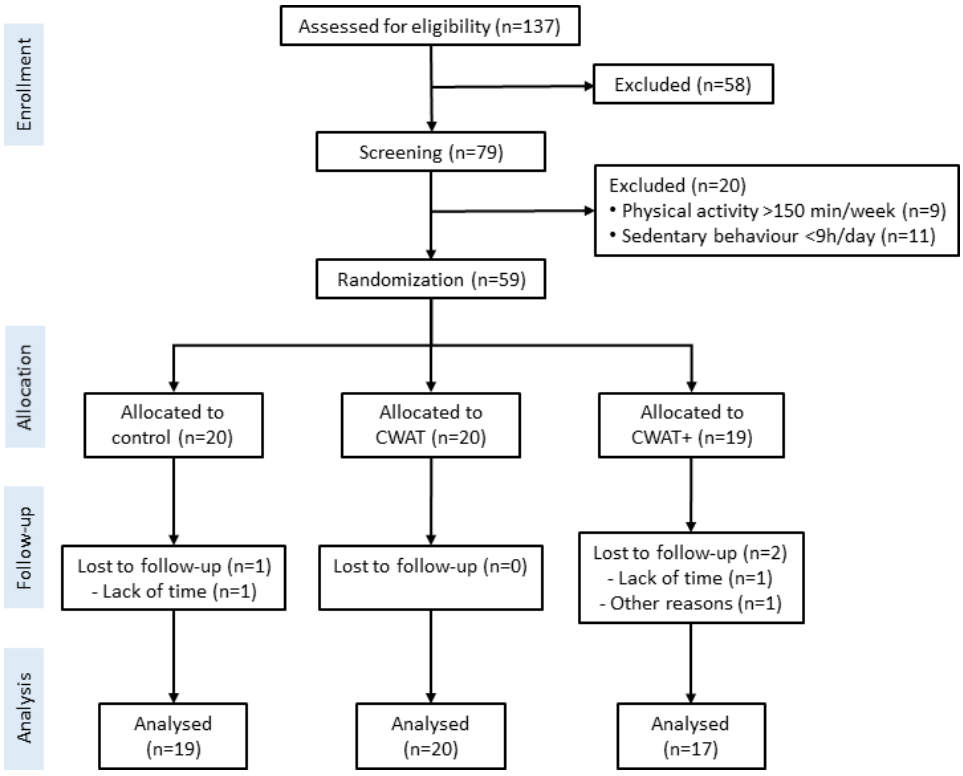

Figure 1 Study flow chart of the eligible and ultimately included participants. CWAT, consumer wearable activity tracker.

study eligibility (figure 1). 20 subjects were excluded due to a sedentary time <9 hours/day (n=11) or spending more than 150 min of structured physical activity per week (n=9). A total of 59 individuals were randomly assigned to either the control (n=20), CWAT (n=20) or CWAT+ (n=19) group. Three participants from both the control (n=1) and the CWAT+ (n=2) group dropped out mainly due to lack of time. In addition, no significant differences between subject characteristics were found between groups at baseline (table 1).

Physical activity and SB

Linear mixed-effects models revealed significant group by time interactions for SB, standing time, LPA and MVPA (all p<0.05, see online supplemental Appendix I). General linear models indicated that, compared with the CON group, a 12-week intervention combining CWATs and motivational interviewing (CWAT+) significantly reduced time spent in SB. (−77 (−148, −9), p=0.031), mainly due to spending less time in bouts of more than 1 hour. Here, sedentary time was replaced by significant increases in standing time (62 (14, 110), p=0.017), LPA (28, (7 50) p=0.032) and MVPA (23, (4 40) p=0.040).

Systemic low-grade inflammation and markers of microvascular endothelial function

No significant differences were found between groups (pre vs post intervention) for markers of vascular endothelial function and low-grade systemic inflammation (table 2).

