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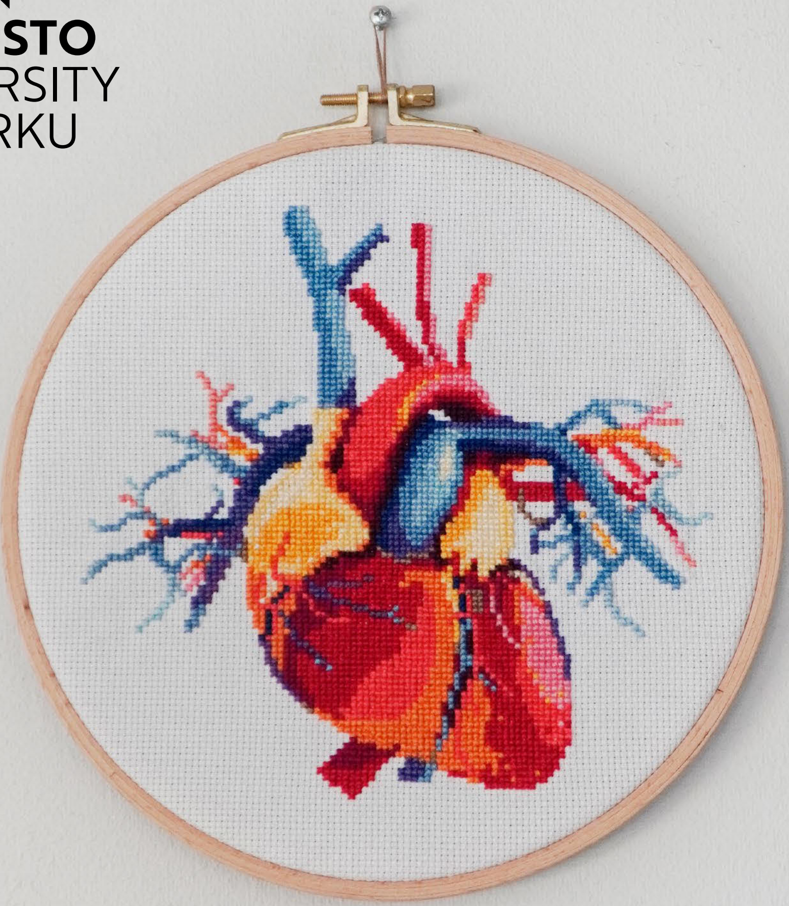

THE EFFECTS OF REDUCING SEDENTARY BEHAVIOR ON CARDIOVASCULAR HEALTH

A Randomized Controlled Trial in Adults with Metabolic Syndrome

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Jooa Norha

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Cover Image: Kaisa Koski

ISBN 978-952-02-0132-6 (PRINT)
ISBN 978-952-02-0133-3 (PDF)
ISSN 0355-9483 (Print)
ISSN 2343-3213 (Online)
Painosalama, Turku, Finland, 2025

To Kaisa

UNIVERSITY OF TURKU
Faculty of Medicine
Department of Clinical Medicine
Clinical Physiology and Nuclear Medicine
Turku PET Centre
JOOA NORHA: The Effects of Reducing Sedentary Behavior on Cardiovascular Health: A Randomized Controlled Trial in Adults with Metabolic Syndrome
Doctoral Dissertation, 138 pp.
Doctoral Programme in Clinical Research
April 2025

ABSTRACT

Observational evidence suggests that a high volume of sedentary behavior (SB) associates with adverse cardiovascular health, yet interventional evidence remains limited. The aim of this doctoral thesis was to investigate the effects of a SB reducing intervention on cardiovascular health.

