Master's thesis

NTNU
Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
Department of Circulation and Medical Imaging

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The effect of Personal Activity Intelligence (PAI) on ambulatory blood pressure in adults with elevated blood pressure: a 12-week pilot randomized controlled trial

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Supervisor: Ulrik Wisløff and Emma Ingeström

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Abstract

Background: High blood pressure (BP), or *hypertension*, is estimated to affect over one billion individuals worldwide and is considered a leading risk factor for cardiovascular disease. Low cardiorespiratory fitness is independently associated with all-cause mortality in hypertensives. Regular physical activity is routinely recommended in the prevention, treatment and control of hypertension. Personal Activity Intelligence (PAI) is a physical activity metric where obtaining ≥100 PAI per week is associated with longer life, higher fitness and lower incidence of hypertension compared to peers obtaining 0 PAI per week. The primary objective of this randomized controlled pilot trial was to evaluate the effect of a physical activity goal of ≥100 PAI per week compared to following current physical activity guidelines on 24h ambulatory BP (ABP) in adults with elevated BP. Secondary outcomes include automated office BP, arterial stiffness, cardiac function and cardiorespiratory fitness.

Methods: This 12-week parallel two-arm pilot trial took place in Trondheim, Norway (October 2019 to May 2020). Twenty-six inactive (<50 PAI per week based on self-reported physical activity) but otherwise healthy adults (45-64 years), meeting the automated office BP criteria of 130-179 mmHg systolic and/or 80-109 mmHg diastolic BP, were recruited (50% women). Participants were randomized (1:1) to an intervention group (n = 12), that were instructed to obtain ≥100 PAI per week guided by a heart rate monitor with a PAI app, or to a control group (n = 14), recommended to follow current physical activity guidelines. Both groups were equipped with a heart rate monitor tracking PAI, but only the intervention group was aware of their PAI level during the intervention period. The primary outcome was assessed with 24h ABP monitoring, and the secondary outcomes were measured by automated BP readings at the clinical office, carotid-femoral pulse wave velocity (cf-PWV), stroke volume by echocardiography and peak oxygen uptake (VO_{2peak}) during cardiopulmonary exercise testing. The outcome measures were assessed at baseline and after 6 and 12 weeks, and subsequently analyzed using linear mixed models on an intention-to-treat and post-hoc basis comparing participants who obtained ≥100 PAI per week to those who obtained <100 PAI per week (on >70% of the days in the intervention period).

Results: The average 24h systolic and diastolic BP was 135 and 81 mmHg, respectively, at baseline, with an average body mass index of 28 kg/m^2 and VO_{2peak} of 36 ml/kg/min. We observed no differences between the intervention (n = 10) and the control group (n = 13) in 24h ABP, automated office BP, cf-PWV, stroke volume or VO_{2peak} following 12 weeks. There were no significant differences between participants who obtained ≥100 PAI on at least 70% of the days compared to those who did not on any outcomes except on automated office systolic BP, which was 7.5 mmHg (95% Confidence interval (CI) -14.2 to -0.8) and 6.4 mmHg (95% CI -13.5 to 0.8) lower in those who achieved ≥100 PAI following 6 and 12 weeks, respectively.

Conclusions: Our findings indicate that there is no difference in 24h ABP between the intervention, obtain ≥100 PAI/week with PAI monitoring for 12 weeks, compared to the control, recommended to follow current physical activity guidelines. Obtaining ≥100 PAI/week may be effective in reducing automated office BP but not 24h ABP. No change in 24h ABP and VO_{2peak} indicate that future PAI trials should examine the effect of higher PAI levels and look for ways to increase adherence.

Trial registration: Clinicaltrials.org identifier: NCT04151537.

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The clinical examinations of the present study were performed at the core facility NeXt Move, NTNU.

Table of Contents

List of Figures

List of Tables

List of Abbreviations

A	Peak late diastolic mitral inflow velocity
ABP	Ambulatory blood pressure
AOBP	Automated office blood pressure
BP	Blood pressure
cf-PWV	Carotid-femoral pulse wave velocity
CI	Confidence interval
CRF	Cardiorespiratory fitness
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
E	Peak early diastolic mitral inflow velocity
e’	Early diastolic mitral annular velocity
ESC	European Society of Cardiology
ESH	European Society of Hypertension
HIIT	High-intensity interval training
HR	Heart rate
MICT	Moderate-intensity continuous training
NO	Nitric oxide
PA	Physical activity
PAI	Personal Activity Intelligence
RAAS	Renin-angiotensin-aldosterone system
RCT	Randomized controlled trial
SBP	Systolic blood pressure
SD	Standard deviation
SE	Standard error
SNS	Sympathetic nervous system
SV	Stroke volume
VO_{2max}	Maximal oxygen uptake
VO_{2peak}	Peak oxygen uptake

Definitions

Afterload

Sum of the resistance, or load, that oppose heart contraction.

Ambulatory blood pressure

Blood pressure measured during daily life with a wearable monitor. Typically worn for 24h with blood pressure measured every 20 minutes to every hour.

Aneurysm

An abnormal bulge, or distention, of an artery caused by arterial wall weakness.

Arterial conduit function

The function of the arteries to supply blood and deliver oxygen to tissues.

Arterial cushioning function

The function of the arteries to distend and attenuate the pressure by intermittent heart ejections to provide steady blood flow.

Automated office blood pressure

Blood pressure recorded in an office where the individual sits alone without disturbance and the monitoring device is set on an automated timer.

Blood pressure

The pressure in the large arteries of the systemic circulation.

Cardiorespiratory fitness

The ability of the body to transport oxygen during sustained physical activity.

High-intensity interval training

Repeated bouts of intense effort interspersed with recovery periods. Interval intensity is high enough to accumulate lactate and muscular fatigue (typically ≥85% of maximal heart rate), such that intermittent recovery is needed to avoid failure.

Hypertension

High blood pressure, defined as systolic blood pressure and/or diastolic blood pressure of ≥140/90 mmHg in Europe and ≥130/80 mmHg in the US based on repeated office readings. The corresponding thresholds for 24h ambulatory blood pressure monitoring are ≥130/80 and ≥125/75 mmHg, respectively (1).

Inotropy

Intrinsic strength of cardiac contraction independent of pre- and afterload.

Left ventricular hypertrophy

Increased size of cardiomyocytes which may be concentric (increased left ventricular wall thickness) and eccentric (dilation of the left ventricular chamber) hypertrophy.

Masked Hypertension

The opposite of white coat hypertension; normal blood pressure in a clinical setting, but high blood pressure in other settings.

Moderate-intensity continuous training

Steady-state bouts of exercise, typically around 70% of maximal heart rate, typically longer duration is needed to achieve similar caloric expenditure to that of high-intensity training.

Preload

Initial stretch of cardiomyocytes prior to heart contraction.

White Coat Hypertension

Exhibition of hypertension in a clinical setting (such as a doctor's office), but normal blood pressure in other settings.

1 Introduction

High blood pressure (BP), or *hypertension*, is estimated to affect over one billion individuals worldwide and is considered the leading risk factor for cardiovascular disease (CVD), making it a major contributor to all-cause mortality and health care expenditures worldwide (2, 3). While the European Society of Cardiology (ESC)/European Society of Hypertension (ESH) definition of hypertension is systolic BP (SBP) ≥140 mmHg and/or diastolic BP (DBP) ≥90 mmHg, the American College of Cardiology and American Heart Association recently lowered their definition to SBP/DBP of ≥130/80 mmHg (4, 5). The exact cut off facilitates decision making, however, CVD risk increases continuously from a BP of 115/75 mmHg (6). For example, above this threshold, each 20 mmHg increment of SBP or 10 mmHg increment of DBP is associated with a two-fold increase of CVD mortality (6).

Blood pressure is the pressure in the large arteries of the systemic circulation generated by the pumping action of the heart, which creates the pressure gradient required for continuous blood flow, oxygen delivery and tissue perfusion (arterial conduit function) (7, 8). BP is pulsatile and can be divided into two phases based on the cardiac cycle: systole and diastole. During heart relaxation, diastole, DBP is determined by heart rate and systemic vascular resistance (9). This resistance mainly depends on vascular tone, the sum of many competing vasoconstricting and vasodilating forces acting on small arteries and arterioles further down in the systemic circulation (10). Whereas heart rate is regulated by the intrinsic firing rate of the heart and neurohormonal influences, such as catecholamines (7).

During systole, which represent the contraction phase of the heart, SBP depends on the underlying DBP, the amount of blood ejected per heartbeat, *i.e.* stroke volume, and ventricular and arterial stiffness (9). Stroke volume is regulated by the preload, inotropy and afterload of the heart. This can be exemplified by the Frank-Starling mechanism: an increase in venous return increases preload, which puts an initial stretch on the cardiomyocytes (11, 12). This stretch lengthens the sarcomeres and increase the force generating capacity of the cardiac muscle by optimizing its length-tension relationship, which results in a larger stroke volume. When heart rate is kept constant, an increase in stroke volume leads to a larger cardiac output and arterial pressure, which then increase afterload and reduce ejection velocity, thereby offsetting part of the initial stroke volume increase (12). Increases in the strength of muscular contraction (inotropy) may increase ejection velocity and stroke volume, but would similarly increase afterload and reduce end-diastolic volume (preload) (12). The converse cascade is also true. In summary, changes to the heart whether by hemodynamics (movement or flow of blood) or neurohormonal influences have several downstream effects, and ultimately it is the sum of the changes that decides the outcome.

Ventricular and arterial stiffness can be mathematically explained as the change in pressure for a given change in ventricular and arterial volume (13). An important function of the large arteries of the systemic circulation is to distend and partially attenuate the pressure generated by the left ventricle (arterial cushioning function), thereby protecting the systemic circulation from too high pressures (13).

While BP forms a vital function, excessive hemodynamic load caused by persistent high BP may lead to CVD and organ damage (7, 14). Particularly susceptible organs are those who rely on high blood flow, such as the brain and kidneys (14). Furthermore, the blood vessels themselves are consistently disposed to dysfunction which may lead to arterial disease, aneurysms and/or stroke (15, 16). The initial response of the heart to overcome the increased afterload caused by persistent high BP and maintain adequate ejection fraction is left ventricular concentric hypertrophy (17). Concentric left ventricular hypertrophy is compensatory to maintain adequate cardiac function and blood flow, but may deleteriously lead to heart failure and other CVDs (17-19).

Cardiovascular load is preferably measured with 24h ambulatory BP (ABP) monitoring as this closely reflects the cardiovascular load faced by the individual in their everyday life and target organ damage (20). Although, office based BP measurements are more routinely used in clinical and research settings due to constrains with 24h ABP monitoring, it is susceptible to white coat or masked hypertension, making 24h ABP monitoring the gold standard (5). Of note, there is emerging evidence that office BP measurements can be improved by using an automated approach where the patients sit alone without disturbance. This is known as an automated office BP measurement and is shown to more closely relate to values seen using 24h ABP monitoring and thus cardiovascular load (21).

