Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Cardiometabolic Effects of Physical Activity guideline adherence and additional Sedentary Behaviour reduction in free-living sedentary adults: a randomised controlled trial

Jen Vanherle

jen.vanherle@uhasselt.be

Hasselt University

Ine Nieste

Hasselt University

Peter J. Joris

Maastricht University Medical Centre

Wouter M.A. Franssen

Hasselt University

Bert Op 't Eijnde

Hasselt University

Research Article

Keywords: Sedentary behaviour, physical activity, cardiometabolic health, insulin sensitivity, sit-to-stand, cardiorespiratory fitness, metabolic health, vascular health

Posted Date: July 21st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10313086/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Both physical inactivity and prolonged sedentary behaviour are risk factors for the development of cardiometabolic disease, yet the long-term benefits of reducing sedentary behaviour in addition to increasing physical activity remain unclear. This study investigated whether increasing physical activity combined with reducing sedentary behaviour additionally improves insulin sensitivity in sedentary and inactive adults, compared to increasing physical activity alone.

Methods

Sedentary, physically inactive adults (18–65 years) were randomised to an 8-week intervention of either increased physical activity alone (PA) or physical activity combined with reduced sedentary behaviour by installing sit-to-stand workstations (PA-SB) to evaluate the effect on insulin sensitivity. Body composition, anthropometrics, activity behaviour, cardiorespiratory fitness, blood pressure, vascular endothelial function, blood parameters and health-related questionnaires were also assessed before and after the intervention periods. Linear mixed-effects models were used to explore effects.

Results

Twenty-nine participants (18 female), aged 47.4 ± 12.3 years were included. Insulin sensitivity improved after the intervention, with significantly greater improvements in the PA group than in the PA-SB group group (-11948 [-23142 to -754] pmol/L*120min; group x time effect $p = 0.038$). Participants in both groups improved cardiorespiratory fitness, body composition and quality of life. Vascular endothelial function and blood pressure remained unchanged.

Conclusions

Guideline-based physical activity improved insulin sensitivity and induced favourable cardiometabolic adaptations in sedentary adults. Adding a sedentary behaviour reduction component did not result in additional improvements in insulin sensitivity or other cardiometabolic outcomes. More effective strategies to reduce prolonged sedentary behaviour in free-living settings should be explored in future research.

Trial registration

The study was registered at clinicaltrials.gov as NCT07363499.

Introduction

Cardiometabolic diseases, including cardiovascular diseases and type 2 diabetes mellitus, are a major global public health concern, accounting for 74% of all deaths worldwide.[1, 2] The efforts of the United Nations to reduce premature deaths resulting from chronic diseases by 2030 highlight the importance of improving prevention strategies. Despite modest progress, the rate of decline is insufficient[1], and scalable interventions targeting reductions in modifiable risk factors are essential.

Lifestyle factors[3, 4] such as tobacco use, excessive alcohol consumption, unhealthy diet and physical inactivity play a central role in the development of cardiometabolic risk factors including insulin resistance and impaired vascular endothelial function.[5, 6] This indicates that structured physical activity (PA) is important for prevention and management of cardiometabolic diseases.[7] Consequently, to promote health, the World Health Organization (WHO) recommends weekly PA of either 150–300 minutes at moderate intensity, 75–150 minutes at vigorous intensity or an equivalent combining moderate and vigorous physical activity (MVPA).[8]

In addition to promoting PA, the WHO also recommends to limit sedentary behaviour (SB) as much as possible by replacing it with PA of any intensity. Here, SB refers to any waking behaviour with a low energy expenditure while in a sitting, reclining or lying position.[9] Importantly, high levels of prolonged SB are associated with increased disease risk and all-cause mortality even in people who meet PA guidelines.[10] This indicates that SB and PA are interrelated constructs that both influence cardiometabolic health and that SB is not just the opposite of PA.[11, 12]

Studies have already shown that brief PA interruptions during prolonged SB are associated with improvements in postprandial glucose and insulin responses.[13] Most evidence is derived from short-term, laboratory-controlled studies and it remains unclear if these findings translate to longer intervention periods. This is an important research gap as healthy lifestyle management should not only include sufficient PA but also consider reducing and interrupting prolonged SB integrated into our daily life.[14]

Replacing sitting time with standing by using sit-stand work stations has emerged as a practical strategy to reduce occupational SB.[15] This strategy might lead to health benefits as acutely alternating between sitting and standing reduces postprandial glucose and insulin responses compared to prolonged SB in obese office workers[16, 17], whereas other studies showed no effects.[18] Furthermore, sit-stand work stations can be used to interrupt prolonged sitting and potentially resolve sitting-induced impaired vascular endothelial function.[19, 20] In addition, it has been shown that exercise training (i.e. structured PA) leads to improved endothelial function.[21, 22]

Acute studies demonstrated that combining exercise with interruptions of prolonged sitting improves cardiometabolic responses under strictly controlled conditions.[23, 24] Extending these acute findings,

Kozey-Keadle *et al.* reported improved insulin sensitivity following a longer-term intervention combining exercise with reduced SB, while highlighting the need for studies in free-living conditions using practical strategies such as sit-to-stand workstations.[25] Supporting this approach, Graves *et al.* showed that sit-to-stand desks can effectively reduce sedentary time and increase standing time in office workers.[26]

The aim of the present study was to investigate the effects of increasing PA and additionally reducing SB on cardiometabolic health and vascular endothelial function, in sedentary and inactive men and women. We hypothesized that both interventions would improve insulin sensitivity and endothelial function, and we explored if reducing SB in addition to increasing PA would lead to additional improvements.

Methodology

Subjects

Sedentary (sitting time > 9h/day) adults aged 18 to 65 years, who did not meet the minimal PA recommendations (weekly MVPA <150 min), were recruited. Exclusion criteria were medical conditions that limit engagement in PA, pregnancy, excessive alcohol consumption (over 10 weekly units), weight loss (>2kg) in the last month, change in dietary habits, or metabolic disorders and unresolved cardiovascular diseases. Eligibility criteria were assessed during a screening visit, including medical history and general health questionnaires. In addition, a resting electrocardiogram was performed and evaluated by a cardiologist to identify possible underlying cardiovascular conditions. All participants provided written informed consent. The study was approved by the medical ethical committee of Hasselt University and was performed at Hasselt University (Diepenbeek, Belgium) between February 2025 and January 2026 in accordance with the principles of the Declaration of Helsinki. The study was registered at clinicaltrials.gov as NCT07363499.

Study design

A two-armed randomised controlled design was used. For practical reasons, subjects were aware of their intervention arm. After a baseline study visit, all participants followed a two-week control period where they continued their habitual PA levels. After this control period, a second study visit was scheduled after which participants were randomised in a 1:1 ratio to one of two intervention arms via a software program (www.randomisation.com). Allocation was concealed until the start of the intervention. The intervention period lasted for eight weeks after which the participants returned for a final study visit.