Cardiac autonomic function

Linear mixed-effects models revealed significant group by time interactions for RMSSD, LF and HF (all p<0.05). Measurements of HRV reflected by RMSSD (CWAT+vs. control: 12[4 27] ms; p=0.014), LF (CWAT+vs control: 1378 (57, 2744) ms^2; p=0.034) and HF (CWAT+vs control: 493 (33, 911) ms^2; p=0.023) were all significantly increased in subjects allocated to the CWAT+group, compared with the CON group (figure 2). However, VLF and the LF/HF ratio were not statistically different between groups. No significant differences were found between subjects from the CWAT group compared with the CON and CWAT+group.

Exercise-onset oxygen uptake kinetics and functional exercise capacity

No significant differences (p>0.05) in $\dot{V}O_2$ throughout exercise prior to or after the intervention period were found between groups (table 2). Similarly, no significant difference was observed in the amplitude (A) between the different interventions or in the time at which exercise response emerged (T_d). On the other hand, a significant group by time interaction effect (p=0.026) was found for the time constant τ. General linear models showed that the time constant τ was significantly reduced in the CWAT+-intervention (−4.7 s±2.9 s; p=0.012), compared with the CON. Although this faster $\dot{V}O_2$ response did not significantly affect the O_2 deficit, both parameters were significantly correlated with each other (r=0.483, p<0.001). A significant group by time interaction effect

Table 1 Subject characteristics of the control, CWAT and CWAT+ groups

General features	Control (n=20)	CWAT (n=20)	CWAT+ (n=19)	P value
Age (years)	53.8±8.5	52.4±8.7	53.8±9.2	0.853
Sex (m/f)	6/14	7/13	8/11	0.745
Body weight (kg)	75.8±11.5	76.6±14.6	74.7±12.7	0.899
Body height (cm)	169.7±7.9	171.1±7.9	171.3±10.3	0.812
BMI (kg/m²)	26.3±3.8	26.2±4.9	25.4±3.6	0.738
Waist circumference (cm)	88.5±10.0	89.2±13.9	87.2±10.1	0.866
Hip circumference (cm)	98.2±9.3	99.7±11.2	97.4±8.0	0.739
Waist-to-hip ratio	0.90±0.08	0.89±0.08	0.90±0.07	0.916
Lean mass (kg)	46.5±7.1	48.3±6.5	47.9±9.1	0.782
Fat mass (%)	34.0±9.6	31.9±9.5	31.5±6.6	0.619
HbA1c (%)	5.3±0.3	5.4±0.3	5.3±0.4	0.747
Total sedentary time (min/day)	637±68	633±83	669±75	0.266
Standing time (min/day)	213±61	239±67	203±51	0.161
LPA (min/day)	71±15	72±17	63±17	0.143
MVPA (min/day)	24±15	22±13	20±13	0.680
Steps per day	7424±1828	7336±1884	6597±1765	0.311
Smoking status (n)				0.447
Current	0	0	1	
Former	5	7	3	
Never	15	13	15	
Chronic disease (n)				0.110
Respiratory	1	0	1	
Cardiovascular	0	5	3	
Medication (n)				0.272
Beta blocker	0	3	2	
Angiotensin II-antagonist	0	2	1	
Bronchodilator	1	0	1	

Data are expressed as mean±SD.
BMI, body mass index; CWAT, consumer wearable activity tracker; HbA1c, glycated haemoglobin A1c; LPA, light-intensity physical activity; MVPA, moderate-to-vigorous intensity physical activity.

(p=0.041) was found with regard to the 6 min walking distance significantly, which increased in CWAT+-intervention (+43 (9 – 89) m; p=0.014) as compared with the CON.

Associations between cardiovascular risk, SB and physical activity

Reallocating sedentary time with standing was not associated with improvements in cardiac autonomic function and skeletal muscle oxidative capacity (figure 3). In addition, LPA beneficially affected LF (SC β=0.313 (0.033–0.517); r^2=0.098; p=0.029). However, after adjusting for all covariates, the association remained not significant. In addition, reallocating sedentary time with MVPA was associated with a higher RMSSD (SC β=0.496 (0.229–0.724); r^2=0.246; p<0.001), LF (SC β=0.572 (0.311–0.772); r^2=0.327; p<0.001), HF (SC β=0.570 (0.323–0.807); r^2=0.325; p<0.001) and 6MWD (SC β=0.378 (0.243–1.239); r^2=0.293; p=0.004) and a lower $\dot{V}O_2$ kinetic time constant τ (SC β=–0.381 (–0.394 to –0.062); r^2=0.318; p=0.008) when adjusted for all covariates.