The underlying reasons for hypertension are often unknown, complex, and can vary greatly. Only 5-10% of hypertensives have an identifiable cause, known as secondary hypertension, with the rest being considered idiopathic and commonly referred to as primary hypertension (22). The causes of hypertension are thought to be associated with genetic predispositions and lifestyle risk factors (4). Hypertension is estimated to have a heritability of around 35-50% (23). A recent genetic association study in over one million individuals with European ancestry identified 901 loci for BP traits, explaining 5.7% of the variance of SBP in this population (24). Genetic studies are opening pathways for improved understanding of hypertension, but much remains to be elucidated. Lifestyle factors associated with hypertension include poor diet, overweight and obesity, low physical activity and excessive alcohol intake (25-28). A healthy lifestyle, as opposed to the above, plays an integral part in not only the prevention but also the treatment of hypertension (4, 5).

Low cardiorespiratory fitness (CRF) is independently associated with all-cause mortality in healthy and hypertensive individuals, as well as in CVD patients (29). Additionally, both high physical activity and CRF are associated with reduced risk of hypertension in a graded fashion (30-32). Regular physical activity, particularly aerobic exercise, is thus recommended in the prevention, treatment and control of hypertension (4, 5). Physical activity exerts its effect on BP by acting on various structural and neurohumoral systems. This includes improvements in endothelial function, arterial stiffness, the renin-angiotensin-aldosterone system and the autonomic nervous system (33-39). Due to the integrated and interindividual ways physical activity affects the body, it is often difficult to find meaningful improvements in all BP-relevant parameters and mechanisms. However, at least hemodynamically, aerobic exercise is thought to lower BP by decreasing systemic vascular resistance (33). A summary of the main mechanisms explaining how aerobic exercise acts to lower BP is illustrated in **Figure 1**.

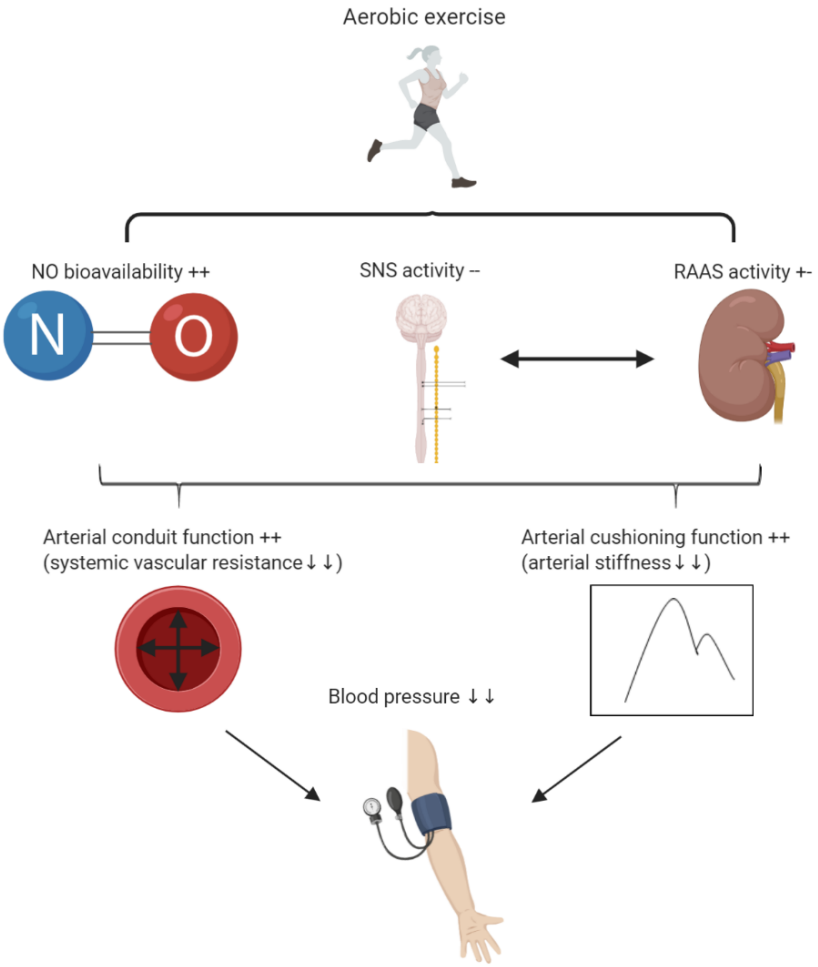

Figure 1. Main mechanisms of reduced blood pressure following aerobic exercise (33-39). Aerobic exercise affects local factors controlling vascular tone, in particular improved vasodilation by increased NO bioavailability but also reduced endothelin-1 activity. Systemic factors promoting vasoconstriction from RAAS and SNS activity, that often reinforce each other, are reduced. Collectively, by improved arterial conduit and cushioning function, blood pressure is reduced. NO, nitric oxide; SNS, sympathetic nervous system; RAAS, renin-angiotensin-aldosterone system.

It is well supported by numerous meta-analyses of randomized controlled trials (RCTs) that aerobic exercise lowers BP (40-44). Findings indicate that the reduction in BP following regular aerobic exercise ranges from 2-10 mmHg in SBP and 1-5 mmHg in DBP (40-44). It is important to note that most research has been on individuals that are normotensive (*i.e.* have lower BP than what is considered hypertensive), and that the reductions are on the higher-end in hypertensive individuals (40, 41). For example, a recent and comprehensive meta-analysis by Naci *et al.* (2018) found a reduction in SBP of 4.1-5.7 mmHg following aerobic exercise training based on 115 RCTs and >8000 normo- and hypertensive individuals (40). They found that SBP was reduced by an average of 8.7 mmHg in the hypertensive group, which is equally effective as current pharmacological treatments (40).

Although aerobic exercise is effective medicine for hypertension, there is a lot of ambiguity on the optimal dose. However, there is some consensus that exercise should be performed

on most days, as there is a drop in BP immediately following exercise, known as post-exercise hypertension (45). Accumulation of this response is thought to be important for chronic BP reduction (46).

High CRF is associated with a reduced risk of hypertension in epidemiological studies (26, 30, 47) and RCTs have found improvements in CRF to be intensity-dependent in cardiometabolic disease populations including hypertension (48). It therefore appears logical that there is an intensity-interaction where high-intensity exercise is superior in reducing BP to that of lower intensity exercise. A systematic review and meta-analysis of RCTs by Costa *et al.* (2018) sought to compare the effects of high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) on BP in adults with pre- to established hypertension (*i.e.* SBP/DBP ≥130/85 mmHg) (42). They found no significant difference between HIIT and MICT based on 7 RCTs and 164 participants, with mean reductions of 6.3/3.8 mmHg in the HIIT group and 5.8/3.5 mmHg in the MICT group, respectively (42). However, HIIT improved CRF measured as maximal oxygen uptake (VO_{2max}) significantly more than MICT (4.3 vs 1.6 ml/kg/min), which results in greater cardioprotective benefits (49, 50). This interestingly indicate that there may be different time courses in the changes of VO_{2max} and BP when comparing the results of shorter RCTs to that of longitudinal epidemiological studies.

It is noteworthy that only a small number of studies have used 24h ABP monitoring. Molmen-Hansen *et al.* (2011) used 24h ABP monitoring and reported that 12-weeks of HIIT reduced 24h SBP by 12 mmHg and 24h DBP by 8 mmHg whereas the effect of MICT was about half of the HIIT group (51). The fact that the participants were hypertensives not currently on medication likely contributed to effect sizes that are generally associated with pharmacological interventions (40). In contrast, a study by Guimarães *et al.* (2010) found no effect of HIIT or MICT on BP compared to controls in medically treated hypertensives (52). Although, this may be due to lower adherence (61%), an unsupervised exercise intervention, lower baseline BP or mechanistic interactions between exercise and medical interventions (52).

Even though the optimal dose-response relationship between exercise and reducing high BP is not known, the aforementioned effects indicate that it is important to get hypertensives more physically active and increase their fitness levels. The World Health Organization recommends at least 150 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity per week, or a combination thereof (53). However, the problem is likely not the guidelines themselves, but getting people to adhere to them. Based on US survey data, merely about 23% of those with diagnosed hypertension and 29% of those with undiagnosed hypertension adhere to current physical activity guidelines (54). These numbers are even more disturbing considering that self-reported activity data severely overestimates activity levels when compared to accelerometer data (55). A promising strategy to improve physical activity is physical activity monitors with a specific activity goal, which has been shown to increase physical activity levels by about 27% (56). An individualized and scientifically validated physical activity goal would, therefore, be an ideal way to improve physical activity levels and ensure it is enough to maximize health benefits.

To quantify the amount of physical activity needed to improve health and reduce CVD mortality, the Cardiac Exercise Research Group (CERG) recently developed a physical activity metric, coined personal activity intelligence (PAI) (57). The PAI metric incorporates almost all aspects of an exercise dose and accounts for age, sex, resting and maximum

heart rate, and translates individual heart rate patterns during physical activity into one continuous, easily understandable and personalized metric of physical activity. The goal is to achieve ≥100 PAI per week, which translates to roughly 60 minutes per week at an intensity of 75% of heart rate reserve. As previous findings have shown that higher intensity exercise leads to greater improvements in CRF in a shorter time period, PAI scores are accumulated faster at higher intensities.

Based on large epidemiological data (>1 million person-years), apparently healthy adults who were physically active (≥100 PAI per week) lived on average 4.7 years longer, had a lower prevalence of hypertension and CVD risk factors, as well as lower all cause (13-17%) and CVD (17-23%) mortality, compared to those who were physically inactive (0 PAI per week) (57, 58). The apparent reduction in CVD mortality was even greater in hypertensives (30%) and established CVD (36%) (57, 58). Importantly, these results applied for all obtaining ≥100 PAI, regardless if they met current physical activity guidelines or not. The basis of using PAI as an improved measure of adequate physical activity compared to current guidelines is appealing, however, it is based on self-reported physical activity and PAI has not yet been tested in an RCT using continuous heart rate monitors.

1.1 Study objective

The objective of this pilot RCT was to evaluate the effect of a physical activity goal to obtain ≥100 PAI per week with PAI monitoring compared to being recommended to follow current physical activity guidelines on 24h ABP in adults with elevated BP (SBP ≥130 mmHg and/or DBP ≥80 mmHg). Secondary outcomes were automated office BP, arterial stiffness, cardiac function and CRF. It was hypothesized that the goal of obtaining ≥100 PAI per week would result in superior improvements in these parameters compared to following national physical activity guidelines.

2 Methods

2.1 Study design

This was a 12-week pilot RCT, where the participants were randomly assigned to two parallel groups (**Figure 2**). The intervention group had a goal of obtaining ≥100 PAI per week with continuous heart rate monitoring, whereas the control group was recommended to follow current national physical activity guidelines. Computerized, unstratified block randomization was conducted by the unit of applied clinical research at NTNU. Randomization order was blinded to the test personnel and spouses (2 pairs) were randomized as a cluster to the same group.