Study Visits

During the study visits, participants arrived after an overnight fasting period (starting from 8 p.m.). Alcohol consumption and engaging in structured PA (exercise) was prohibited during the day before each study visit. Cardiovascular function was assessed by means of resting heart rate, resting blood pressure and macrovascular endothelial function (flow-mediated dilation [FMD]). Next, body composition

and anthropometrics were evaluated. A fasting blood sample was collected after placing an indwelling catheter in the brachial vein. Participants then consumed a standardised test drink during an oral glucose tolerance test (OGTT) to assess insulin sensitivity. During the OGTT, participants were asked to fill in a food questionnaire to evaluate habitual dietary intake (MEDAS), the Pittsburgh sleep quality index (PSQI) and the Euroqol questionnaire (EQ-5D). At the end of the study visit, participants performed a cardiopulmonary exercise test (CPET) to evaluate cardiorespiratory fitness.

Intervention period

Each participant followed one intervention arm during eight weeks. The intervention arms will be further described as “PA arm” and “PA-SB arm”. Participants in both intervention arms were instructed to adhere to the minimal requirements of the WHO guidelines for PA. This consisted of at least two weekly 50-minute sessions of moderate-intensity PA (MPA) and one weekly 30-min session of vigorous-intensity PA (VPA). Heart rate monitoring was used, where heart rate zones matching 40-60% and 60-90% of maximal oxygen capacity (based on CPET) represent MPA and VPA respectively.[27] In the PA-SB arm a SB reduction component was added to this PA component. Participants were provided with a sit-to-stand working station at their workplace and they were stimulated to replace seated work with standing work for at least one hour every working day.[15] Furthermore, they were advised to limit prolonged sitting bouts (>60 minutes) as much as possible. Participants were allowed to engage in light activities (e.g., stretching or walking) during standing periods. In both groups, participants were provided with a Fitbit Inspire 3 (Google, San Francisco (CA), USA) activity tracker and were assisted in creating a Fitbit account to monitor the PA sessions. The intervention was carried out under free-living conditions and weekly contact moments (via phone calls or mail) were scheduled to evaluate adherence. Participants were instructed to maintain their habitual diet throughout the study trial.

Outcome measures

Insulin sensitivity (primary outcome)

An oral glucose tolerance test (OGTT) was performed to assess whole body insulin sensitivity. Participants ingested water (250ml) containing 75g dextrose, and five venous blood samples were obtained every 30 minutes for assessment of plasma glucose and serum insulin concentrations. From glucose and insulin concentrations, homeostatic model assessment for insulin resistance (HOMA-IR) was calculated by: fasting glucose (mg/dL) * fasting insulin (μU/mL)/405.[28] In addition, whole-body insulin sensitivity index (WBISI) was calculated by: 10.000/√[fasting glucose (mg/dL) * fasting insulin (μU/mL)) * (mean glucose during OGTT (mg/dL) * mean insulin during OGTT (μU/mL)].[29] Beta cell function was estimated by calculation of the insulinogenic index (IGI) by: ratio of increment of insulin (μU/mL) and glucose (mg/dL) in the first 30 min of OGTT.[30] The area under the curve (AUC) for glucose and insulin for the 2 hour period was calculated using the trapezoidal rule.[31]

Body composition and anthropometrics

Total fat mass (in kg), lean tissue mass (in kg), visceral adipose tissue (in grams) and fat percentage were evaluated using Dual Energy X-ray Absorptiometry (Hologic Series Delphi-A Fan Beam X-ray Bone Densitometer, Vilvoorde, Belgium).

Body height was measured to the nearest 0.1cm using a wall-mounted Harpenden stadiometer, with participants barefoot. Body weight was determined using a digital-balanced weighting scale to the nearest 0.1kg. Body mass index (BMI [in kg/m²]) was calculated from weight and height measurements (weight/height^2). Waist and hip circumferences were measured to the nearest 0.1 cm using a flexible metric measuring tape with participants in standing position. Waist circumference was measured at the midpoint between the lower rib margin and the top of the iliac crest.

Physical activity and sedentary behaviour

Physical activity (PA) and body postures were quantified during one week using the activPAL3™ activity monitor (PAL Technologies Ltd, Glasgow, Scotland), a triaxial accelerometer and inclinometer.[32] The device was enclosed with a nitrile sleeve and attached to the anterior mid-thigh of the participants' right leg using an adhesive dressing (Tegaderm, 3M).

The activPAL™ accurately measures posture allocation and free-living activity in which discriminations are made between time spent in SB (sitting or lying), standing and PA including step count and step cadence (low intensity physical activity (LIPA) and moderate to vigorous physical activity (MVPA)).[33]

In addition to the activPAL monitor, participants kept track of their sleeping and exercise time in a paper diary. Self-reported sleeping time (time in and out bed and time waking up and trying to fall asleep and naps during daytime) were used to adjust the sleeping time determined by the activPAL algorithm (CREA), as recommended in literature.[34] Details on structured exercise session were also administered (time, duration, rate of perceived exertion and average heart rate) in the same paper diary. Outcomes that were included in the analysis are daily step count, time spent in LIPA, MVPA, standing and SB. In addition, time spent in sedentary bouts >30min, the daily number of sit-to-stand transitions and time spent in prolonged sedentary bouts (>60 minutes/bout), were also included in the analysis.

Cardiorespiratory fitness

Cardiorespiratory fitness was defined as peak oxygen uptake ($\dot{V}O_{2peak}$), and was assessed via a graded CPET on an electronically braked cycle ergometer (eBike Basic®, General Electric GmbH, Bitz, Germany) with gas exchange analysis (Metalyzer IIB® Cortex, Leipzig, Germany). After a five-minute warm-up period (@40W for women; @60W for men), the workload was increased every minute (+10W/min for women; +15W/min for men). Participants were instructed to maintain a cadence of >75 revolutions per minute. Exercise testing was terminated by volitional exhaustion or failure to maintain 45 rpm. The maximal heart rate, respiratory exchange ratio, post-test lactate levels (2 min after termination), and perceived exertion were used to verify maximal effort.[35] Heart rate was continuously monitored via a Polar chest strap (Polar®, Oy, Finland).

Blood pressure and endothelial function

After an initial resting period of at least ten minutes with participants in a supine position in a quiet room with constant temperature (21°C), blood pressure (BP) was measured at least 3 times at 2-min intervals until BP was stable using an electronic sphygmomanometer (Omron®, Omron Healthcare, IL, USA) from the left arm and documented as the mean value of the three final measurements.

Vascular endothelial function was assessed by femoral artery flow-mediated dilation (FMD), with participants in a supine position and according to published guidelines.[36] These measurements took place at 9 a.m. and involve doppler ultrasound imaging of the superficial femoral artery (MyLab™ Sigma, Esaote S.p.A., Genova, Italy). A pneumatic cuff was placed around the upper part of the right calf. The superficial femoral artery was imaged longitudinally using a linear probe (L3-11) above the knee (antero-medial side of the thigh), proximal to the pneumatic cuff. Femoral artery diameter profiles were assessed using B-mode which was combined with Doppler mode to assess velocity profiles as recommended.[37] After a two-minute reference period, the pneumatic cuff was inflated to >250 mmHg for a duration of five minutes. FMD was measured during the reference period and during three minutes after this 5-min occlusion phase (reactive hyperaemia response). FMD was quantified as the percentage difference between the post-occlusion peak and baseline diameter (FMD%).[36] Ultrasound images were analysed offline using a custom-written Matlab program which uses automatic edge-detection and wall tracking (MyFMD, Prof. A.P.G. Hoeks, Department of Biomedical Engineering, Maastricht University, Maastricht, The Netherlands).