DISCUSSION AND CONCLUSION

In this randomised controlled trial, we observed that the behaviour change intervention combining self-monitoring with motivational interviewing (CWAT+group) led to significant improvements in cardiac autonomic function, skeletal muscle oxidative capacity and functional exercise capacity compared with participants who either only wore a CWAT (CWAT group) or maintained their usual sedentary and activity patterns (CON group). These findings highlight the potential of a multicomponent behavioural intervention to induce

Table 2 Cardiovascular health and muscle function markers at baseline and after the 12-week intervention period

	Control		CWAT		CWAT+		
	Baseline (n=20)	12 weeks (n=19)	Baseline (n=20)	12 weeks (n=20)	Baseline (n=19)	12 weeks (n=17)	Time×group (p value)
Blood pressure							
Systolic BP (mm Hg)	120±13	117±12	123±12	120±12	124±12	125±15	0.742
Diastolic BP (mm Hg)	79±8	77±7	83±9	80±8	81±8	81±9	0.715
Resting heart rate (bpm)	62±6	61±7	59±9	60±8	57±7	60±8	0.450
Low-grade inflammation							
C reactive protein (mg/L)	2.69±3.53	2.33±3.10	2.51±3.79	2.38±3.36	2.07±2.44	1.91±1.62	0.984
Serum amyloid A (mg/L)	3.77±2.51	3.07±1.95	4.63±5.58	3.46±2.70	3.30±2.42	3.96±2.84	0.464
zLGI	0.05±1.03	0.16±0.46	−0.20±0.53	0.16±0.43	−0.28±0.46	0.68±2.41	0.239
Endothelial function							
sICAM (µg/L)	437±143	410±97	399±52	393±59	402±65	397±91	0.512
sVCAM (µg/L)	470±121	443±103	440±62	435±70	440±73	422±65	0.850
sE-selectin (µg/L)	10.6±7.1	10.0±4.4	11.2±4.88	9.9±4.2	9.3±3.6	10.2±4.6	0.621
zEF	0.04±1.03	−0.23±0.44	−0.18±0.49	−0.26±0.41	−0.28±0.58	−0.29±0.41	0.642
RHI	2.09±0.43	2.07±0.59	2.11±0.51	2.17±0.58	2.21±0.47	2.46±0.50	0.516
Muscle function							
$\dot{V}O_2$ baseline (ml/min)	268±58	238±57	298±51	233±60	270±95	260±80	0.253
$\dot{V}O_2$ steady-state (mL/min)	789±101	794±124	822±126	784±164	795±192	814±166	0.465
τ (s)	26.2±9.1	29.0±8.6	27.8±12.6	25.3±8.6	28.1±12.6	23.2±6.8*	**0.026**
A (mL/min)	524±69	565±89	540±114	558±145	532±128	559±110	0.910
T_d (s)	9.9±10.5	9.1±11.8	14.9±5.1	14.7±7.4	13.3±6.4	12.7±5.6	0.785
O_2 deficit (L)	0.26±0.09	0.35±0.13	0.28±0.20	0.30±0.13	0.30±0.14	0.29±0.08	0.425
6MWD (m)	608±68	626±70	627±77	655±84	644±77	692±80*	**0.041**

Data represented cardiovascular risk factors before and after a 12-week CWAT-based intervention period within the control, CWAT and CWAT+ groups (see the Methods section) and are expressed as mean±SD.
Bold values indicate statistical significance.
*p<0.05 indicates a significant between-group difference of change scores (baseline–12-week postintervention) based on pairwise comparisons.
BP, blood pressure; CWAT, consumer wearable activity tracker; 6MWD, 6 min walking distance; O_2, oxygen uptake; RHI, reactive hyperaemia index; sICAM, soluble intercellular adhesion molecule; sVCAM, soluble vascular cell adhesion molecule; $\dot{V}O_2$, oxygen uptake; zEF, endothelial function overall z-score; zLGI, low-grade inflammation overall z-score; τ, time constant tau.