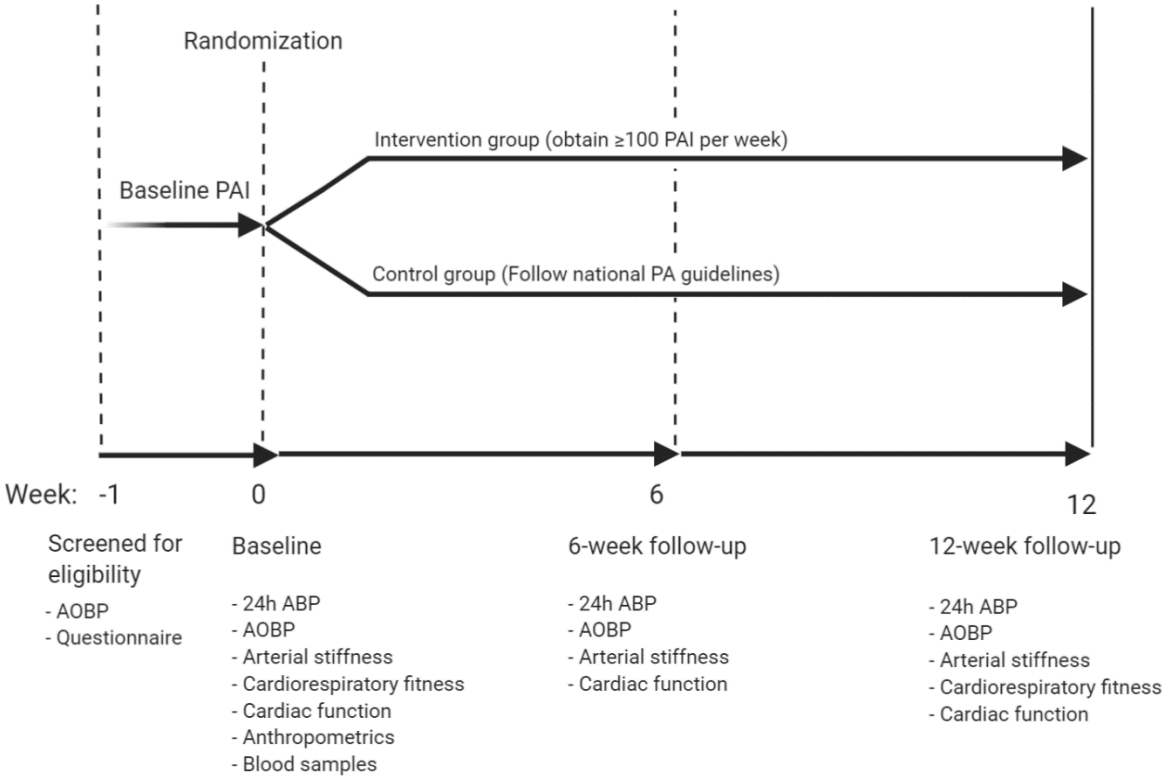

Figure 2. Schematic of the study design and study timeline. Abbreviations: ABP, ambulatory blood pressure; AOBP, automatic office blood pressure; PA, physical activity; PAI, Personal Activity Intelligence.

2.2 Study population

Twenty-six participants were recruited through advertisements on Facebook (facebook.com/cergforskning/) and in a local newspaper. Inclusion criteria were automated office SBP 130-179 mmHg and/or DBP 80-109, age 45-64 years and not currently engaging

in regular physical activity (<50 PAI per week based on self-reported physical activity (57)). Exclusion criteria were self-reported usage of BP or lipid modifying medication, medical history of diabetes or CVD, diagnosed secondary hypertension or other current disease or disability that would prevent participation. Eligibility was assessed during an initial screening visit at least one week prior to baselines testing.

2.3 Ethical concerns

The study followed the directives of the Declaration of Helsinki, was approved by the regional medical ethics committee (REK 2019/1084) and written informed consent was obtained by all participants. The study is registered on clinicaltrials.org (Identifier: NCT04151537).

The inclusion criteria were updated on 30 October 2019. This was due to a lower than expected inclusion rate, merely 3 out of 16 (19%) potential participants attending screening were included between 11-29 October 2019. The initial inclusion criteria regarding BP were SBP 140-179 mmHg and/or DBP 90-109 mmHg. The updated inclusion criteria enabled callback of 5 previously excluded participants, of which 4 were subsequently enrolled in the study. The remaining 19 participants were enrolled after 30 October 2019.

2.4 Personal Activity Intelligence (PAI)

The PAI score is calculated from resting heart rate, max heart rate and sex, and translate individual heart rate patterns to a weekly physical activity score. Further information regarding the algorithm and how PAI can be obtained has been described elsewhere (59, 60). All participants were fitted with a continuous heart rate monitor (Lynk2, Accurofit, Il, US), which was connected to a mobile app to measure PAI throughout the whole study period. At least six days of baseline PAI score were collected before other baseline assessments to evaluate current PAI level, where the participants were unable to see their own PAI level to avoid potential bias. During baseline monitoring the participants were asked to do physical activity as usual without changes in their current habits. Throughout the intervention period PAI was measured on all participants, but only the intervention group was aware of their current PAI level.

2.5 Study interventions

The study had two parallel arms:

- The intervention group that was instructed to obtain ≥100 PAI on a weekly basis. The heart rate monitor was connected to an app with a user interface that showed their current weekly PAI level and PAI scores obtained the last 7 days. Information on how to gain PAI was given verbally and in writing. Adherence to the intervention was predefined as >70% of days ≥100 PAI.

- The control group was recommended to follow physical activity guidelines, meaning 150 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity per week, or a combination thereof (53). The heart rate monitor was connected to an app with a user interface that tracked but did not show current PAI level or obtained score.

2.6 Clinical examinations

The primary outcome of this study was the difference between the two groups in 24h SBP and DBP following a 12-week intervention period. Secondary outcomes were automated office SBP and DBP, arterial stiffness, cardiac function and CRF. All primary and secondary outcomes except CRF were collected at baseline, 6 and 12-week follow-up. Participants fasted for >2h before hemodynamic variables were obtained. The clinical examinations were performed at the core facility NeXt Move, Norwegian University of Science and Technology (NTNU), Trondheim, Norway.

2.6.1 24-hour ambulatory blood pressure monitoring

A validated oscillometric device (Oscar 2, model 250, SunTech Medical, NC, US) was used to measure 24h ABP at baseline, 6 and 12-week follow-up (61, 62). BP and heart rate were measured in 20-minute intervals during daytime (0600-2200) and 30-minute intervals at nighttime (2200-0600). At least 70% of the measurements had to be successful for the 24h ABP to be defined as valid (63). If a measurement failed, another was taken automatically. The participants were instructed to avoid strenuous physical the 24h before and during the 24h ABP measurement, but otherwise asked to go on as usual. Awake and asleep time was individualized based on participant logs.

2.6.2 Automated office blood pressure

Automated office BP measurements were performed using an automatic BP monitor (Tango M2, Suntech, NC, USA) according to recent guidelines (64) at screening, baseline, 6 and 12-week follow-up. Initially, arm circumference was measured, and cuff size chosen according to manufacturer's instructions. The cuff was placed on the upper arm at the level of the heart. When set up with feet flat on the floor and back-and arms supported, the participants rested (unattended) in a seated position for five minutes. Three BP measurements were taken with 1 min 30 s rest in-between. Additional recordings were taken if the two first readings differed in SBP/DBP by more than 10 mmHg, and the average of the last two recordings were used. During the screening sessions both arms were measured, starting with the left arm and then the right arm following 2 minutes rest. All following BP measurements were taken on the arm with the highest measurement. In case of arm discrepancies, the reading with the highest percentage difference was used. All automated office BP measurements were unattended, which has been found to reduce the chance of white-coat hypertension and more closely reflect awake ambulatory BP readings (21).

2.6.3 Arterial stiffness

Applanation tonometry (Sphygmocor CvMS v9, AtCor Medical, Sydney, Australia) was used to measure carotid-femoral pulse wave velocity (cf-PWV) following 10 minutes of supine rest. Carotid to femoral artery distance was determined prior to the assessment by subtracting the carotid site to the suprasternal notch distance from the suprasternal notch to the femoral site distance using a tape measure. Two 10 s long sequential readings at the carotid and femoral site were gated to the R wave of an ECG signal to determine cf-PWV. All measurements were done on the right side and in duplicate as recommended (65, 66). If the measurements differed by more than 0.5 m/s a third measure was taken and the median used, otherwise the mean of two measurements was used.

2.6.4 Cardiac function

Cardiac function was assessed by echocardiographic readings examined at rest by an experienced sonographer using a Vivid e95 scanner (GE Vingmed Ultrasound, Horten, Norway) with a 4VC phased array three-dimensional transducer. The echocardiographic protocol followed international recommendations (67). All measurements were analyzed in EchoPAC SWO, v. 203 (GE Ultrasound). Left ventricular dimension and wall thickness were measured in two-dimensional parasternal gray-scale recordings. Measurements of left ventricular end-diastolic diameter and end-diastolic interventricular septum thickness were measured at the level according to the tips of the mitral leaflets. Mitral inflow pattern was assessed by pulsed-wave Doppler with sample volume at the tip of the mitral leaflets. Peak early diastolic (E) and late diastolic (A) mitral inflow velocities were measured. Mitral annular velocities were assessed by pulsed wave tissue Doppler with sample volumes in the basal part of the mitral annulus at the septal and lateral points. Peak early diastolic velocity (e') was measured as the average of the septal and lateral measurements. Ratios of early to late mitral inflow (E/A) and early mitral inflow to early myocardial velocities (E/e') were calculated. Tricuspid annular plane systolic excursion (TAPSE, *i.e.* longitudinal shortening of the right ventricular free wall) was measured in apical four-chamber views aligned to the right ventricle. Cardiac function was assessed as stroke volume that was measured using Doppler flow and diameter measurements in the left ventricular outflow tract. Cardiac output was automatically calculated by multiplying stroke volume and heart rate. Systemic vascular resistance was estimated by dividing mean arterial pressure (from 24h ABP) by cardiac output and multiplying by 80.

2.6.5 Cardiorespiratory fitness

Peak oxygen uptake (VO_{2peak}) was measured using an individualized ramp protocol on a treadmill (Woodway PPS 55, Waukesha, Wisconsin, USA) with Metalyzer II (Cortex, Leipzig, Germany) as previously described (68). The participants warmed-up for 15 minutes at a moderate intensity, approximately 70% of estimated maximal heart rate (69), with a rating of perceived exertion corresponding to 13-15 on the Borg scale (70). Heart rate was measured with a heart rate monitor (H7, Polar Electro, Kempele, Finland). Following the warm-up, the participants were fitted with a facemask (7450 Series V2 CPET mask, Hans Rudolph, Shawnee, Kansas, USA). Workload was increased by 0.5-1 km/h and/or 1-2% inclination per minute until volitional exhaustion or VO_{2max} criteria were met with gas measurements recorded every 10 seconds. VO_{2max} was defined as a plateau in VO_2 despite an increase in workload and respiratory exchange ratio >1.05. Twenty-two of 26 participants reached these criteria at baseline (10 in the intervention group and 12 in the control group), therefore the term VO_{2peak} was used instead. Maximal heart rate that was used in the PAI algorithm was estimated by adding 2 bpm to peak heart obtained during the test based on previous findings in our lab (71).

2.6.6 Anthropometrics

Waist circumference was measured with a stretch-resistant tape and according to World Health Organization guidelines (72). Specifically, the measurement site was the midpoint between the lower margin of the last palpable rib and the top of the iliac crest. The participants were asked to remove upper body clothing and keep their feet close together with weight evenly distributed and arms to the sides. When the participants were relaxed, waist circumference was measured at the end of a normal expiration. Measurements were

taken in duplicate and averaged if they were within 1 cm of each other. In case of discrepancies the measurements were repeated.