Blood parameters

After antecubital catheter placement, fasting blood samples were obtained to measure glucose, insulin, serum lipids and lipoproteins (total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triglycerides (TG)). For blood glucose assessment, blood was collected in fluoride-oxalate tubes (4mL). For the assessment of insulin, blood was collected in serum separator (SST) tubes (5mL) and for the assessment of lipid profile, blood was collected in Lithium-Heparin tubes (6mL). The SST tubes were allowed to clot for at least 30min at room temperature. All tubes were centrifuged during 15min at 1300 x *g* at a temperature of 20°C (brake 9). After centrifugation, plasma and serum samples were immediately portioned into aliquots that were stored at -80°C until the analysis at the end of the trial.

Questionnaires

During the screening visit, participants completed a questionnaire to inquire personal information such as date of birth, biological sex, general health status (familial chronic disorders; dietary habits; smoking habits; alcohol consumption), employment, exercise habits, and medication use.

During each study visit, health-related quality of life (QOL) was measured using the Euroqol 5-D questionnaire (EQ-5D). The EQ-5D is a widely used and validated generic instrument consisting of five

dimensions: mobility, self- care, usual activities, pain/discomfort and anxiety/depression. Sleep quality over a period of one month was also assessed using the Pittsburgh sleep quality index (PSQI) which is a self-administered questionnaire consisting of 19 items that is reliable and valid to assess sleep problems. Dietary intake was assessed using a validated 14-item validated Mediterranean Diet Adherence Screener (MEDAS) questionnaire that evaluates adherence to the Mediterranean diet.[38] Feasibility of using a sit-stand workstation was assessed by means of a 17-item Likert scale based on a questionnaire that has been previously used in similar research.[26] An average feasibility score is achieved after negative scores were multiplied by -1. Higher scores on the scale (ranging from -2 to +2) indicate increased feasibility.

Statistical analysis

Statistical analyses were performed by IBM SPSS® version 30.0 (IBM SPSS Statistics for Windows, Chicago, IL, USA). Data are expressed as mean ± SD, unless otherwise indicated. Shapiro-Wilk test was used to test normality of the data (p<0.05). Data were analysed using an intention-to-treat analysis. Baseline characteristics were compared between intervention groups using t-tests or non-parametric alternatives. Intervention effects between baseline and post-intervention were analysed using linear mixed-effects models. The models included fixed effects for intervention group (PA arm vs PA-SB arm), time (baseline vs post), and their interaction, with an unstructured repeated covariance structure and a random intercept for participant.

Estimated marginal means were derived from the mixed models, and changes over time within each group, as well as between-group differences in change, were calculated. The primary effect of interest was the effect of time while also exploring the group-by-time interaction, indicating whether changes differed between intervention groups. Missing data were handled by the maximum likelihood estimation procedure under the assumption of missing at random (MAR). Statistical significance was set at p-value < 0.05.

A total study sample of 24 participants was anticipated for the study based on results on insulin sensitivity (postprandial area under the curve) from previous research[23, 25] (Cohen's d effect size = 0.77, one-sided alpha = 0.05, power = 80%) to evaluate the effect of reducing SB in addition to engaging in PA on insulin sensitivity (primary outcome). Accounting for a drop-out rate of 20%, this results in a final sample of 30 participants.

Results

In total, 192 individuals were assessed for eligibility of which 57 individuals were eventually screened. After screening, 28 individuals were excluded due to spending more than 150 minutes per week in MVPA (n=19) or other reasons (n=9). The remaining 29 participants were randomised to the PA arm (n=15) and the PA-SB arm (n=14). Two participants (PA group) dropped out; one due to cancer diagnosis and one due too practical issues (Figure 1 – Consort 2025 flow diagram). Baseline characteristics are presented

in Table 1. No significant differences between groups were found for baseline characteristics after randomisation.

Table 1. Participant characteristics (n = 29)

Sex (female [n, %])	18, 62
Age (y)	47.4 ± 12.3
Anthropometrics	26.5 ± 3.4
BMI (kg/m²)	89.3 ± 11.8
Waist circumference (cm)	33.1 ± 7.2
Fat percentage (%)	617 ± 281
Visceral adipose tissue (g)	
Blood pressure	59 ± 12
Resting heart rate (bpm)	113 ± 9
Systolic blood pressure (mmHg)	74 ± 7
Diastolic blood pressure (mmHg)	
Fasting metabolic risk markers	4.7 ± 1.1
Total cholesterol (mmol/L)	1.3 ± 0.3
HDL-C (mmol/L)	2.9 ± 0.9
LDL-C (mmol/L)	1.1 ± 0.4
Triglycerides (mmol/L)	5.1 ± 0.4
Glucose (mmol/L)	42 ± 24
Insulin (pmol/L)	
Calorimetry	27.0 ± 6.4
Peak oxygen uptake (mL/min•kg)	77.8 ± 14.6
Peak oxygen uptake as % of predicted value	
Questionnaires	
Pittsburgh Sleep Quality Index (PSQI)	5 ± 2
EQ-5D Quality of Life score (0-100)	73 ± 12
MEDAS food questionnaire	5.3 ± 1.7

Abbreviations: BMI = body mass index; HDL-C = high-density lipoprotein cholesterol; LDL-C= low-density lipoprotein cholesterol; EQ-5D:EuroQol five dimensions
Data are expressed as mean ± standard deviation

Physical activity behaviour

PA behaviour changed throughout the intervention period. Daily steps were significantly increased by 2389 steps/day (time effect $p<0.001$) and this increase was significantly greater in the PA group (group x time effect $p=0.029$). Light intensity physical activity was significantly increased by 10 minutes/day (time effect $p=0.008$), and MVPA increased by 13 minutes/day (time effect $p<0.001$).

Time spent in sedentary behaviour significantly decreased by 55 minutes/day (time effect $p<0.001$). Standing time significantly increased by 36 minutes/day ($p<0.001$) and no interaction effect was observed. Results for activity behaviour per group are presented in Figure 2.

Further analysis revealed a significant decrease in time spent in sedentary bouts that were longer than 30 minutes (time effect $p<0.001$), however time spent in prolonged (>60 minutes) sedentary bouts remained unchanged (time effect $p>0.05$). Other outcomes related to activity behaviour that remained unchanged over the course of the intervention (time effect $p>0.05$) include number of sit-to-stand transitions and total sleeping time.

Insulin sensitivity (primary outcome) and metabolic risk markers

Insulin total area under the curve during the OGTT significantly improved over time and a significant interaction effect revealed that this reduction was significantly greater in the PA group compared with the PA-SB group (-11948 [-23142 to -754] pmol/L*120min; group x time effect $p=0.038$; Figure 3). Additional outcomes from the mixed model analysis related to insulin sensitivity and other metabolic blood markers did not change over the course of the eight-week intervention periods (time effect $p>0.05$; presented in Supplementary Table 1). Glucose concentrations during the OGTT are presented in Supplementary Figure 1.