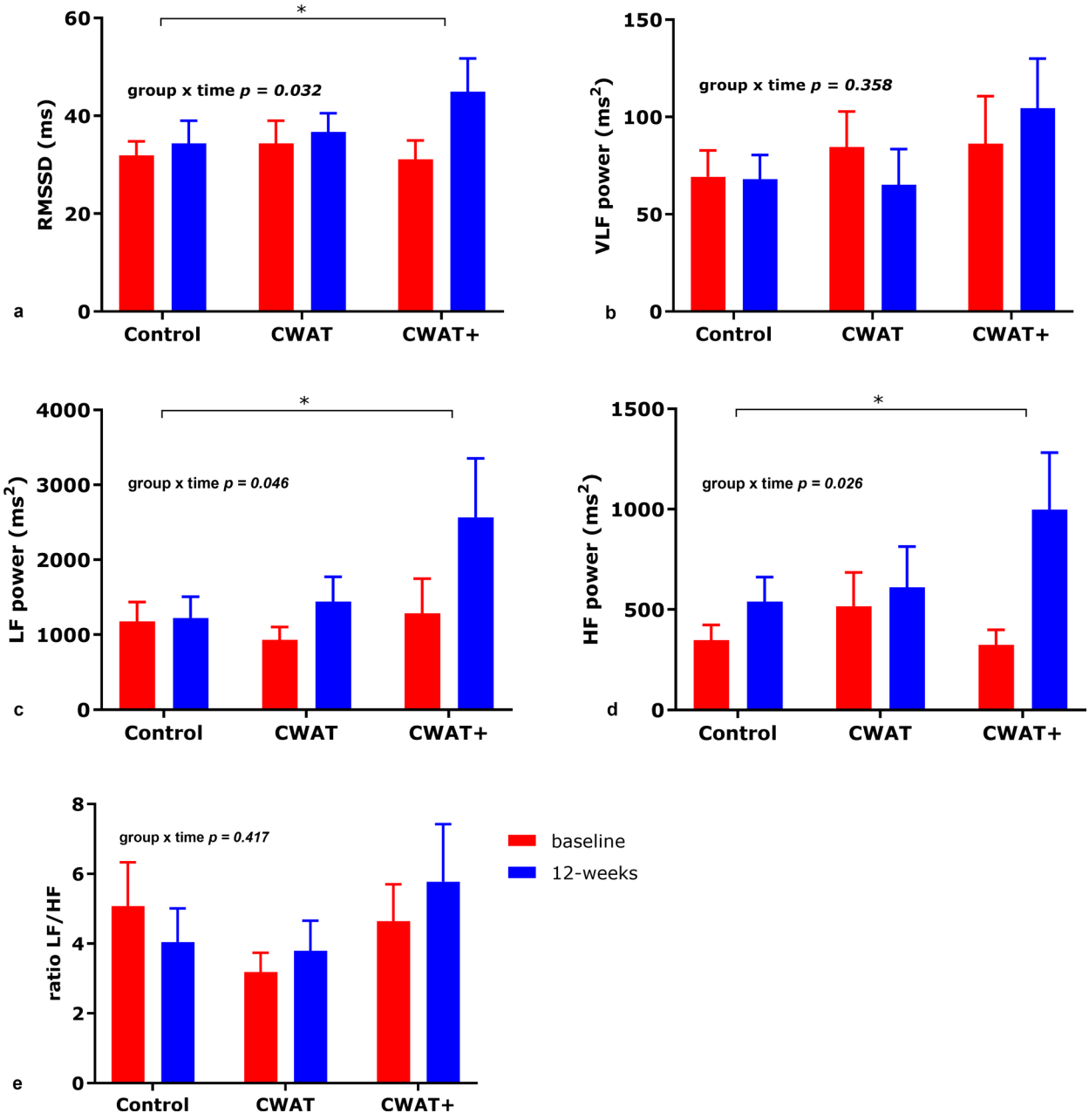

Figure 2 Cardiac autonomic function, reflected by (a) RMSSD, (b) VLF, (c) LF, (d) HF and (e) the ratio of LF/HF, before and after a 12-week CWAT-based intervention period within the control, CWAT and CWAT+ groups. Data are presented as means±SEs. *p<0.05 indicates a significant between-group difference of change scores (baseline–12-week postintervention) based on pairwise comparisons. CWAT, consumer wearable activity tracker; HF, high frequency; LF, low frequency; RMSSD, root mean square of the successive difference; VLF, very low frequency.

meaningful physiological adaptations, extending beyond changes in SB and physical activity alone.

Our previous publication reported reductions in sedentary time accompanied by corresponding increases in physical activity of different intensities.[36] The present study extends these findings by demonstrating that such behavioural changes lead to modest improvements in cardiac autonomic function and muscle oxidative capacity, indicating small benefits for cardiovascular health. Although these results demonstrate that significant short-term reductions in SB and modest improvements in cardiovascular health are achievable, the sustainability of these