Body weight and composition was measured using bioelectrical impedance (Inbody 770, Seoul, Korea). The participants stood bear-foot on the device with hands on the handles and arms slightly abducted as per the manufacturer's instructions.

2.6.7 Blood analyses

Blood samples were obtained from an arm vein at baseline by experienced hospital personnel. All participants fasted for at least 10 hours prior to testing. Creatinine, total cholesterol, high-density lipoprotein, low-density lipoprotein, fasting glucose and glycosylated hemoglobin were measured using standard and quality-assured procedures at St Olavs Hospital, Trondheim, Norway. Glomerular filtration rate was estimated based on creatinine level, sex and age.

2.7 Sample size and statistical analyses

The PAI intervention consists of unsupervised physical activity and ≥100 PAI can be obtained using a range of exercise patterns. As the optimal exercise dose (frequency, duration and intensity) for reducing BP is yet to be determined, and there are no published RCTs using PAI monitoring, a pilot study was warranted. According to previous RCTs, the average reduction in 24h SBP following aerobic exercise range from 5 to 12 mmHg (51, 73-75). The standard deviation is about 12 mmHg. Power calculations with a selected significance level ($\alpha = 0.05$) and statistical power ($1 - \beta = 0.80$) gives a required sample size of 36-182 participants. Considering the uncertainty regarding adherence to the physical activity goal (100 PAI) and estimated effect size on 24h ABP and an extensive testing protocol, we found it reasonable to start with a smaller sample size, *e.g.* 30 participants, in this pilot study.

Linear mixed models for repeated measurements were conducted on all primary and secondary outcomes (except VO_{2peak}) with repeated measures with the interaction between group and time as fixed effects, as recommended by Twisk *et al.* (76). Analyzed results are shown by its model estimations. Normality of residuals were checked by visual inspection of Q-Q plots. Three variables (*i.e.* resting heart rate, cf-PWV and systemic vascular resistance) had borderline-normality. These results were tested with and without bootstrap, and the results were substantially the same. Therefore, all linear mixed model analyses are presented without bootstrapping. A sensitivity analysis to assess the potential effects of coronavirus disease 2019 (COVID-19) was conducted where participants who were affected by lockdown measures and had clinical examinations delayed were removed from the analysis at time points affected and completely.

The intervention effect on VO_{2peak} was examined for normality, homogeneity of variances, collinearity, homoscedasticity and homogeneity of the regression slope. The difference between intervention and control was compared with analysis of covariance (ANCOVA). Baseline values were used as a covariate. Additionally, a pooled post-hoc analysis was conducted similarly to the intention-to-treat analysis. Here, participants who obtained ≥100 PAI on >70% days were compared to those who did not, regardless of original group allocation.

All statistical analyses were two-sided with a significance level set at $\alpha = 0.05$. All measurements are presented as mean ± standard error (SE) unless otherwise stated. Statistical analyses were conducted with IBM SPSS v. 26 (IBM Corp, NY, US).

3 Results

Between October 2019 and January 2020, 49 participants were screened for inclusion at St. Olavs Hospital, Trondheim, Norway (**Figure 3**). Twenty-six participants were included, of which 12 were randomized to the intervention group (obtain ≥100 PAI per week) and 14 to the control group (recommended to follow national PA guidelines). The last participants completed follow-ups in May 2020 (Three participants did not show up for the 12-week follow-up due to personal reasons (n = 1) or COVID-19-related symptoms that made testing contraindicated (n = 2). Nine participants, including two COVID-19-related dropouts, were still in the intervention period at time of the national lockdown following the COVID-19 pandemic (13th of March to 30th of April). Thus, the national lockdown affected the time for post-intervention assessment for 4 and 5 participants from the intervention and control group, respectively, resulting in a 3-week extension of the of the intervention period. A sensitivity analysis was conducted to assess whether the national lockdown and extended intervention period affected the results by excluding the nine participants with 12-week follow-up after the national lockdown (**Appendix**). Similar estimates were observed in the primary analysis and sensitivity analysis.

At screening, 65% reported that they have been told they have high BP by a health care provider, and 50% reported a family history of high BP. None of the participants took any BP lowering medications at least 6 months prior to screening nor during the study period. Fourteen participants were classified as having high normal BP (SBP/DBP of ≥130/80 mmHg) and 12 as having hypertension (≥140/90 mmHg) at screening. Of the 14 participants with high normal BP, 7 would be classified as hypertensive based on their 24h ABP at baseline. In total, 17 participants were classified as hypertensive based on baseline 24h ABP. At screening, twelve participants had highest BP on their left arm and 14 on the right arm. The sample consisted of non- and moderate drinkers, aside from one heavy drinker in the intervention group. Further baseline characteristics are found in **Table 1**. One participant in the intervention group reported experiencing a rash by the activity monitor. Overall, 8 participants reached the predefined adherence criteria of at least 70% of days with ≥100 PAI, of which 5 were in the intervention group and 3 in the control group. Objectively measured PAI levels and associated data are found in **Table 2**.

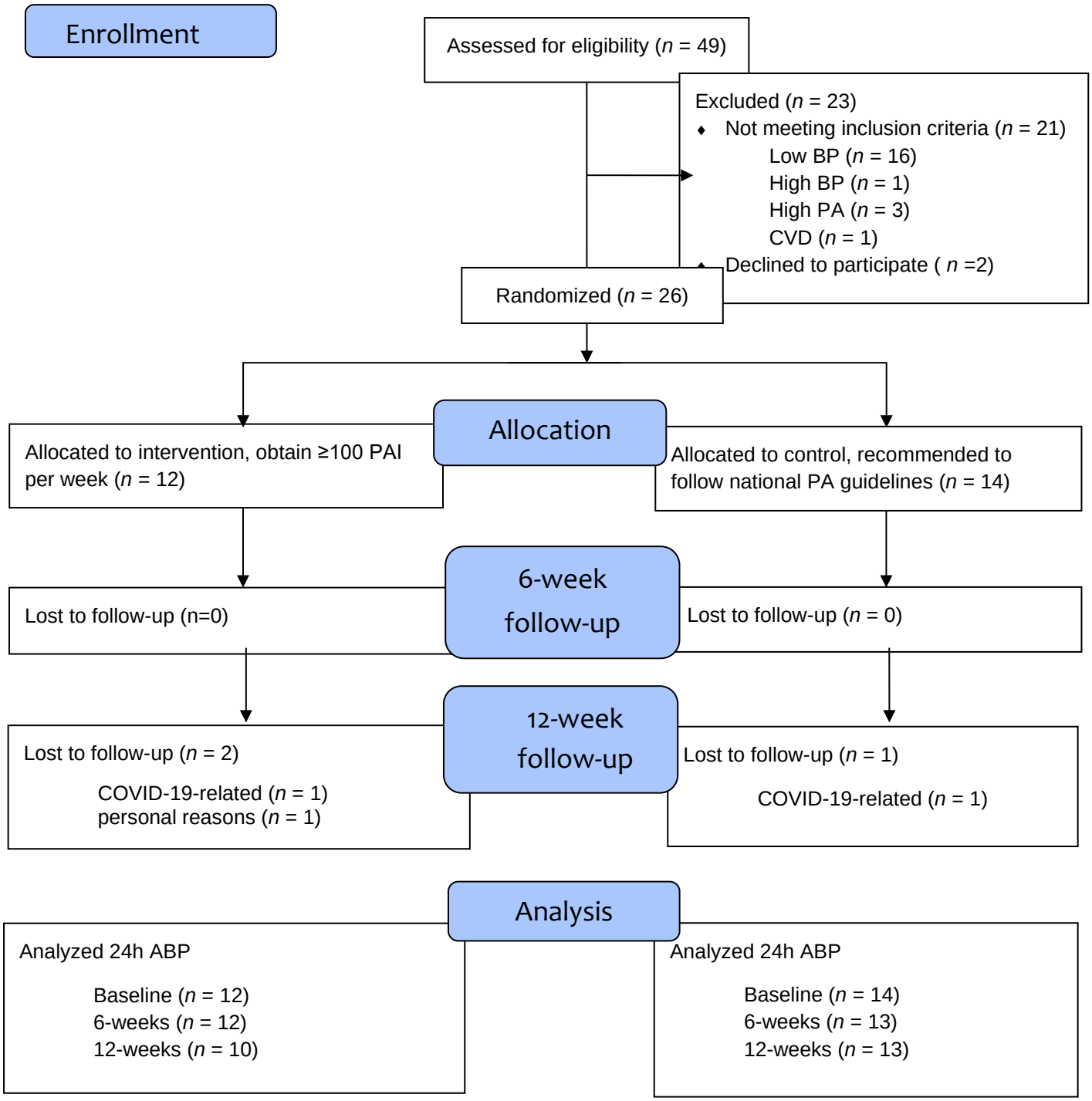

Figure 3. CONSORT statement flow diagram of screened, included and analyzed participants. Abbreviations: ABP, ambulatory blood pressure; BP, blood pressure; CVD, cardiovascular disease; PA, physical activity; PAI, Personal Activity Intelligence.

Table 1. Baseline characteristics.

	Obtain ≥100 PAI/wk (N = 12)	Follow PA guidelines (N = 14)
	Mean (SD)	Mean (SD)
Age (years)	55.5 (3.0)	54.6 (4.6)
Male/female	6/6	7/7
Anthropometrics		
BMI (kg/m^2)	29.2 (3.8)	27.6 (3.4)
Body fat (%)	31.5 (7.8)	28.4 (8.9)
Waist circumference (cm)	99.0 (10.1)	95.0 (8.9)
Personal Activity Intelligence (PAI) levels		
Estimated from self-reported activity levels	13 (17)	12 (15)
Objectively measured with heart rate monitor	52 (47)	67 (63)
Blood samples		
Creatinine (µmol/L)	77.3 (9.2)	72.3 (9.8)
Estimated GFR (ml/min/1.73m^2)	83.7 (6.0)	87.1 (5.4)
Cholesterol (mmol/L)	5.7 (0.4)	5.1 (1.1)
High-density lipoprotein (mmol/L)	1.4 (0.4)	1.5 (0.3)
Low-density lipoprotein (mmol/L)	4.0 (0.7)	3.4 (1.0)
Fasting glucose (mmol/L)	5.5 (0.6)	5.3 (0.4)$^{n = 13}$
Glycosylated hemoglobin (HbA1c, mmol/mol)	36.8 (3.4)	34.6 (4.5)
Echocardiographic measures*		
End-diastolic intraventricular septum thickness (mm)	8.8 (1.9)	8.0 (1.8)
Left ventricle end-diastolic diameter (mm)	48.6 (3.7)	48.4 (3.7)
E/A ratio	1.1 (0.3)	1.0 (0.2)
Left atrium end-systolic volume (ml)	59.7 (19.0)	56.1 (13.1)
Tricuspid annular plane systolic excursion (mm)	21.7 (3.2)	24.6 (4.0)
E/e' ratio	8.6 (1.2)	7.2 (1.7)
Outcome measures		
24h SBP (mmHg)	135.2 (12.7)	134.2 (14.2)
24h DBP (mmHg)	79.6 (9.0)	81.6 (9.7)
24h HR (bpm)	67.3 (6.3)	68.5 (7.1)
SBP (mmHg)	135.5 (10.2)	140.0 (14.5)
DBP (mmHg)	86.5 (7.4)	88.0 (9.7)
Heart rate (bpm)	67.0 (10.0)	65.4 (9.9)
cf-PWV (m/s)	8.4 (1.9)	7.0 (0.8)
Stroke volume (ml)	80.9 (27.1)	79.2 (14.3)
Cardiac output (L/min)	5.2 (1.3)	5.2 (1.2)
SVR (dyn*s*cm^{-5})	1606 (417)	1589 (319)
VO_{2peak} (ml/kg/min)	34.1 (6.6)	37.7 (6.9)

* all other left and right heart chamber structural and functional variables were also within normal limits (77, 78). Abbreviations: A, late mitral peak inflow velocity; cf-PWV, carotid-femoral pulse wave velocity; DBP, diastolic blood pressure; E, early mitral peak inflow velocity; e', early diastolic mitral annular velocity; GFR, glomerular filtration rate; PA, physical activity; PAI, Personal Activity Intelligence; SBP, systolic blood pressure; SV, stroke volume; SVR, systemic vascular resistance.