Secondary health-related outcomes

Cardiorespiratory fitness significantly improved in both experimental arms (+3.1 [1.8 to 4.4] ml/kg*min, $p<0.001$) with no between-group differences. Body composition improved in both intervention groups, indicated by significant decreases in visceral adipose tissue (-30 [-60 to -1] gram, $p=0.042$), fat percentage (-1.0 [-1.8 to -0.3] %, $p=0.009$), total fat mass (-0.9 [-1.7 to -0.1] kg, $p=0.032$) BMI (-0.4 [-0.7 to -0.0] kg/m², $p=0.035$) and waist circumference (-2.5 [-3.6 to -1.4] cm, $p<0.001$).

Systolic and diastolic BP did not change ($p=0.596$ and $p=0.371$ respectively). Vascular endothelial function, quantified by femoral artery FMD, did not change either over the course of the intervention ($p=0.203$; Figure 4).

Quality of life significantly improved (+6 [2 to 9], $p=0.003$) and overall sleep quality scores remained unchanged ($p=0.992$). Dietary habits slightly improved during the intervention (+0.60 [0.02 to 1.19], $p=0.042$), but this was not associated with improvements in health outcomes. Based on the feasibility

questionnaire in the PA-SB group (n=14), participants rated the use of sit-to-stand working stations as moderately positive (1.1 ± 0.2 on a Likert scale ranging from -2 to +2).

Discussion

The present study investigated the effects of complying with current physical activity guidelines, either alone (PA) or in combination with sedentary behaviour reduction (PA-SB), on cardiometabolic health in sedentary and inactive adults. The main finding was that insulin sensitivity, assessed by insulin total area under the curve (tAUC) during an OGTT, improved following the intervention period, with a significantly greater improvement observed in the PA arm compared with the PA-SB arm. In contrast, most secondary cardiometabolic outcomes improved similarly following both interventions.

The greater reduction in insulin tAUC observed in the PA arm may be explained by the larger increase in daily step count and MVPA observed in this group. This is in line with indications that greater volumes and intensities of PA are associated with superior improvements in insulin sensitivity and glycaemic control.[39, 40] In contrast to our findings, Kozey-Keadle et al. reported improvements in insulin sensitivity only following a combined intervention targeting both exercise and SB reduction in overweight adults.[25] Interestingly, participants with the least favourable metabolic profile at baseline demonstrated the greatest metabolic improvements, which is also in line with our results. Although no statistically significant baseline differences were observed between groups in the present study, baseline insulin tAUC values were higher in the PA arm, which may have increased the potential for improvement in this group.

Both intervention arms successfully modified activity behaviour. Daily step count, MVPA and light-intensity PA increased, while sedentary time decreased following the intervention period. Despite the additional SB reduction component in the PA-SB arm, no between-group differences in the decrease of sedentary time were observed at the end of the intervention. This suggests that increasing PA to comply with current guidelines may indirectly reduce sedentary time under free-living conditions. Although total sedentary time decreased, prolonged sedentary bouts (longer than 60 minutes) were not significantly reduced. Previous laboratory-based studies demonstrated beneficial metabolic effects of frequently interrupting prolonged sitting[16, 23, 24], however translating these behavioural changes into free-living settings remains challenging, particularly as the number of sedentary breaks did not significantly change throughout the intervention. This may explain why the additional SB reduction component did not result in additional metabolic improvements.

The sit-to-stand workstations used in the PA-SB arm were generally well perceived by participants, supporting the feasibility of this strategy in occupational settings. Similarly, Graves *et al.* demonstrated that sit-to-stand desks can effectively reduce occupational sedentary time.[26] Nevertheless, the present findings suggest that modest reductions in sitting time through standing-based strategies may not provide additional metabolic benefits when individuals also comply with current PA guidelines. It is

possible that larger reductions in prolonged sedentary time or more frequent interruptions involving activities at higher intensity are required to induce additional metabolic effects.[13]

Several secondary health-related outcomes improved following both interventions. Cardiorespiratory fitness increased significantly, which is clinically relevant given the strong association between cardiorespiratory fitness and reduced cardiovascular and all-cause mortality.[41] In addition, body composition improved, reflected by reductions in visceral adipose tissue, body fat percentage, total fat mass and waist circumference. Visceral adiposity is strongly associated with insulin resistance and cardiometabolic disease risk[42], supporting evidence that even relatively short-term behavioural interventions may induce meaningful metabolic adaptations in sedentary adults.[43, 44]

No significant changes were observed for blood pressure or femoral artery vascular endothelial function. This may be explained by the relatively healthy cardiometabolic risk profile of the study participants at baseline, thereby limiting the potential for improvement as previously reported.[21] In addition, we evaluated the femoral artery and current evidence is mostly based on brachial artery FMD. Lastly, the intensity of the intervention may have been insufficient to induce measurable vascular adaptations as high intensity training result in superior effects on vascular endothelial function.[21] Sleep quality and total sleeping time remained unchanged throughout the intervention period, suggesting that the observed cardiometabolic improvements were unlikely to be associated with sleep behaviour. This is also in line with previous findings that sleep quality, assessed with the PSQI, is not affected by daily MVPA.[45] Although dietary habits modestly improved over the course of the intervention, these changes were not associated with changes in cardiometabolic outcomes.

The present findings contribute to the ongoing discussion regarding the additional value of SB reduction in individuals who already comply with PA guidelines. While both intervention strategies resulted in favourable cardiometabolic adaptations, the findings suggest that adding a modest SB reduction strategy to guideline-based PA may not provide additional improvements in insulin sensitivity. This is consistent with previous reviews indicating that the metabolic effects of reducing SB alone are generally smaller than those achieved through structured MVPA interventions.[46] Nevertheless, reducing SB remains relevant as a complementary lifestyle strategy, particularly for individuals with high occupational sitting time or difficulty engaging in higher volumes of PA.

Several strengths of this study should be acknowledged. First, the intervention was performed under free-living conditions, thereby increasing ecological validity compared with laboratory-based studies. Second, objective measurements of PA and SB were used throughout the intervention period. Third, the intervention strategy closely reflected current WHO recommendations by targeting both MVPA and SB. Finally, several non-invasive gold-standard assessments (FMD, CPET, OGTT) were used to evaluate cardiometabolic and vascular health and improvements in several cardiometabolic outcomes were observed despite the relatively short intervention duration and inclusion of generally healthy participants.

Some limitations should also be considered. The relatively small sample size may have limited statistical power for secondary outcomes. Within-group differences are therefore presented in a supplementary table to facilitate sample size calculations for future studies. In addition, participants and researchers could not be blinded due to the behavioural nature of the intervention. Although sedentary time decreased, prolonged sedentary bouts remained largely unchanged, suggesting limited effectiveness of the intervention to change SB patterns. Finally, the relatively healthy study population may limit generalisability to populations with established cardiometabolic disease or more pronounced insulin resistance. As a result, findings of this study should be interpreted in the context of primary prevention and future studies should also include clinical populations to investigate potential benefits in a secondary prevention context.

In conclusion, guideline-based PA improved insulin sensitivity and induced favourable cardiometabolic adaptations in sedentary adults. Adding a SB reduction component using sit-to-stand workstations did not result in additional improvements in insulin sensitivity or other cardiometabolic outcomes beyond those achieved through guideline-based PA alone. These findings support current public health recommendations emphasising the importance of regular MVPA, while also suggesting that future interventions should investigate more effective strategies to interrupt prolonged SB under free-living conditions.