effects remains uncertain because outcomes were assessed only immediately after the 12-week intervention. Long-term interventions (6–24 months) targeting SB generally produce modest (20–60 min/day) but sustained reductions, particularly in workplace settings.[52–54] Reductions in workplace sitting were largely replaced by standing, which may explain the minimal or non-significant effects on cardiovascular risk factors. These findings suggest that multilevel interventions can achieve long-term reductions in SB in the workplace.

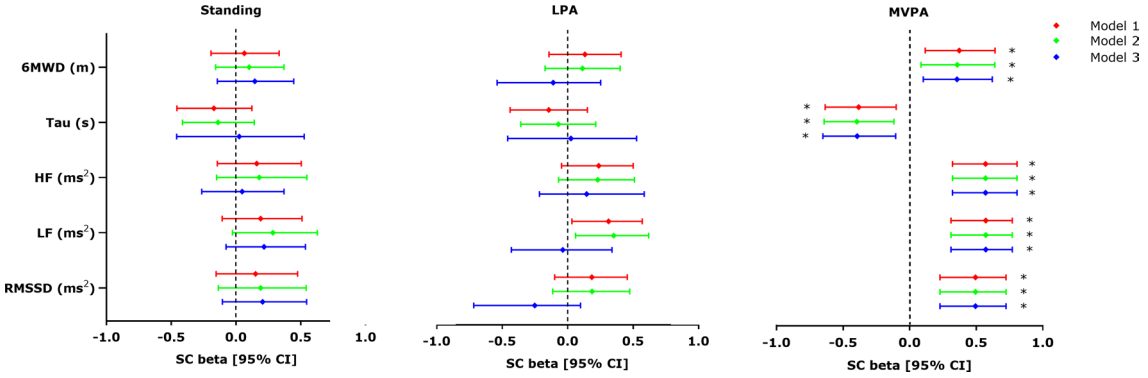

Figure 3 Multivariate regression analyses for the associations between standing, LPA, MVPA and different cardiovascular health, skeletal muscle oxidative capacity and functional exercise capacity outcomes. Model 1: unadjusted; model 2: adjusted for covariates age and sex; model 3: adjusted for all covariates from model 2 and standing, LPA and/or MVPA. Data are presented as standardised coefficient (SC) of beta (95% CI). *p<0.05. 6MWD, 6 min walking distance; HF, high frequency; LF, low frequency; LPA, light-intensity physical activity; MVPA, moderate-to-vigorous physical activity; RMSSD, root mean square of the successive differences; τ, time constant tau.