Table 2. Personal Activity Intelligence (PAI) data.

	Obtain ≥100 PAI/wk			Follow PA guidelines		
	N	Mean (SD)		N	Mean (SD)	
Average PAI						
Baseline – 6 weeks	12	114 (47)		14	99 (65)	
6 – 12 weeks	10	107 (45)		13	80 (49)	
Baseline – 12 weeks	10	115 (33)		13	91 (51)	
Missing days*						
Baseline – 6 weeks	12	3 (7)		14	4 (8)	
6 – 12 weeks	10	2 (4)		13	5 (5)	
Baseline – 12 weeks	10	3 (5)		13	8 (9)	
	N	Mean (SD)	Mean percentage of days (SD)	N	Mean (SD)	Mean percentage of days (SD)
Days of 0-49 PAI						
Baseline – 6 weeks	12	6 (8)	14 (20)	14	14 (13)	31 (31)
6 – 12 weeks	10	7 (9)	14 (17)	13	16 (12)	41 (34)
Baseline – 12 weeks	10	9 (9)	10 (10)	13	28 (22)	34 (27)
Days of 50-99 PAI						
Baseline – 6 weeks	12	11 (10)	26 (23)	14	11 (8)	25 (19)
6 – 12 weeks	10	9 (7)	19 (10)	13	10 (8)	23 (18)
Baseline – 12 weeks	10	20 (14)	22 (13)	13	20 (15)	24 (16)
Days of ≥100 PAI						
Baseline – 6 weeks	12	26 (14)	60 (32)	14	19 (16)	44 (38)
6 – 12 weeks	10	27 (8)	67 (25)	13	17 (17)	36 (34)
Baseline – 12 weeks	10	57 (16)	68 (21)	13	37 (30)	42 (32)

*Missing days are days where no heart rate data have been recorded. Abbreviations: PA, physical activity, PAI, Personal Activity Intelligence.

3.1 Intention-to-treat analysis

3.1.1 Primary outcomes

In an intention-to-treat analysis, the linear mixed model found no statistically significant difference in 24h ABP between the groups at any time points (**Figure 4** and **Table 3**). However, there was a statistically significant difference in 24h heart rate at the 12-week follow-up (0.21 to 7.80 bpm, 95% confidence interval (CI), p = 0.04), with heart rate being 4 beats per minute higher in the ≥100 PAI group (66.9 vs 62.9 bpm).

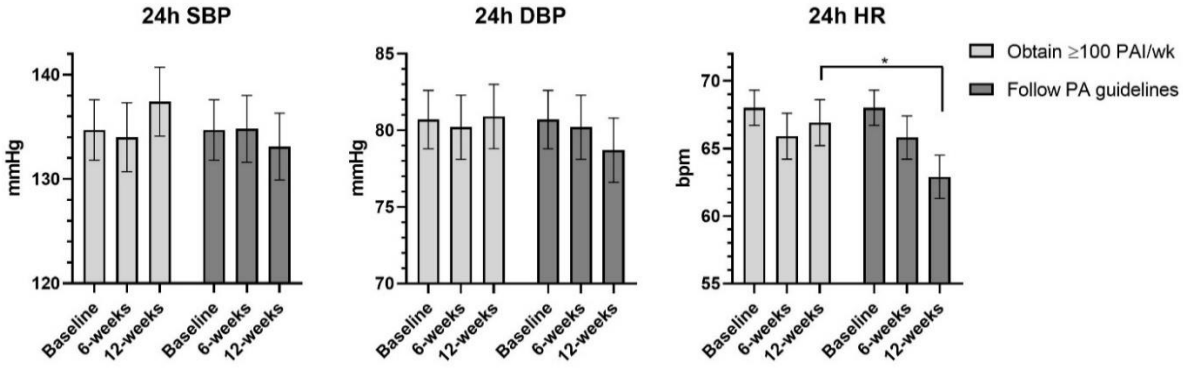

Figure 4. Intention-to-treat analysis of 24h ambulatory blood pressure and heart rate. Estimated means with standard error at baseline, 6 and 12-week follow-up adjusted for baseline differences. Abbreviations: DBP, diastolic blood pressure; HR, heart rate; PA, physical activity; PAI, Personal Activity Intelligence; SBP, systolic blood pressure. * represents statistically significant group-time interaction ($p < 0.05$).

Table 3. Intention-to-treat analysis of 24h, awake and asleep ambulatory blood pressure and heart rate at baseline, 6 and 12-week follow-up.

	Obtain ≥100 PA/wk		Follow PA guidelines		Difference	
	N	Mean (SE)	N	Mean (SE)	Estimate (95% CI)	p-value
24h SBP (mmHg)						
Baseline	12	134.7 (2.9)	14	134.7 (2.9)		
6-weeks	12	134.0 (3.3)	13	134.8 (3.2)	-0.75 (-6.08 to 4.58)	0.78
12-weeks	10	137.4 (3.2)	13	133.1 (3.2)	4.22 (-1.33 to 9.76)	0.13
24h DBP (mmHg)						
Baseline	12	80.7 (1.9)	14	80.7 (1.9)		
6-weeks	12	80.2 (2.1)	13	80.2 (2.1)	-0.14 (-3.18 to 3.15)	0.99
12-weeks	10	80.9 (2.1)	13	78.7 (2.1)	2.27 (-1.02 to 5.56)	0.17
24h HR (bpm)						
Baseline	12	68.0 (1.3)	14	68.0 (1.3)		
6-weeks	12	65.9 (1.7)	13	65.8 (1.6)	0.84 (-3.56 to 3.73)	0.96
12-weeks	10	66.9 (1.7)	13	62.9 (1.6)	4.01 (0.21 to 7.80)	0.04*
Awake SBP (mmHg)						
Baseline	12	140.3 (3.1)	14	140.3 (3.1)		
6-weeks	12	140.3 (3.5)	13	140.1 (3.4)	0.18 (-5.58 to 5.94)	0.95
12-weeks	10	142.1 (3.6)	13	138.6 (3.4)	3.53 (-2.46 to 9.52)	0.24
Awake DBP (mmHg)						
Baseline	12	84.9 (2.0)	14	84.9 (2.0)		
6-weeks	12	84.8 (2.2)	13	84.2 (2.2)	0.57 (-2.89 to 4.03)	0.74
12-weeks	10	84.5 (2.3)	13	82.4 (2.2)	2.18 (-1.42 to 5.78)	0.23
Awake HR (bpm)						
Baseline	12	71.0 (1.4)	14	71.0 (1.4)		
6-weeks	12	69.3 (1.7)	13	68.4 (1.7)	0.88 (-2.94 to 4.70)	0.65
12-weeks	10	69.2 (1.8)	13	65.8 (1.7)	3.38 (-0.59 to 7.36)	0.09
Asleep SBP (mmHg)						
Baseline	12	118.1 (2.7)	14	118.1 (2.7)		
6-weeks	12	118.8 (3.2)	13	118.5 (3.1)	0.34 (-6.11 to 6.79)	0.92
12-weeks	10	123.8 (3.3)	13	117.2 (3.1)	6.61 (-0.11 to 13.33)	0.05
Asleep DBP (mmHg)						
Baseline	12	67.8 (1.8)	14	67.8 (1.8)		
6-weeks	12	68.5 (2.0)	13	69.1 (2.0)	-0.59 (-4.47 to 3.29)	0.76
12-weeks	10	70.2 (2.1)	13	68.6 (2.0)	1.59 (-2.44 to 5.63)	0.43
Asleep HR (bpm)						
Baseline	12	59.1 (1.4)	14	59.1 (1.4)		
6-weeks	12	57.3 (1.7)	13	58.6 (1.6)	-1.29 (-4.73 to 2.16)	0.46
12-weeks	10	58.0 (1.8)	13	55.5 (1.5)	2.55 (-1.04 to 6.14)	0.16

Means adjusted for baseline differences and estimates are presented. Abbreviations: DBP, diastolic blood pressure; HR, heart rate; PA, physical activity; PAI; Personal Activity Intelligence; SBP, systolic blood pressure. * represents statistically significant group-time interaction ($p < 0.05$).

3.1.2 Secondary outcomes

In an intention-to-treat analysis, linear mixed models found no statistically significant differences in automated office BP, cf-PWV, stroke volume or VO_{2peak} between the groups at the 12-week follow-up (**Table 4**).

Table 4. Intention-to-treat analysis of automated office blood pressure, cf-PWV, SV, VO_{2peak} and associated secondary outcomes at baseline, 6 and 12-week follow-up.

	Obtain ≥100 PAI/wk		Follow PA guidelines		Difference	
	N	Mean (SE)	N	Mean (SE)	Estimate (95% CI)	p-value
SBP (mmHg)						
Baseline	12	137.9 (2.8)	14	137.9 (2.8)		
6-weeks	12	137.2 (3.3)	14	136.2 (3.1)	0.97 (-5.53 to 7.47)	0.77
12-weeks	9	135.7 (3.5)	13	133.4 (3.2)	2.32 (-4.71 to 9.36)	0.51
DBP (mmHg)						
Baseline	12	87.3 (2.0)	14	87.3 (2.0)		
6-weeks	12	84.2 (2.4)	14	85.8 (2.3)	-1.54 (-6.61 to 3.53)	0.54
12-weeks	9	82.2 (2.6)	13	84.9 (2.3)	-2.63 (-8.13 to 2.87)	0.34
HR (bpm)						
Baseline	12	66.1 (2.1)	14	66.1 (2.1)		
6-weeks	12	60.5 (2.5)	14	60.8 (2.4)	-0.27 (-5.85 to 5.30)	0.92
12-weeks	9	66.6 (2.8)	13	62.9 (2.5)	3.70 (-2.35 to 9.75)	0.23
cf-PWV (m/s)						
Baseline	12	7.6 (0.3)	14	7.6 (0.3)		
6-weeks	11	7.9 (0.4)	13	7.9 (0.4)	0.16 (-0.88 to 0.91)	0.97
12-weeks	7	7.5 (0.4)	13	7.6 (0.4)	-0.01 (-1.01 to 1.00)	0.99
SV (ml)						
Baseline	12	80.0 (3.5)	14	80.0 (3.5)		
6-weeks	12	74.7 (4.3)	14	84.7 (4.1)	-10.08 (-19.42 to -0.73)	0.04*
12-weeks	8	74.5 (4.9)	13	78.6 (4.2)	-4.06 (-14.51 to 6.38)	0.44
CO (L/min)						
Baseline	12	5.2 (0.2)	14	5.2 (0.2)		
6-weeks	12	4.6 (0.3)	14	5.0 (0.3)	-0.35 (-0.99 to 0.28)	0.27
12-weeks	8	5.1 (0.3)	13	4.6 (0.3)	0.48 (-0.23 to 1.19)	0.18
SVR ($dyn*s*cm^{-5}$)						
Baseline	12	1597 (68)	14	1597 (68)		
6-weeks	12	1755 (90)	13	1657 (87)	97.4 (-126.2 to 321.0)	0.39
12-weeks	8	1616 (105)	13	1723 (87)	-106.9 (-354.5 to 140.6)	0.39
VO_{2peak} (ml/kg/min)						
Baseline	9	36.0 (1.5)	13	36.0 (1.5)		
12-weeks	9	35.1 (0.6)	13	36.8 (0.5)	-1.6 (-3.41 to 0.11)	0.065

Means adjusted for baseline differences and estimates are presented. Abbreviations: cf-PWV, carotid-femoral pulse wave velocity; CO, cardiac output; DBP, diastolic blood pressure; HR, heart rate; VO_{2peak}, peak oxygen uptake; SBP, systolic blood pressure; SV, stroke volume; SVR, systemic vascular resistance. * represents statistically significant group-time interaction ($p < 0.05$).