Sixty-four adults with metabolic syndrome, physical inactivity, and high sedentary time were randomized into the intervention (n=33) and control (n=31) groups. The intervention group aimed at reducing daily SB by 1 h/day for six months, compared to a four-week screening period. The SB was advised to be replaced with other physical activity than exercise training, such as standing up, everyday tasks, and light physical activities. The control group maintained their usual physical activity behavior. All participants wore accelerometers throughout the study to monitor SB and physical activities. The outcomes were maximal cardiorespiratory fitness, and blood pressure and echocardiographic measures at rest and during exercise testing.

The intervention group reduced their SB by 40 min/day and increased moderate-to-vigorous intensity physical activity by 20 min/day, on average, while no statistically significant changes in the control group were observed.

No statistically significant intervention effects on cardiorespiratory fitness or resting or exercise blood pressure and echocardiography were observed. However, among all participants, increased physical activity correlated with improved cardiorespiratory fitness, left ventricular mass index, and submaximal exercise blood pressure and left ventricular global longitudinal strain.

In conclusion, the SB-reducing intervention did not affect the health of the cardiovascular system, although successful SB reduction provided some benefits. Therefore, increasing physical activity is recommended to improve cardiovascular health.

KEYWORDS: Blood pressure, cardiovascular health, exercise, fitness, metabolic syndrome, physical activity, physical inactivity, randomized controlled trial, sedentary behavior

TURUN YLIOPISTO
Lääketieteellinen tiedekunta
Kliininen laitos
Kliininen fysiologia ja isotooppilääketiede
Valtakunnallinen PET-keskus
JOOA NORHA: Paikallaanolon vähentämisen vaikutukset sydämen ja verenkiertoelimistön terveyteen: satunnaistettu kontrolloitu tutkimus aikuisilla, joilla on metabolinen oireyhtymä
Väitöskirja, 138 s.
Kliininen tohtoriohjelma
Huhtikuu 2025

TIIVISTELMÄ

Havainnoivien tutkimusten mukaan runsas paikallaanolo on yhteydessä heikompaan sydän- ja verisuoniterveyteen, mutta interventiotutkimuksia aiheesta on vasta rajatusti. Tämän väitöskirjatutkimuksen tavoitteena oli tutkia paikallaanolon vähentämisen vaikutuksia kestävyyskuntoon sekä sydämen ja verenkiertoelimistön terveyteen fyysisesti inaktiivisilla keski-ikäisillä aikuisilla, joilla on metabolinen oireyhtymä.

Yhteensä 64 vähän liikkuvaa aikuista, joilla oli metabolinen oireyhtymä ja jotka viettivät suurimman osan hereilläoloajastaan paikallaan istuen tai makoillen, satunnaistettiin koe- (n=33) ja verrokkiryhmiin (n=31). Koeryhmässä tavoitteena oli vähentää päivittäistä paikallaanoloa neljän viikon sisäänottovaiheeseen verrattuna tunnilla päivässä puolen vuoden ajan. Paikallaanoloa suositeltiin korvaamaan tuolista ylös nousemalla, arkiliikkumisella ja kevyellä aktiivisuudella. Verrokkiryhmää ohjeistettiin säilyttämään tavanomaiset paikallaanolo- ja liikkumistottumukset. Kaikki tutkittavat käyttivät liikemittareita koko puolen vuoden ajan paikallaanolon ja liikkumisen seuraamiseksi. Sydän- ja verisuoniterveyttä tutkittiin maksimaalisella polkupyöräergometritestillä sekä verenpainemittauksilla ja sydämen kaikukuvauksella sekä levossa että fyysisen rasituksen yhteydessä.

Koeryhmä vähensi paikallaanoloa keskimäärin 40 min/pv ja lisäsi reipasta tai rasittavaa liikkumista 20 min/pv, kun taas verrokkiryhmässä ei havaittu tilastollisesti merkitseviä muutoksia.