Evidence from free-living settings is more mixed.[14] Some interventions reduced SB without improving cardiovascular health, while others showed small significant effects.[55 56] Overall, these studies indicate that the magnitude of health-related benefits may depend on the intensity of replacement activities and the broader context of the intervention. Workplace-based interventions appear particularly effective at sustaining reductions, whereas free-living interventions may require additional support or higher-intensity activity to translate behavioural changes into meaningful cardiovascular improvements.

To achieve more durable effects, future interventions should shift focus from initiating change to sustaining it. This may involve permanent environmental or policy modifications (eg, standing meetings, flexible active breaks) that reduce reliance on continuous individual effort.

The reduction in sedentary time within the CWAT+group resulted in significant improvements in cardiovascular risk factors, as compared with the CON. We observed an increased HRV (RMSSD, LF and HF), whereas no significant differences were found in markers of endothelial function and low-grade inflammation. A robust level of HRV is a positive indicator of cardiovascular health status[57] and recent studies showed that objective accelerometer-derived PA had a positive association with HRV.[58] We showed as one of the first that the HRV, reflected by RMSSD, LF and HF, was significantly improved when sedentary time was replaced by MVPA since an increase in MVPA was significantly associated with a higher HRV. Indeed, de Sousa *et al* found a dose-response association between intensity of physical activity and HRV.[4] Interestingly, our results might have important implications for a potential clinical tool for cardiovascular health given the widespread availability of sophisticated CWATs, which are often able to monitor heart rate and provide information on HRV, and thus cardiovascular health status.

An additional goal of the current study was to explore the role of different SB interventions in the $\dot{V}O_2$-onset kinetics during submaximal exercise testing. We found that the CWAT+intervention significantly speeds the $\dot{V}O_2$ response at the onset of light-intensity exercise. Previous studies have already found that exercise-onset $\dot{V}O_2$ kinetics are improved by exercise training interventions.[59] Our results confirm these findings as a significant positive association was found between the difference in MVPA and skeletal muscle oxidative capacity, reflected by faster $\dot{V}O_2$ kinetics. Moreover, we also found that these improvements led to a significantly higher functional exercise capacity (i.e. increase in 6MWD), which was negatively correlated with the faster $\dot{V}O_2$ kinetics (r=−0.561; p<0.001). It is hypothesised that the reasons for these improvements might be related to an increased activation of oxidative muscle enzymes.[59] In addition, another explanation could be due to changes in peripheral blood flow, which result in an improved skeletal muscle oxygen supply at exercise onset,[46] although this is controversial in the literature.[60]

Although prolonged sedentary time was significantly reduced within the CWAT+group, mainly due to an increase in standing time and LPA, no improvements in endothelial function and low-grade inflammation were found. Findings of epidemiological and early experimental studies demonstrated that MVPA outperformed LPA[61] and that replacing sitting time with a continuous bout of approximately 60 min of MVPA a day is likely to gain benefits in cardiometabolic biomarkers.[62] In the current study, the CWAT+group accumulated 41 min/day in MVPA, which may have been insufficient to elicit measurable improvements in both endothelial function and inflammatory markers. Importantly, reductions in SB should not be interpreted as a replacement for MVPA. The physiological adaptations associated with improved cardiovascular health are primarily driven by the intensity of the activity replacing sedentary time rather than by sedentary reduction per se. In the present study,

reductions in SB occurred alongside increases in MVPA, suggesting that SB reduction alone is insufficient to elicit the observed physiological benefits.

Interruptions that involve moderate-to-vigorous intensity movement, by contrast, appear more likely to produce acute improvements in cardiovascular-related outcomes. For example, breaking up prolonged SB with brief bouts of high-intensity activity (eg, stair climbing) has been shown to improve cardiovascular health.[63–65] Notably, short high-intensity interruptions have, in some cases, elicited greater improvements than moderate continuous exercise, suggesting that the intensity of the movement stimulus is a critical determinant of benefit.[66] However, much of this evidence comes from short-term, laboratory-based studies and, therefore, long-term investigations conducted under free-living conditions are warranted. This emphasis on intensity is consistent with findings showing that higher-intensity activity (75%–90% of maximal oxygen uptake) induces the greatest improvements in endothelial function in lean adults, likely through elevations in BP and the associated increases in shear stress.[67] In our study, MVPA was classified from approximately three metabolic equivalents (50%–60% of maximal oxygen uptake), meaning that the activity intensity may not have been sufficiently high to produce measurable improvements in endothelial function.