3.2 Post-hoc analysis of ≥100 PAI/week vs <100 PAI/week

3.2.1 Primary outcomes

In a post-hoc analysis comparing participants that obtained ≥100 PAI on >70% of the days (*n* = 8) to those that obtained <100 PAI per week (*n* = 18), the linear mixed model found no statistically difference in 24h ABP between the groups at any time points (**Figure 5** and **Table 5)**.

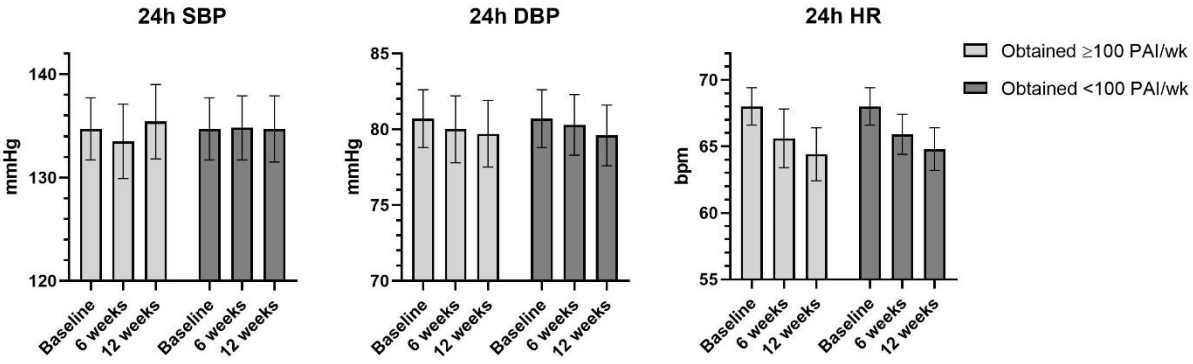

Figure 5. Post-hoc analysis of 24h ambulatory blood pressure and heart rate, comparing participants that obtained ≥100 PAI on >70% of the days with those who obtained <100 PAI. Estimated means with standard error at baseline, 6 and 12-week follow-up adjusted for baseline differences. Abbreviations: DBP, diastolic blood pressure; HR, heart rate; PAI, Personal Activity Intelligence; SBP, systolic blood pressure.

Table 5. Post-hoc analysis of 24h, awake and asleep ambulatory blood pressure and heart rate at baseline, 6 and 12-week follow-up.

	Obtained ≥100 PAI/wk		Obtained <100 PAI/wk		Difference	
	N	Mean (SE)	N	Mean (SE)	Estimate (95% CI)	p-value
24h SBP (mmHg)						
Baseline	8	134.7 (3.0)	18	134.7 (3.0)		
6-weeks	8	133.5 (3.6)	17	134.8 (3.1)	-1.30 (-7.19 to 4.59)	0.66
12-weeks	8	135.4 (3.6)	15	134.7 (3.2)	0.69 (-5.30 to 6.68)	0.82
24h DBP (mmHg)						
Baseline	8	80.7 (1.9)	18	80.7 (1.9)		
6-weeks	8	80.0 (2.2)	17	80.3 (2.0)	-0.29 (-3.77 to 3.19)	0.87
12-weeks	8	79.7 (2.2)	15	79.6 (2.0)	0.11 (-3.43 to 3.65)	0.95
24h HR (bpm)						
Baseline	8	68.0 (1.4)	18	68.0 (1.4)		
6-weeks	8	65.6 (2.0)	17	65.9 (1.5)	-0.26 (-4.35 to 3.84)	0.90
12-weeks	8	64.4 (2.0)	15	64.8 (1.6)	-0.40 (-4.56 to 3.77)	0.85
Awake SBP (mmHg)						
Baseline	8	140.3 (3.1)	18	140.3 (3.1)		
6-weeks	8	139.7 (3.8)	17	140.5 (3.3)	-0.73 (-6.98 to 5.51)	0.81
12-weeks	8	141.1 (3.8)	15	139.6 (3.3)	1.54 (-4.81 to 7.88)	0.63
Awake DBP (mmHg)						
Baseline	8	84.9 (2.0)	18	84.9 (2.0)		
6-weeks	8	84.0 (2.4)	17	84.7 (2.1)	-0.61 (-4.38 to 3.15)	0.75
12-weeks	8	83.7 (2.4)	15	83.1 (2.1)	0.57 (-3.26 to 4.39)	0.77
Awake HR (bpm)						
Baseline	8	71.0 (1.4)	18	71.0 (1.4)		
6-weeks	8	68.4 (2.0)	17	69.1 (1.6)	-0.68 (-4.89 to 3.53)	0.75
12-weeks	8	67.6 (2.0)	15	67.1 (1.6)	0.48 (-3.81 to 4.76)	0.82
Asleep SBP (mmHg)						
Baseline	8	118.1 (2.7)	18	118.1 (2.7)		
6-weeks	8	116.1 (3.6)	17	119.7 (2.9)	-3.66 (-10.83 to 3.50)	0.31
12-weeks	8	118.1 (3.6)	15	121.0 (3.0)	-2.94 (-10.23 to 4.35)	0.42
Asleep DBP (mmHg)						
Baseline	8	67.8 (1.7)	18	67.8 (1.7)		
6-weeks	8	68.2 (2.2)	17	69.1 (1.9)	-0.90 (-5.06 to 3.25)	0.67
12-weeks	8	67.3 (2.2)	15	70.3 (1.9)	-2.99 (-7.21 to 1.24)	0.16
Asleep HR (bpm)						
Baseline	8	59.1 (1.4)	18	59.1 (1.4)		
6-weeks	8	58.1 (1.9)	17	57.9 (1.6)	0.23 (-3.54 to 4.00)	0.90
12-weeks	8	55.3 (1.9)	15	57.2 (1.6)	-1.99 (-5.82 to 1.85)	0.30

Means adjusted for baseline differences and estimates are presented. Abbreviations: DBP, diastolic blood pressure; HR, heart rate; PAI, Personal Activity Intelligence; SBP, systolic blood pressure.

3.2.2 Secondary outcomes

There were no statistically significant differences between the groups at the 12-week follow-up in automated office BP, cf-PWV, stroke volume, VO_{2peak} or any other associated secondary outcome (**Table 6**). At the 6-week follow-up, the estimated difference in office SBP was 7.5 mmHg lower in those who obtained ≥100 PAI on >70% of the days compared to those who did not ($p = 0.03$). This difference was not supported statistically at the 12-week follow-up, but SBP was still lower (-6.36 mmHg, $p = 0.08$) in those who obtained ≥100 PAI per week (**Table 6**).

Table 6. Post hoc analysis of automated office blood pressure, cf-PWV, SV, VO_{2peak} and associated secondary outcomes at baseline, 6 and 12-week follow-up.

	Obtained ≥100 PAI/wk		Obtained <100 PAI/wk		Difference	
	N	Mean (SE)	N	Mean (SE)	Estimate (95% CI)	p-value
SBP (mmHg)						
Baseline	8	137.9 (2.7)	18	137.9 (2.7)		
6-weeks	8	131.5 (3.5)	18	139.0 (2.9)	-7.50 (-14.2 to -0.78)	0.03*
12-weeks	7	130.0 (3.7)	15	136.4 (3.0)	-6.36 (-13.49 to 0.77)	0.08
DBP (mmHg)						
Baseline	8	87.3 (1.9)	18	87.3 (1.9)		
6-weeks	8	83.4 (2.7)	18	85.8 (2.1)	-2.42 (-7.84 to 3.00)	0.38
12-weeks	7	80.6 (2.8)	15	85.2 (2.2)	-4.61 (-10.37 to 1.16)	0.12
HR (bpm)						
Baseline	8	66.1 (2.1)	18	66.1 (2.1)		
6-weeks	8	61.6 (3.0)	18	60.2 (2.3)	1.45 (-4.62 to 7.52)	0.63
12-weeks	7	64.2 (3.1)	15	64.6 (2.4)	-0.38 (--6.84 to 6.09)	0.91
cf-PWV (m/s)						
Baseline	8	7.6 (0.3)	18	7.6 (0.3)		
6-weeks	8	7.9 (0.4)	16	7.9 (0.3)	0.01 (-0.94 to 0.95)	0.99
12-weeks	7	7.5 (0.5)	13	7.6 (0.4)	-0.13 (-1.14 to 0.88)	0.80
SV (ml)						
Baseline	8	80.0 (3.5)	18	80.0 (3.5)		
6-weeks	8	83.4 (5.1)	18	78.6 (3.9)	4.78 (-5.68 to 15.24)	0.36
12-weeks	6	75.7 (5.5)	15	77.0 (4.1)	-1.35 (-13.00 to 10.31)	0.82
CO (L/min)						
Baseline	8	5.2 (0.2)	18	5.2 (0.2)		
6-weeks	8	5.1 (0.3)	18	4.7 (0.2)	0.36 (-0.35 to 1.06)	0.31
12-weeks	6	4.7 (0.4)	15	4.8 (0.3)	-0.82 (-0.87 to 0.71)	0.84
SVR ($dyn*s*cm^{-5}$)						
Baseline	8	1597 (68)	18	1597 (68)		
6-weeks	8	1583 (106)	17	1762 (79)	-178.9 (-415.4 to 57.5)	0.14
12-weeks	6	1738 (118)	15	1667 (82)	71.3 (-191.3 to 333.9)	0.59
VO_{2peak} (ml/kg/min)						
Baseline	7	36.0 (1.5)	15	36.0 (1.5)		
12-weeks	7	35.6 (0.8)	15	36.3 (0.5)	-0.73 (-2.79 to 1.3)	0.47

Means adjusted for baseline differences and estimates are presented. Abbreviations: cf-PWV, carotid-femoral pulse wave velocity; CO, cardiac output; DBP, diastolic blood pressure; HR, heart rate; VO_{2peak}, peak oxygen uptake; SBP, systolic blood pressure; SV, stroke volume; SVR, systemic vascular resistance. * represents statistically significant group-time interaction ($p < 0.05$).