Declarations

Ethics approval and consent to participate

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 their informed consent to participate in the study before taking part.

Consent for publication

Not applicable.

Availability of data and materials

Study data are available on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

The research was funded by the special research fund (BOF) of Hasselt University.

Author's contributions

JV, WMAF and PJJ wrote the manuscript. JV, WMAF and IN performed the clinical measurements. JV, WMAF and PJJ were involved in data acquisition. JV, WMAF and BOE performed the data cleaning and statistical analysis of the data. JV, WMAF and BOE conceived and designed the study. JV 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.

Acknowledgements

The authors thank the participants in the study. We also want to thank Anne Bogaers for taking the blood samples and dr. Sevda Ece Kizlic for assessing the ECGs during the study trial.

References

1. Nations U. Sustainable Development goals, sdgs.un.org/goals/goal3 (2023).
2. Organization WH. *Global action plan for the prevention and control of noncommunicalbe diseases 2013-2020*. 2013, p.55.
3. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J* 2018; 39: 3021–3104. DOI: 10.1093/eurheartj/ehy339.
4. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014; 129: S76–99. 20131112. DOI: 10.1161/01.cir.0000437740.48606.d1.
5. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; 390: 1345–1422. DOI: 10.1016/s0140-6736(17)32366-8.
6. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2224–2260. DOI: 10.1016/s0140-6736(12)61766-8.
7. Reiner M, Niermann C, Jekauc D, et al. Long-term health benefits of physical activity--a systematic review of longitudinal studies. *BMC Public Health* 2013; 13: 813. 20130908. DOI: 10.1186/1471-2458-13-813.
8. Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *British Journal of Sports Medicine* 2020; 54: 1451–1462. DOI: 10.1136/bjsports-2020-102955.
9. Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 Compendium of Physical Activities: a second update of codes and MET values. *Med Sci Sports Exerc* 2011; 43: 1575–1581. DOI: 10.1249/MSS.0b013e31821ece12.

10. Biddle SJ, Bennie JA, Bauman AE, et al. Too much sitting and all-cause mortality: is there a causal link? *BMC Public Health* 2016; 16: 635. 20160726. DOI: 10.1186/s12889-016-3307-3.
11. Duvivier BM, Schaper NC, Bremers MA, et al. Minimal intensity physical activity (standing and walking) of longer duration improves insulin action and plasma lipids more than shorter periods of moderate to vigorous exercise (cycling) in sedentary subjects when energy expenditure is comparable. *PLoS One* 2013; 8: e55542. 20130213. DOI: 10.1371/journal.pone.0055542.
12. Franssen WMA, Nieste I, Verboven K, et al. Sedentary behaviour and cardiometabolic health: Integrating the potential underlying molecular health aspects. *Metabolism* 2025; 170: 156320. 20250606. DOI: 10.1016/j.metabol.2025.156320.
13. Vanherle J, Franssen G, Ivanova A, et al. Optimizing physical activity bouts to interrupt sedentary behaviour for cardiometabolic health: a systematic review and meta-analyses of randomized controlled trials. *Eur J Prev Cardiol* 2026 20260401. DOI: 10.1093/eurjpc/zwag079.
14. Janssen I, Clarke AE, Carson V, et al. A systematic review of compositional data analysis studies examining associations between sleep, sedentary behaviour, and physical activity with health outcomes in adults. *Appl Physiol Nutr Metab* 2020; 45: S248–s257. DOI: 10.1139/apnm-2020-0160.
15. Shrestha N, Kukkonen-Harjula KT, Verbeek JH, et al. Workplace interventions for reducing sitting at work. *Cochrane Database Syst Rev* 2018; 6: Cd010912. 20180620. DOI: 10.1002/14651858.CD010912.pub4.
16. Thorp A, Kingwell B, Sethi P, et al. Alternating Bouts of Sitting and Standing Attenuate Postprandial Glucose Responses. *Medicine and science in sports and exercise* 2014; 46. DOI: 10.1249/MSS.0000000000000337.
17. Saeidifard F, Medina-Inojosa JR, Supervia M, et al. The Effect of Replacing Sitting With Standing on Cardiovascular Risk Factors: A Systematic Review and Meta-analysis. *Mayo Clin Proc Innov Qual Outcomes* 2020; 4: 611–626. 20201201. DOI: 10.1016/j.mayocpiqo.2020.07.017.
18. Hoffmann SW, Schierbauer J, Zimmermann P, et al. Effects of light-intensity physical activity on cardiometabolic parameters in young adults with overweight and obesity: The SED-ACT randomized controlled crossover trial. *Diabetes Obes Metab* 2024; 26: 3849–3859. 20240625. DOI: 10.1111/dom.15732.
19. Bodker A, Visotcky A, Gutterman D, et al. The impact of standing desks on cardiometabolic and vascular health. *Vasc Med* 2021; 26: 374–382. 20210405. DOI: 10.1177/1358863x211001934.
20. Soto-Rodríguez FJ, Cabañas EI and Pérez-Mármol JM. Impact of prolonged sitting interruption strategies on shear rate, flow-mediated dilation and blood flow in adults: A systematic review and meta-analysis of randomized cross-over trials. *J Sports Sci* 2022; 40: 1558–1567. 20220622. DOI: 10.1080/02640414.2022.2091347.
21. Khalafi M, Sakhaei MH, Kazeminasab F, et al. The impact of high-intensity interval training on vascular function in adults: A systematic review and meta-analysis. *Frontiers in Cardiovascular Medicine* 2022; Volume 9 - 2022. Systematic Review. DOI: 10.3389/fcvm.2022.1046560.