Another reason why no significant improvements were found could be due to the measurement site. Taylor *et al* showed in a systematic review that mainly the lower-limb vascular function (ie, femoral or popliteal artery) will be improved after breaking up sedentary time due to a higher shear stress within the leg vasculature,[68] instead of measuring endothelial function in the fingertips. However, these results were only based on acute effects rather than effects on the longer term as in our study.

Next to endothelial function, no differences were found on low-grade inflammatory markers. Because it has been shown that prolonged sitting leads to impaired low-grade systemic inflammatory markers,[69] we would expect that this impairment was reversible when sedentary time was reduced. A possible reason why no differences in low-grade inflammation were found is that we evaluated inflammation using adhesion molecules rather than interleukins (IL), which may be more sensitive. This is in line with a study from Karch *et al* who found lower resting IL-6 levels in athletes as compared with non-athletes and IL-6 levels were increased after exercise, whereas no differences were found in sICAM.[70] In addition, Henson *et al* showed that substituting sedentary time with MVPA was associated with lower IL-6 levels.[62] Taken together, it seems that longer periods of interrupting sedentary time (>5 min) and/or physical activity of higher intensities will improve vascular endothelial function and low-grade inflammation.

This study has multiple strengths which include the use of an accelerometer, which can distinguish postures and is the most accurate to assess time spent in SB.[71] Due to the randomised controlled study design, we were able to discriminate between the effectiveness of mono- and multicomponent intervention strategies. Furthermore, we only included sedentary adults (10.8±1.2 hours per day) based on objective measurements. Here, only a few clinical trials in the current literature included individuals based on sedentary time. So far, most of the studies included participants based on physical (in)activity levels, which does not guarantee a sedentary population. Hence, based on physical activity measurements, people could both be physically inactive and not sedentary at the same time.

Our study also had some limitations. First, although participants were randomly allocated to the CON group or one of the intervention groups, we were not able to blind the assessors and participants themselves. However, all assessments were performed in an objective way, resulting in less performance bias. In addition, although we measured two different aspects of endothelial function (small vascular reactivity with endoPAT and microvascular function with soluble endothelial markers), it is warranted to also investigate other sensitive endothelial function markers. For example, flow-mediated dilation responses are the current non-invasive gold standard approach, especially for measurements of the lower-limb vasculature. Finally, the sample size was determined by power calculations for another outcome, triglyceride concentration, which was the primary outcome of this trial.[36]

In conclusion, a 12-week multiple behaviour change intervention combining self-monitoring and motivational interviewing reduced sedentary time and was associated with modest improvements in cardiac autonomic function, muscle oxidative capacity and functional exercise capacity. These improvements were largely linked to increases in MVPA, indicating that engaging in more structured MVPA in place of SB may contribute to better cardiovascular health.

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Contributors WMAF, IN, PJ, KK and FV wrote the manuscript. WMAF and FV performed the motivational interviewing techniques. WMAF, IN and PJ performed the clinical measurements. WMAF, IN, PJ, FV and KK were involved in data acquisition. WMAF, IN, PJ, KK, HHCMS and BOE performed the data cleaning and statistical analysis of the data. WMAF, HHCMS and BOE conceived and designed the study. WF is the guarantor of the study. All authors contributed to the interpretation of the data and critical revision of the manuscript and approved the final draft. All authors took responsibility for the integrity of the data and the accuracy of the data analysis.

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Patient consent for publication Consent obtained directly from patient(s).

Ethics approval The study was approved by the medical ethical committee of Hasselt University and was in accordance with the principles of the Declaration

of Helsinki. Participants gave informed consent to participate in the study before taking part.

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