Paikallaanolon vähentämiseen pyrkineellä interventiolla ei ollut tilastollisesti merkitseviä vaikutuksia kestävyyskuntoon eikä levossa mitattuun tai rasituksen aikaiseen verenpaineeseen tai sydämen rakenteeseen tai toimintaan. Koko tutkimusjoukkoa tarkasteltaessa lisääntynyt liikkuminen oli kuitenkin yhteydessä parantuneeseen kestävyyskuntoon sekä sydämen vasemman kammion massaindeksiin ja matalampaan verenpaineeseen sekä parempaan vasemman kammion pitkittäissupistumiseen kevyen–reippaan liikkumisen aikana.

Paikallaanolon vähentämiseen pyrkineellä interventiolla ei ollut vaikutusta sydän- ja verisuoniterveyteen, joskin onnistunut paikallaanolon vähentäminen ja liikkumisen lisääminen edistivät maksimaalista kestävyyskuntoa sekä sydän- ja verisuoniterveyttä. Siispä liikkumisen lisääminen on suositeltavaa kunnon sydän- ja verisuoniterveyden parantamiseksi.

AVAINSANAT: Fyysinen aktiivisuus, fyysinen inaktiivisuus, kestävyyskunto, liikunta, metabolinen oireyhtymä, paikallaanolo, satunnaistettu kontrolloitu tutkimus, sydän- ja verisuoniterveys, verenpaine

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Abbreviations

A	Peak atrial contraction transmitral flow velocity
A2CH	Apical two-chamber view
A3CH	Apical three-chamber view
A4CH	Apical four-chamber view
ACC/AHA	American College of Cardiology/American Heart Association
APE	Angle for posture estimation
BMI	Body mass index
BP	Blood pressure
BP/MET	Blood pressure change per 1-unit increase in metabolic equivalent of task during the exercise test
BSA	Body surface area
CI	Confidence interval
cm	Centimeter
E	Peak early diastolic transmitral flow velocity
e’	Early mitral annulus velocity
ESC/ESH	European Society of Cardiology/European Society of Hypertension
GLS	Global longitudinal strain
g	Gram
g	Gravity
h	Hour
HFmrEF	Heart failure with mildly reduced ejection fraction
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
kg	Kilogram
LPA	Light physical activity
LV	Left ventricle
m	Meter
M-mode	Motion mode
MAD	Mean amplitude deviation
MET	Metabolic equivalent of task
m*g*	Milligravity
min	Minute
ml	Milliliter
mm	Millimeter
MVPA	Moderate-to-vigorous intensity physical activity

n	Number of participants
O_2	Oxygen
PA	Physical activity
PLAX	Parasternal long axis
Q1, Q3	First and third quartile
RER	Respiratory exchange ratio
s	Second
SB	Sedentary behavior
SD	Standard deviation
WHO	World Health Organization
VO_2max	Maximal oxygen uptake
W	Watt
wk	Week

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Norha, J., Sjöros, T., Garthwaite, T., Laine, S., Saarenhovi, M., Kallio, P., Laitinen, K., Houttu, N., Vähä-Ypyä, H., Sievänen, H., Löyttyniemi, E., Vasankari, T., Knuuti, J., Kalliokoski, K. K. & Heinonen, I. H. A. Effects of reducing sedentary behavior on cardiorespiratory fitness in adults with metabolic syndrome: A 6-month RCT. *Scandinavian Journal of Medicine & Science in Sports*, 2023; 33: 1452- 1461.
doi:10.1111/sms.14371

II Norha, J., Sjöros, T., Garthwaite, T., Laine, S., Saarenhovi, M., Kallio, P., Laitinen, K., Houttu, N., Vähä-Ypyä, H., Sievänen, H., Löyttyniemi, E., Vasankari, T., Knuuti, J., Kalliokoski, K. K., & Heinonen, I. H. A. Effects of reduced sedentary time on resting, exercise and post-exercise blood pressure in inactive adults with metabolic syndrome – a six-month exploratory RCT. *Journal of Human Hypertension*, 2024; 38(4), 314–321.
doi:10.1038/s41371-024-00894-6