22. Kleinloog JPD, Mensink RP, Roodt JO, et al. Aerobic exercise training improves not only brachial artery flow-mediated vasodilatation but also carotid artery reactivity: A randomized controlled, cross-over trial in older men. *Physiol Rep* 2022; 10: e15395. DOI: 10.14814/phy2.15395.
23. Wheeler MJ, Green DJ, Cerin E, et al. Combined effects of continuous exercise and intermittent active interruptions to prolonged sitting on postprandial glucose, insulin, and triglycerides in adults with obesity: a randomized crossover trial. *Int J Behav Nutr Phys Act* 2020; 17: 152. 20201214. DOI: 10.1186/s12966-020-01057-9.
24. Homer AR, Fenemor SP, Perry TL, et al. Regular activity breaks combined with physical activity improve postprandial plasma triglyceride, nonesterified fatty acid, and insulin responses in healthy, normal weight adults: A randomized crossover trial. *Journal of Clinical Lipidology* 2017; 11: 1268–1279.e1261. DOI: https://doi.org/10.1016/j.jacl.2017.06.007.
25. Kozey Keadle S, Lyden K, Staudenmayer J, et al. The independent and combined effects of exercise training and reducing sedentary behavior on cardiometabolic risk factors. *Appl Physiol Nutr Metab* 2014; 39: 770–780. 20140107. DOI: 10.1139/apnm-2013-0379.
26. L EFG, R CM, Shepherd SO, et al. Evaluation of sit-stand workstations in an office setting: a randomised controlled trial. *BMC Public Health* 2015; 15: 1145. 20151119. DOI: 10.1186/s12889-015-2469-8.
27. Garber C, Blissmer B, Deschenes M, et al. Quantity and Quality of Exercise for Developing and Maintaining Cardiorespiratory, Musculoskeletal, and Neuromotor Fitness in Apparently Healthy Adults: Guidance for Prescribing Exercise. *Medicine and science in sports and exercise* 2011; 43: 1334–1359. DOI: 10.1249/MSS.0b013e318213fefb.
28. Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; 28: 412–419. DOI: 10.1007/bf00280883.
29. Matsuda M and DeFronzo RA. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. *Diabetes Care* 1999; 22: 1462–1470. DOI: 10.2337/diacare.22.9.1462.
30. Yeckel CW, Weiss R, Dziura J, et al. Validation of insulin sensitivity indices from oral glucose tolerance test parameters in obese children and adolescents. *J Clin Endocrinol Metab* 2004; 89: 1096–1101. DOI: 10.1210/jc.2003-031503.
31. Matthews JN, Altman DG, Campbell MJ, et al. Analysis of serial measurements in medical research. *Bmj* 1990; 300: 230–235. DOI: 10.1136/bmj.300.6719.230.
32. Nieste I, Franssen WMA, Duvivier B, et al. Replacing sitting with light-intensity physical activity throughout the day versus 1 bout of vigorous-intensity exercise: similar cardiometabolic health effects in multiple sclerosis. A randomised cross-over study. *Disabil Rehabil* 2022: 1–10. 20221003. DOI: 10.1080/09638288.2022.2122601.
33. Lyden K, Keadle SK, Staudenmayer J, et al. The activPALTM Accurately Classifies Activity Intensity Categories in Healthy Adults. *Med Sci Sports Exerc* 2017; 49: 1022–1028. DOI:

10.1249/mss.0000000000001177.

34. Courtney JB, Nuss K, Lyden K, et al. Comparing the activPAL software's Primary Time in Bed Algorithm against Self-Report and van der Berg's Algorithm. *Meas Phys Educ Exerc Sci* 2021; 25: 212–226. 20201228. DOI: 10.1080/1091367x.2020.1867146.
35. Medicine ACoS. *ACSM's health-related physical fitness assessment manual.* IV ed.: Chris Johnson, 2013.
36. Thijssen DH, Black MA, Pyke KE, et al. Assessment of flow-mediated dilation in humans: a methodological and physiological guideline. *Am J Physiol Heart Circ Physiol* 2011; 300: H2–12. 20101015. DOI: 10.1152/ajpheart.00471.2010.
37. Thijssen DHJ, Bruno RM, van Mil A, et al. Expert consensus and evidence-based recommendations for the assessment of flow-mediated dilation in humans. *Eur Heart J* 2019; 40: 2534–2547. DOI: 10.1093/eurheartj/ehz350.
38. Bekar C and Goktas Z. Validation of the 14-item mediterranean diet adherence screener. *Clin Nutr ESPEN* 2023; 53: 238–243. 20221229. DOI: 10.1016/j.clnesp.2022.12.026.
39. Bird SR and Hawley JA. Update on the effects of physical activity on insulin sensitivity in humans. *BMJ Open Sport Exerc Med* 2016; 2: e000143. 20170301. DOI: 10.1136/bmjsem-2016-000143.
40. Mann S, Beedie C, Balducci S, et al. Changes in insulin sensitivity in response to different modalities of exercise: a review of the evidence. *Diabetes Metab Res Rev* 2014; 30: 257–268. DOI: 10.1002/dmrr.2488.
41. Weeldreyer NR, De Guzman JC, Paterson C, et al. Cardiorespiratory fitness, body mass index and mortality: a systematic review and meta-analysis. *Br J Sports Med* 2025; 59: 339–346. 20250220. DOI: 10.1136/bjsports-2024-108748.
42. Neeland IJ, Ross R, Després JP, et al. Visceral and ectopic fat, atherosclerosis, and cardiometabolic disease: a position statement. *Lancet Diabetes Endocrinol* 2019; 7: 715–725. 20190710. DOI: 10.1016/s2213-8587(19)30084-1.
43. Ferguson T, Olds T, Curtis R, et al. Effectiveness of wearable activity trackers to increase physical activity and improve health: a systematic review of systematic reviews and meta-analyses. *Lancet Digit Health* 2022; 4: e615–e626. DOI: 10.1016/s2589-7500(22)00111-x.
44. Franssen WMA, Nieste I, Vandereyt F, et al. A 12-week consumer wearable activity tracker-based intervention reduces sedentary behaviour and improves cardiometabolic health in free-living sedentary adults: a randomised controlled trial. *J Act Sedentary Sleep Behav* 2022; 1: 8. 20221201. DOI: 10.1186/s44167-022-00007-z.
45. Andriessen C, Rutters F, Hoeks J, et al. Amount and timing of physical activity in relation to sleep quality in the general middle-aged Dutch population: A cross-sectional analysis. *Preventive Medicine Reports* 2025; 53: 103035. DOI: https://doi.org/10.1016/j.pmedr.2025.103035.
46. Hadgraft NT, Winkler E, Climie RE, et al. Effects of sedentary behaviour interventions on biomarkers of cardiometabolic risk in adults: systematic review with meta-analyses. *Br J Sports Med* 2021; 55: 144–154. 20200408. DOI: 10.1136/bjsports-2019-101154.