4 Discussion

This pilot RCT sought to evaluate the effect of a 12-week intervention, obtain ≥100 PAI per week with PAI monitoring, compared to a control, recommended to follow physical activity guidelines, on 24h ABP in adults with elevate BP. The main finding was that there were no clinically relevant changes or differences between (or within) the groups in 24h SBP and DBP. Furthermore, no clinically relevant differences between groups were found in automated office BP, cardiac function, arterial stiffness nor CRF. Similarly, comparing participants that obtained ≥100 PAI on >70% of the days to those who obtained <100 PAI, indicated no significant benefits of being above or below the predefined cut-off at 6- and 12-week follow-ups. However, automated office SBP/DBP was lower (-6/-5 mmHg) in those who obtained ≥100 PAI compared to those who did not, but the difference was not supported statistically. Since this was a small sample size pilot RCT, we emphasize that the results are intended as descriptive and should be interpreted with caution. The results may be used to inform and improve adequately powered trials in the future.

Meta-analyses have shown that aerobic exercise reduce 24h SBP by about 3.2 mmHg and 24h DBP by 2.7 mmHg (79). The exercise dose of RCTs used in this meta-analysis was a median duration of 15 weeks, 2-5 sessions per week for 30-60 minutes at an intensity of 50-75% of heart rate reserve (79). In contrast, the observed change in 24h SBP in our study was +2.7 mmHg in the intervention group and -1.6 mmHg in the control group following 12-weeks. Similarly, at 12-week follow-up, 24h DBP reduced by 2.0 mmHg in the control group and remained virtually unchanged in the intervention group. This was coupled with 24h heart rate being reduced in the control group. The PAI algorithm is made to favor higher intensity-exercise due to its importance on CRF and CVD mortality (57). While there is still debate whether HIIT is superior to lower intensities in reducing BP based on short-term RCTs (40, 42), HIIT is superior in improving CRF (80). A discrepancy in the time course of CRF and BP changes following exercise could therefore affect the effectiveness on PAI as a BP-reducing intervention in the short term.

A study by Molmen-Hansen *et al.* (2011) sought to compare 12-weeks of HIIT and MICT in a population of hypertensives but otherwise healthy (51). The HIIT intervention consisted of 4x4 minute intervals at 90-95% of HR_{max}, with a total exercise time of 38 minutes whereas the MICT intervention consisted of 47 minutes at 70% HR_{max}. Both groups had supervised session 3 times per week and was compared to a control group receiving standard physical activity recommendations, similar to our control group. The observed reduction in 24h SBP/DBP was 12/8 mmHg in the HIIT group, ~5/4 mmHg in the MICT group and 2/2 mmHg in the control group, respectively. Associated increases in VO_{2max} was 5.2 ml/kg/min in the HIIT group, 1.8 ml/kg/min in the MICT group and 1.0 ml/kg/min in the control group (51). Albeit improvements have not been as impressive in heart failure patients and young normotensive women with familial risk for hypertension, collectively there are tendencies for HIIT to improve 24h ABP and VO_{2max} more than MICT and control groups (81, 82). We had a hypothesis based on the findings by Molmen Hansen *et al.* (2011) and the notion that the PAI algorithm favors high-intensity exercise and therefore obtaining a high PAI level (≥100 PAI) would be more beneficial than following physical activity guidelines. However, the results from this pilot RCT could not prove that there was a difference as we found neither 24h ABP nor CRF improved in those asked to obtain ≥100

per week, those who actually obtained ≥100 PAI per week on >70% of the days, nor following current physical activity guidelines.

The population in the study by Molmen-Hansen *et al.* (2011) was comparable to ours aside from baseline 24h ABP being lower in our study (~135/80 vs 150/90 mmHg), which begs the question whether the differences observed between our studies are due to intervention effects or baseline BP (51). It is well established that the effects of aerobic exercise on reducing office BP is dependent on the initial BP (40, 83). On the other hand, changes 24h ABP appears to be less dependent on baseline BP, though small number of studies using 24h ABP measurements compared to office measures makes it difficult to draw definitive conclusions (79). It seems likely that the differences in 24h ABP between the present RCT and the RCT by Molmen-Hansen and colleagues may be explained by a combination of different baseline BP and training interventions.

There are multiple ways to obtain ≥100 PAI per week, but it corresponds roughly to 60 minutes at 75% of heart rate reserve or 40 minutes at 85% of heart rate reserve, or a combination thereof, including lower intensity exercise for a considerably longer time (59). Compared to popularly used HIIT protocols, such as the one used by Molmen-Hansen *et al.* (2011), 100 PAI corresponds roughly to 2 sessions of 4x4 minute bouts of HIIT per week (51, 59). Considering the low adherence to the obtain ≥100 PAI per week protocol in the intervention group (5 of 10), and the notion that 100 PAI corresponds to a lower training load than 3 times 4x4 minutes of HIIT (or MICT) per week, it is not surprising that the effect sizes differ. Post-hoc analyses revealed no apparent differences in 24h ABP or VO_{2peak} between those who obtained ≥100 PAI on at least 70% of the days and those who did not. Considering the low baseline VO_{2peak} of the participants and the lack of improvements in any of the groups, it appears the interventions and the prescribed PAI dose was inadequate. Better adherence and a higher PAI dose are thus likely required to improve VO_{2peak} and BP in this population.

Despite no apparent differences in 24h ABP, post-hoc analyses revealed a 6.4 mmHg reduction in automated office SBP after 6 weeks among those who obtained ≥100 PAI/week followed by a 1.5 mmHg reduction the following 6 weeks. A similar pattern was observed in automated office DBP, with an initial reduction of 3.9 mmHg during the first 6 weeks and another 2.8 mmHg during the last 6 weeks. Although this was not supported statistically, it translates to considerable risk reductions of cardiovascular events (6). Greater reductions in office BP compared to 24h ABP have also been found in previous aerobic exercise studies. Pagonas *et al.* (2017) conducted a 12-week RCT in hypertensives (~75% on medication) who exercised unsupervised 3-5 times per week for 30 minutes at a moderate intensity (74). They found that 24h SBP was reduced by ~5 mmHg, whereas office SBP was reduced by ~10 mmHg. Though parts of the discrepancies can be attributed to office SBP being 12.9 mmHg higher than 24h SBP, it indicates a greater effect of aerobic exercise on office BP. One could speculate that the reduction in office SBP found by Pagonas *et al.* and in the present study are due to a reduction in white coat hypertension as the participants expected a BP-lowering effect by adhering to the exercise protocol. However, we found automated office BP to be lower than 24h ABP in those who obtained ≥100 PAI on >70% of the days. Automated office BP is thought to be similar to that of awake ABP and slightly higher than 24h ABP (21), which reduces the potential likelihood of the findings being due to a reduction in white coat hypertension.

Reductions in BP following exercise is mostly attributed to reductions in systemic vascular resistance (83). This is consistent with the two aforementioned RCTs by Molmen-Hansen

et al. and Pagonas *et al.* who found significant reductions in both 24h ABP and systemic vascular resistance after 12-weeks of aerobic exercise (51, 74). In contrast, we found no differences nor clinically relevant effect sizes in 24h ABP, and as expected we found no clinically relevant changes in systemic vascular resistance either. Moreover, we suspect that the lack of changes in arterial stiffness in this study are due to the relatively short intervention period and insignificant changes in SBP. Indeed, significant changes in arterial stiffness seems to require an intervention period of at least 16 weeks and are usually accompanied by a larger reduction in SBP in adults with elevated BP (84).

In the epidemiological study of which PAI was based on, men with a PAI score of ≥100 had on average 4.1 ml/kg/min higher VO_{2peak} whereas women had on average 2.9 ml/kg/min VO_{2peak} compared to those with less than 100 PAI (60). In the present study we found no differences between those at or above compared to those below 100 PAI based on 70% of available days. Stroke volume, whose variation in this study can be explained by test-retest differences (85), is the main contributor to increases in CRF following exercise training (86). Though this was measured at rest, and not at peak exercise, other studies, also using echocardiography, have found increases in VO_{2peak} to be accompanied by increased resting stroke volume in hypertensive and CVD populations (51, 87). Physiologically, an increase in stroke volume should increase SBP, but it appears that other mechanisms override this effect following aerobic exercise (7).

4.1 Future trial directions, strengths and weaknesses

The initial plan of this pilot RCT was to include adults with SBP/DBP of ≥140/90 mmHg as per ESC/ESH hypertension definitions (5). However, due to an initial inclusion rate of merely 19% the inclusion was adjusted to ≥130/80 mmHg, which increased the inclusion rate to approximately 50%. The reason for the low inclusion in the beginning may be due to the notion that we used an automated office BP approach as opposed to traditional office BP. The benefit of this approach is that it more closely relates to the diagnostic and prognostic value of 24h ABP monitoring (21) without having the increased burden of using 24h ABP monitoring prior to inclusion. Compared to using the traditional office BP approach, our automated office readings likely underestimated the BP compared to other studies and hypertension guidelines, and ultimately contributed to the low initial inclusion rate. For example, according to ESC/ESC hypertension guidelines (5), the difference between office and 24h SBP/DBP cut-offs is 10 mmHg, whereas the difference reported in the present study was approximately 3/7 mmHg. It therefore seems reasonable for a future trial to use automated office BP with adjusted cut-offs for inclusions (5, 21).

An issue of the present pilot RCT was that adherence to the ≥100 PAI per week protocol in the intervention group was lower than expected (50%). Both the intervention group with a PAI goal and the control group being monitored but following physical activity recommendations increased physical activity levels in this study (**Table 2**). Participation in the study required repeated clinical follow-ups and the participants knew physical activity levels were monitored, which probably contributed to the observed increase in physical activity levels of all participants. However, having a PAI goal and being able to track PAI via a mobile app was not motivating enough to see a difference in the outcomes between the intervention and the control group. It would thus seem like additional motivation is needed, perhaps from a more interactive app with additional feedback. Additionally, physical activity levels would likely have increased more in both groups if the trial was conducted during warmer months (88). Though this would not improve the trial design in relation to physical activity patterns between the groups, it could provide an avenue for

enhanced adherence to the PAI protocol to examine the physiological effects of obtaining higher PAI levels. Examining the effect of higher PAI levels seems necessary as, contrary to previous studies, we were unable to see an effect of physical activity on 24h ABP, and the lack of improvements in VO_{2peak} indicate an inadequate physical activity dose (80).

While increasing real-world applicability, this study was unsupervised, which may also have contributed to poor adherence and small effect sizes (89). A pragmatic solution to improve adherence in future PAI-studies could be a supervised familiarization period prior to unsupervised activity. For example, Poon *et al.* (2020) compared low-volume HIIT to MICT in overweight/obese middle-aged men consisting of 3 sessions per week for 8 weeks (90). The first 6 sessions were supervised with a gradual increase in exercise duration. The subsequent 6 weeks were unsupervised and in a free-living setting. Overall exercise adherence ended above 90% in both groups. Importantly both groups in that study, though differing in duration and intensity (*i.e.* the basis of PAI), had similar improvements in VO_{2max} (approximately 10%), high levels of enjoyment and similar self-efficacy (90). Supervised familiarization sessions would likely improve adherence but would come with caveats as it increase costs and would reduce the clinical applicability of using PAI as a substitute for physical activity guidelines.