III Norha, J., Saarenhovi, M., Kallio, P., Sjöros, T., Garthwaite, T., Laine, S., Laitinen, K., Houttu, N., Vähä-Ypyä, H., Sievänen, H., Löyttyniemi, E., Vasankari, T., Knuuti, J., Kalliokoski, K. K., & Heinonen, I. H. A. Effects of reducing sedentary behavior on cardiac structure and function at rest and during exercise: a six-month randomized controlled trial. *Manuscript.*

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1 Introduction

Physical activity (PA) has been known to be beneficial for achieving and maintaining good health for millennia (Tipton, 2014). Despite this, physical inactivity (i.e., not meeting the current PA guidelines) affects about one-third of the world's population, especially adults in Western high-income countries, and the number of adults with physical inactivity is increasing (Guthold et al., 2018; Strain et al., 2024). As the prevalence of physical inactivity increases with age, it is likely that physical inactivity continues to increase in the aging population (Strain et al., 2024). Global estimates predict almost 500 million new cases of non-communicable disease that could be attributed to physical inactivity between 2020 and 2030 (Santos et al., 2023). This leads to both high healthcare costs and decreased quality of life (Santos et al., 2023; Vaduganathan et al., 2022). Meanwhile, a concerning trend is seen in the increasing prevalence of cardiovascular diseases and their risk factors, such as hypertension and obesity (Roth et al., 2020; Zhang et al., 2024). Yet, it has been estimated that, for example, most coronary heart disease deaths could be prevented or postponed by improving risk factor profiles on a population level (Capewell et al., 2010). Here, PA behavior plays an important role at all stages of life (Perry et al., 2023).

Sedentary behavior (SB) is defined as any awake sitting, reclining, or lying behaviours that result in energy expenditure of 1.5 times above resting or less (i.e., $\leq$1.5 metabolic equivalents of task (MET) where 1 MET = 3.5 ml O_2/kg/min) (Tremblay et al., 2017). SB is highly prevalent among Finnish adults with over 9 h/day, on average (Husu et al., 2021). In addition to physical inactivity, SB has been recognized as a risk factor for cardiovascular diseases and mortality (Young et al., 2016). Indeed, adults who accumulate the most SB seem to have around 20–30% increased risk for cardiovascular diseases and mortality compared to the least sedentary adults (Jingjie et al., 2022). However, the estimates are based entirely on observational studies which, by nature, cannot fully establish causality. Specifically, a potential confounder for the association between SB and cardiovascular disease risk is PA – time spent sedentary is, by definition, time not spent physically active. Thus, high SB may merely be a reflection of the lack of PA (Van Der Ploeg & Hillsdon, 2017). Controlling for PA in observational studies often includes only moderate-to-vigorous intensity PA (MVPA) (Ross et al., 2024). The approach fails to address light PA (LPA) which is strongly negatively correlated with SB (Mansoubi et al., 2014). Moreover, data from interventional studies show that reduced SB is mostly reallocated to LPA or standing (Segura-Jiménez et al., 2022). Thus, adjusting for only MVPA can lead to ignoring the lack of LPA as a potential cause of increased disease risk with high SB (Chastin et al., 2019).

Intervention studies (i.e., randomized controlled trials) that focus on modifying (reducing) SB help to elucidate the possible independent effect of SB on cardiovascular health. By randomizing participants into a SB-reducing group and a control group, the differences between groups after the intervention should be due to the administered intervention rather than any confounding factors (Zabor et al., 2020). Importantly, several studies show that interventions focusing on the reduction of SB are effective in reducing SB among different populations, such as adults with overweight (Chastin et al., 2021; Lam et al., 2022). In addition, such interventions do result in minor beneficial changes in several cardiovascular disease risk factors (e.g., blood glucose, body adiposity, and blood pressure (BP)) both in healthy and clinical populations (Hadgraft et al., 2021; Nieste et al., 2021). However, data on the effects of SB reduction on the cardiovascular system's function is scarce.