Figures

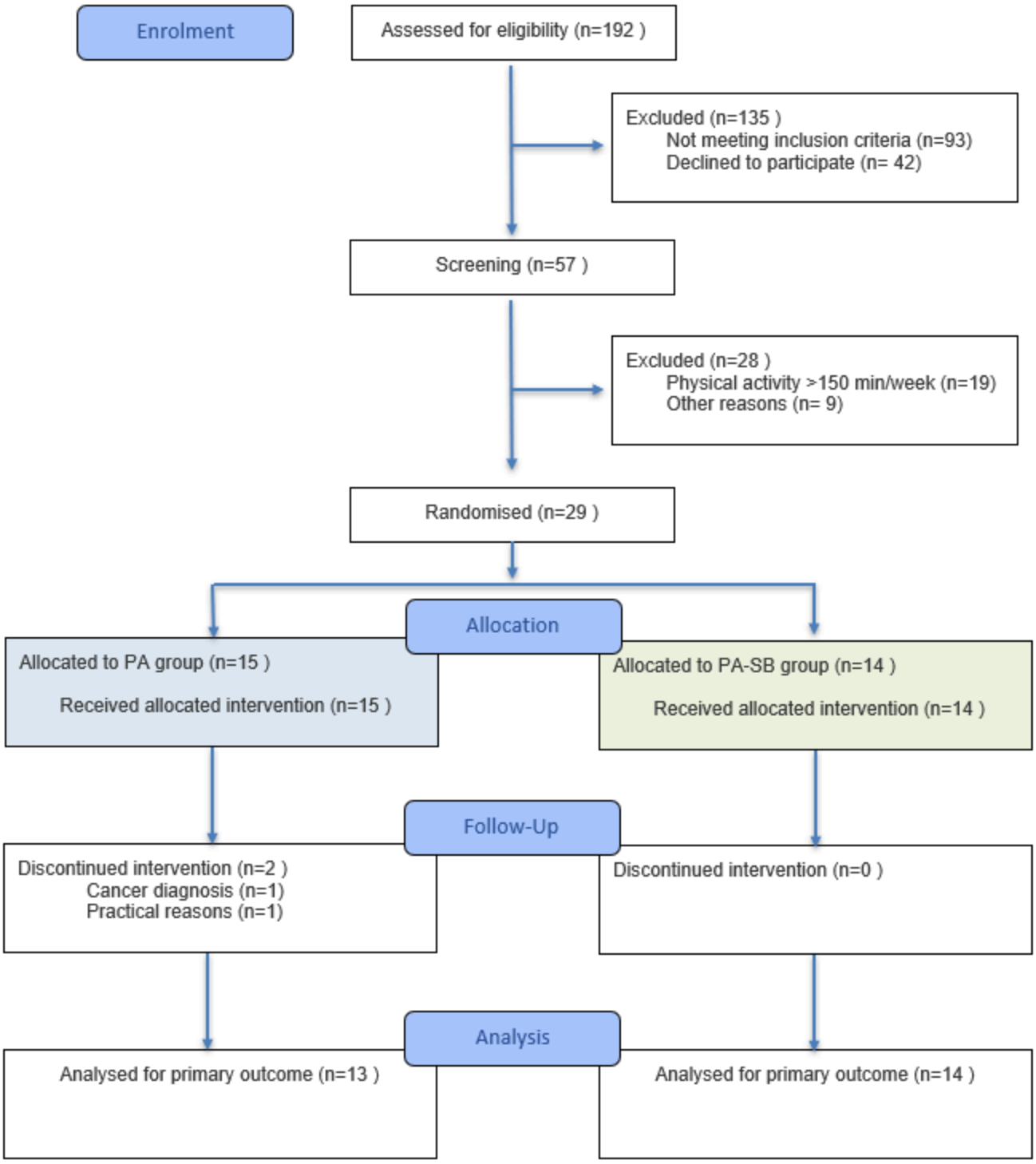


Figure 1

CONSORT 2025 Flow diagram

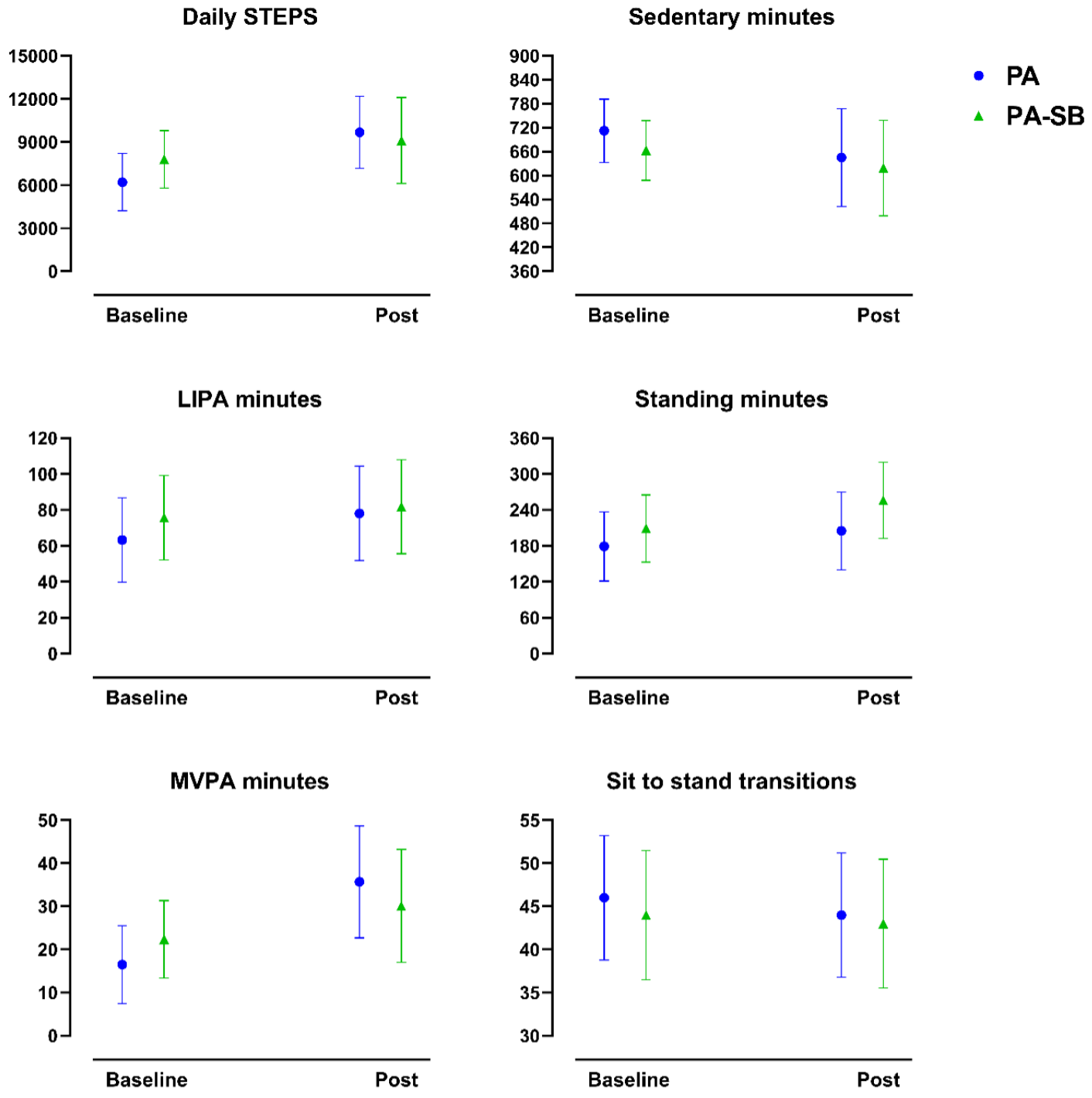


Figure 2

Physical activity behaviour and sedentary time at baseline and at the end of the intervention period per intervention arm. Abbreviations that were used: LIPA = light intensity physical activity; MVPA = moderate to vigorous intensity physical activity;. Data are expressed as mean with standard deviation.