This study has some noteworthy strengths. First, the RCT design is a key strength by being the gold standard in clinical research and inferring causality (91). Second, the outcome measures used are reliable and often considered the gold standard in their domains, *e.g.* VO_{2peak}, 24h ABP, cf-PWV (5, 66, 92). Third, the intervention was conducted in a free-living setting, and thus have high external validity. Fourth, PAI data was collected from both groups, making it possible to look at the effect of obtained PAI level on physiological outcomes regardless of group allocation.

There are also some noteworthy weaknesses in the present study. First, the sample size is low and therefore underpowered to detect statistical differences in the primary outcome. As a pilot RCT this is expected, though this is important to keep in mind when making statistical inferences. Second, it was an unblinded study and the test personnel also analyzed them. An attempt to blind the analyses was implemented, *i.e.* a third party re-coded the participant numerical identified and minimized the data sets, but this was not effective as individuals could still be recognized by test personnel due to the small sample size. Third, some participants experienced technical issues with uploading data from the heart rate monitor to the PAI mobile app, which resulted in days with, or without, activity that are not adequately accounted for. It seems likely that trouble with the PAI platform could have had a negative effect on motivation. Recently, the PAI algorithm has been integrated in smartwatches, which may ease both data transfer and user interaction and thus motivation to adhere to a PAI intervention (93). Fourth, PAI can be obtained in nearly unlimited different ways based on user preferences and only gives a crude estimate. If there are nuances in physical activity patterns that are optimal for reducing BP, *e.g.* intervals vs continuous exercise, or a certain intensity, frequency or duration, obtained PAI alone would not be able to convey or use this information. However, with the emergence of big data and artificial intelligence, continuous heart rate monitoring could clear a path for a highly individualized PAI metric, for example by the use of digital twins (94).

5 Conclusion

Contrary to the hypothesis, this pilot RCT indicate that there is no difference between the intervention, obtaining ≥100 PAI/week and user PAI monitoring, compared to the control, recommended to follow national physical activity guidelines without PAI monitoring, on 24h ABP. Obtaining ≥100 PAI per week may be effective in reducing automated office BP but not 24h ABP. Low effect sizes in cardiac function, arterial stiffness and particularly CRF indicate a higher weekly PAI level or longer intervention period is needed for effective BP control. However, as a small sample size pilot RCT the results are mainly descriptive and should be interpreted with caution. In the future, adequately powered PAI RCTs should consider using a higher PAI goal and consider ways to improve adherence, for example by improving user experience (more feedback, ease of use) and using supervised familiarization sessions.

Statement of conflict of interest & Funding

Ulrik Wisløff, the main supervisor of this thesis, is the inventor of PAI. Wisløff has together with other international experts in their fields (including behavioural psychology, artificial intelligence, machine learning, prototyping, and industrial design) a 20% position as a senior advisor (in exercise physiology related to trends, development and research in sports, as well as health and health-related services) at PAI Health Norway AS. Wisløff has thoroughly discussed all aspects of the Regulations on External Work with Øystein Risa, the head of Department at ISB, and received advice from Hanne Sørgjerd, a legal adviser at the NTNU. To secure transparency, a contract regarding the external work of Wisløff has been described in detail and signed by both Wisløff and Risa. Due to potential conflicts of interests Wisløff was not involved in the acquisition or analyses of data. There are no additional potential conflicts of interest or disclosures to report.

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Appendix

Sensitivity analysis of primary outcome where participants affected by the COVID-19 lockdown are excluded from the analysis where affected (**Table 7**) and completely (**Table 8**). Similar estimates were observed in the primary analysis and sensitivity analysis such that the effect of the lockdown was considered negligible.

Table *7.* Sensitivity analysis of primary outcomes at baseline, 6 and 12-week follow-up where participants affected by COVID-19-related events are excluded at time points affected, *i.e.* 12-week follow-up.

	Obtain ≥100 PAI/wk		Follow PA guidelines		Difference	
	N	Mean (SE)	N	Mean (SE)	Estimate (95% CI)	p-value
24h SBP (mmHg)						
Baseline	12	134.7 (3.0)	14	134.7 (3.0)		
6-weeks	12	134.0 (3.3)	13	134.9 (3.2)	-0.89 (-6.10 to 4.31)	0.73
12-weeks	7	137.7 (3.6)	9	134.3 (3.4)	3.44 (-2.84 to 9.71)	0.28
24h DBP (mmHg)						
Baseline	12	80.7 (2.0)	14	80.7 (2.0)		
6-weeks	12	80.2 (2.1)	13	80.4 (2.1)	-0.16 (-3.20 to 2.88)	0.92
12-weeks	7	81.8 (2.3)	9	79.5 (2.2)	2.25 (-1.41 to 5.92)	0.22
24h HR (bpm)						
Baseline	12	68.0 (1.3)	14	68.0 (1.3)		
6-weeks	12	65.9 (1.6)	13	65.6 (1.5)	0.32 (-3.04 to 3.68)	0.85
12-weeks	7	67.3 (1.8)	9	63.2 (1.7)	4.15 (0.07 to 8.23)	0.05*
Awake SBP (mmHg)						
Baseline	12	140.3 (3.2)	14	140.3 (3.2)		
6-weeks	12	140.3 (3.5)	13	140.2 (3.5)	0.08 (-5.64 to 5.79)	0.98
12-weeks	7	142.6 (3.8)	9	139.3 (3.6)	3.31 (-3.58 to 10.21)	0.34
Awake DBP (mmHg)						
Baseline	12	84.9 (2.0)	14	84.9 (2.0)		
6-weeks	12	84.8 (2.2)	13	84.3 (2.2)	0.44 (-2.98 to 3.86)	0.80
12-weeks	7	85.2 (2.4)	9	83.0 (2.3)	2.18 (-1.94 to 6.30)	0.29
Awake HR (bpm)						
Baseline	12	71.0 (1.4)	14	71.0 (1.4)		
6-weeks	12	69.4 (1.7)	13	68.1 (1.6)	1.28 (-2.29 to 4.85)	0.47
12-weeks	7	70.4 (1.9)	9	65.6 (1.8)	4.77 (0.44 to 9.10)	0.03*
Asleep SBP (mmHg)						
Baseline	12	118.1 (2.7)	14	118.1 (2.7)		
6-weeks	12	118.8 (3.1)	13	118.5 (3.1)	0.29 (-5.97 to 6.55)	0.93
12-weeks	7	122.5 (3.6)	9	118.4 (3.3)	4.08 (-3.51 to 11.67)	0.28
Asleep DBP (mmHg)						
Baseline	12	67.8 (1.8)	14	67.8 (1.8)		
6-weeks	12	68.5 (2.1)	13	69.1 (2.0)	-0.62 (-4.55 to 3.30)	0.75
12-weeks	7	70.3 (2.3)	9	68.9 (2.2)	1.44 (-3.30 to 6.18)	0.54
Asleep HR (bpm)						
Baseline	12	59.1 (1.4)	14	59.1 (1.4)		
6-weeks	12	57.3 (1.7)	13	58.6 (1.6)	-1.22 (-4.63 to 2.19)	0.48
12-weeks	7	58.3 (1.9)	9	55.8 (1.8)	2.52 (-1.61 to 6.66)	0.23

Adjusted means and estimates are presented. Abbreviations: DBP, diastolic blood pressure; HR, heart rate; PA, physical activity; PAI, Personal Activity Intelligence; SBP, systolic blood pressure. * represents statistically significant group-time interaction ($p < 0.05$)

Table 8. Sensitivity analysis of primary outcomes at baseline, 6 and 12-week follow-up where participants affected by COVID-19-related events are excluded at all time points.

	Obtain ≥100 PAI/wk		Follow PA guidelines		Difference	
	N	Mean (SE)	N	Mean (SE)	Estimate (95% CI)	p-value
24h SBP (mmHg)						
Baseline	8	132.5 (3.8)	9	132.5 (3.8)		
6-weeks	8	130.9 (4.2)	9	133.8 (4.1)	-2.91 (-9.59 to 3.77)	0.38
12-weeks	7	135.2 (4.3)	9	132.7 (4.1)	2.47 (-4.40 to 9.34)	0.47
24h DBP (mmHg)						
Baseline	8	78.9 (2.3)	9	78.9 (2.3)		
6-weeks	8	77.7 (2.5)	9	79.3 (2.5)	-1.54 (-5.48 to 2.39)	0.43
12-weeks	7	79.7 (2.5)	9	78.1 (2.5)	1.53 (-2.52 to 5.58)	0.45
24h HR (bpm)						
Baseline	8	67.8 (1.4)	9	67.8 (1.4)		
6-weeks	8	64.3 (1.7)	9	64.6 (1.7)	-0.38 (-4.42 to 3.67)	0.85
12-weeks	7	66.5 (1.8)	9	62.8 (1.7)	3.70 (-0.47 to 7.88)	0.08
Awake SBP (mmHg)						
Baseline	8	138.5 (4.1)	9	138.5 (4.1)		
6-weeks	8	136.8 (4.5)	9	139.5 (4.4)	-2.74 (-9.89 to 4.40)	0.44
12-weeks	7	140.1 (4.6)	9	138.1 (4.4)	1.98 (-5.37 to 9.34)	0.59
Awake DBP (mmHg)						
Baseline	8	83.2 (2.4)	9	83.2 (2.4)		
6-weeks	8	81.6 (2.7)	9	83.7 (2.6)	-2.02 (-6.16 to 2.13)	0.33
12-weeks	7	82.9 (2.7)	9	81.9 (2.6)	0.99 (-3.27 to 5.26)	0.64
Awake HR (bpm)						
Baseline	8	71.1 (1.6)	9	71.1 (1.6)		
6-weeks	8	67.8 (1.9)	9	67.4 (1.9)	0.37 (-4.00 to 4.74)	0.87
12-weeks	7	69.6 (2.0)	9	65.4 (1.9)	4.22 (-0.29 to 8.73)	0.07
Asleep SBP (mmHg)						
Baseline	8	115.5 (3.2)	9	115.5 (3.2)		
6-weeks	8	117.7 (3.8)	9	116.4 (3.7)	1.25 (-6.36 to 8.87)	0.74
12-weeks	7	120.8 (3.9)	9	116.3 (3.7)	4.50 (-3.35 to 12.34)	0.25
Asleep DBP (mmHg)						
Baseline	8	66.1 (2.0)	9	66.1 (2.0)		
6-weeks	8	67.8 (2.4)	9	67.1 (2.3)	0.73 (-4.30 to 5.77)	0.77
12-weeks	7	69.2 (2.5)	9	67.3 (2.3)	1.87 (-3.32 to 7.06)	0.47
Asleep HR (bpm)						
Baseline	8	58.8 (1.3)	9	58.8 (1.3)		
6-weeks	8	56.0 (1.7)	9	56.8 (1.6)	-0.77 (-4.76 to 3.23)	0.70
12-weeks	7	57.7 (1.8)	9	54.9 (1.6)	2.79 (-1.33 to 6.91)	0.18

Adjusted means and estimates are presented. Abbreviations: DBP, diastolic blood pressure; HR, heart rate; PA, physical activity; PAI, Personal Activity Intelligence; SBP, systolic blood pressure.

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