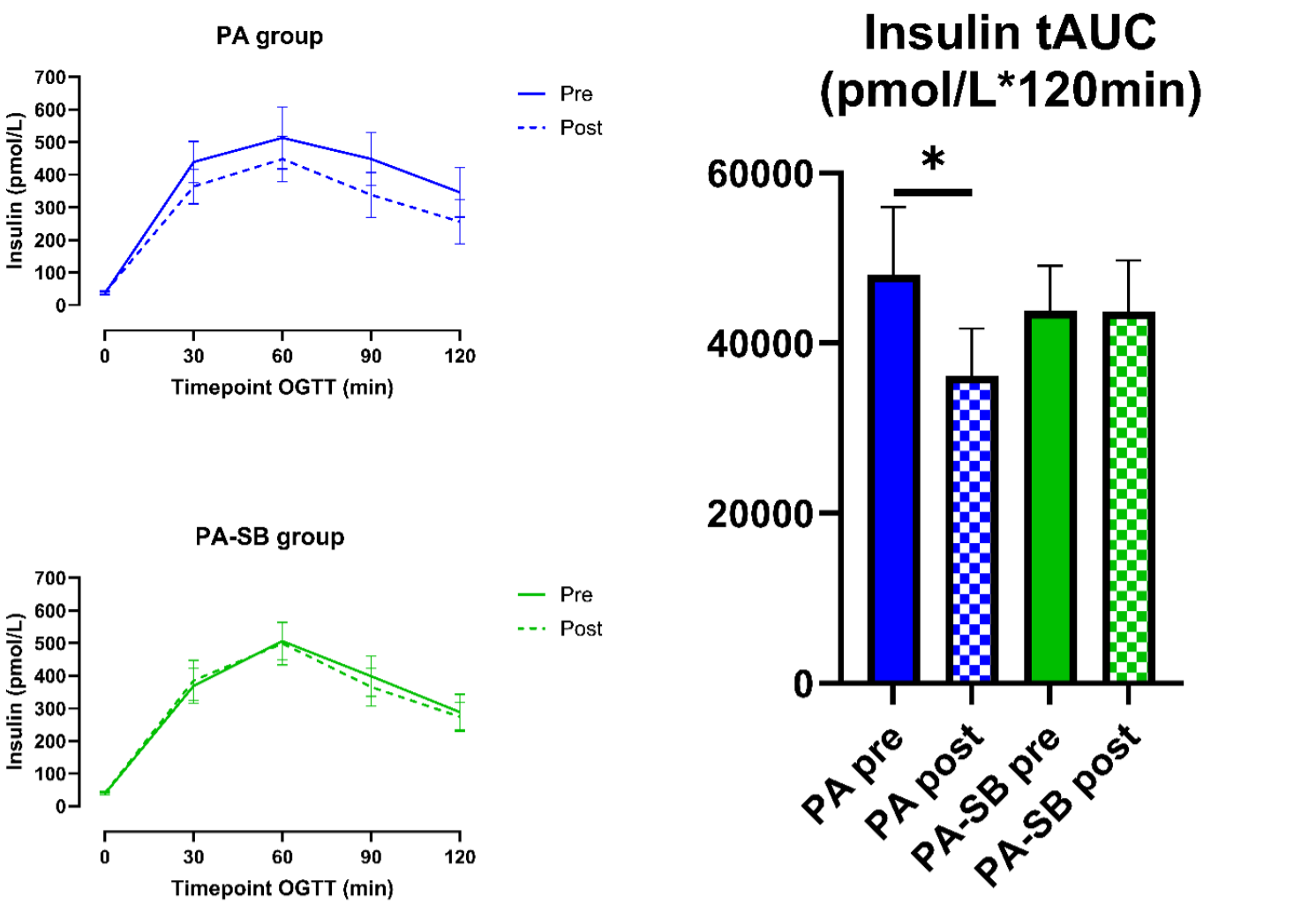


Figure 3

Insulin concentration per timepoint during oral glucose tolerance tests (OGTT) before and after the interventions presented for each intervention arm (left panels); Insulin total area under the curve (AUC) during the OGTT (right panel). * indicates a significant within group difference ($p<0.05$)

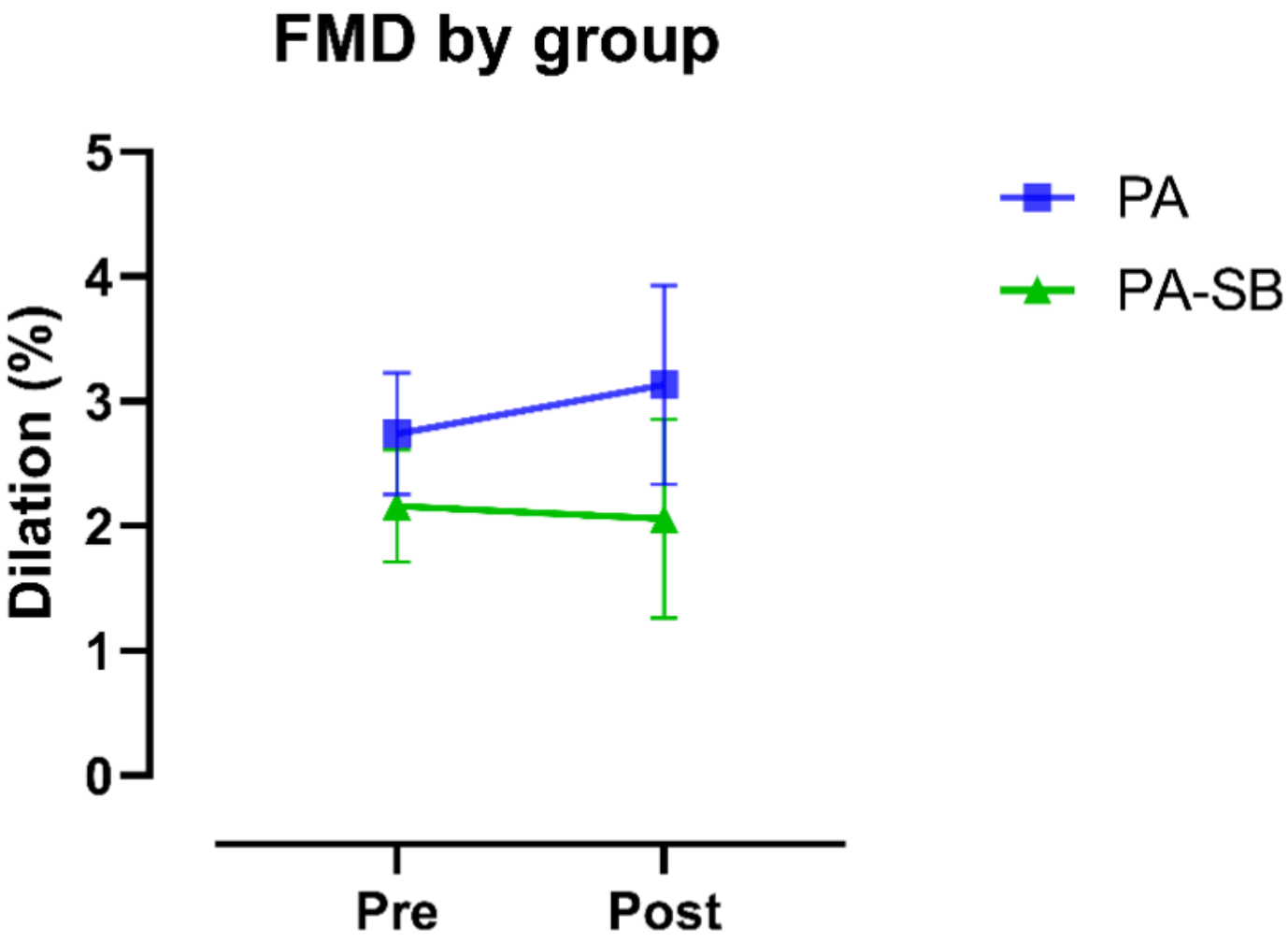


Figure 4

Femoral artery flow-mediated dilation before and after the intervention period presented for each experimental group.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CONSORT2025editablechecklist.docx
- Supplementarymaterials.docx