Besides the scarcity of intervention studies, a second shortcoming of the present research that focused on SB and cardiovascular health is the measurement of SB. Self-report assessments (i.e., questionnaires) of SB are highly susceptible to recall and response biases, and compared to device-based measurements they underestimate SB by over 1.5 h/day (Prince et al., 2020). Furthermore, self-report tools often have limited ability to estimate LPA and standing time. Yet, most studies investigating the health consequences of SB to date have utilized self-reports of SB (Jingjie et al., 2022). Device-based measures, such as accelerometers, are considered more objective with less social desirability bias compared to self-report tools. On the other hand, current studies that do utilize device-based measures often measure PA and SB for only a few days (e.g., 4–7 days). This duration might not be sufficient at capturing the actual SB and PA habits of the study participants and as a result, some health-related associations might be missed (Sjöros et al., 2021).

Detailed measurement of the cardiovascular system is key for understanding the potentially widespread effects of SB on cardiovascular health. As shown by previous intervention studies, the magnitude of the potential health-related effects of SB reduction is small which encourages elaborate measurements to detect and describe the effects in detail (Hadgraft et al., 2021; Nieste et al., 2021). Various measurement conditions (e.g., at rest and during exercise), methods (e.g., cycle ergometry, BP measurement, and echocardiography), and statistical analyses are crucial in understanding the phenomenon of cardiovascular responses to a long-term SB reduction intervention.

With the major limitations of the SB and cardiovascular disease related research acknowledged, this thesis aims to address these gaps by reporting the results of a six-month accelerometer-utilizing randomized controlled trial that focused on SB reduction in middle-aged adults with physical inactivity and an increased risk for cardiovascular disease (i.e., metabolic syndrome). The results discuss the effects on cardiorespiratory fitness, BP in various physiological conditions, and cardiac function and remodeling.

2 Review of the literature

2.1 Definitions of sedentary behavior and physical activity

Human PA behaviors can be displayed as a continuum from total inactivity (e.g., sleeping) to light activities, such as light housework, to the most extreme athletic performances (**Figure 1**). In this thesis, I use the term PA behavior to cover all behavior related to PA; this includes even the activities that are characterized by low PA and energy consumption, such as SB.

A crucial concept in describing SB and PA intensity is the MET value, which is the most commonly adapted measure in the intensity classification. One MET is defined as oxygen consumption of 3.5 ml O_2/kg/min, which is stated to represent the average resting metabolic rate of an adult (Byrne et al., 2005). However, this definition has been questioned as the 3.5 ml O_2/kg/min was measured only from one man decades ago and more recent measurements have recorded lower and varying values for different populations (Byrne et al., 2005). Nevertheless, the definition of 1 MET = 3.5 ml O_2/kg/min remains used in the current SB and PA classifications (Tremblay et al., 2017).

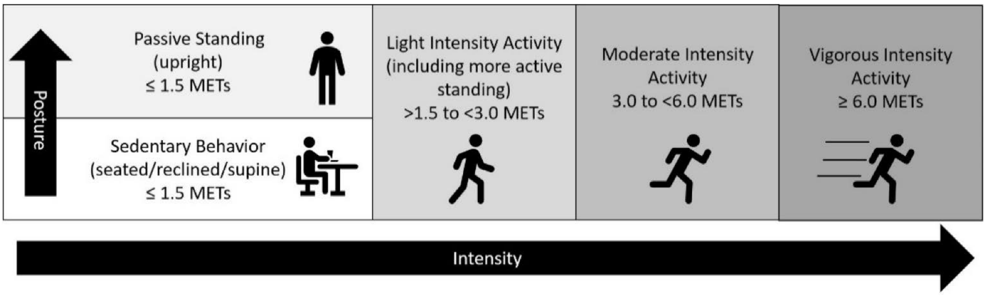


Figure 1. Continuum of the physical activity intensities. Reprinted from Kowalsky et al., 2021. Published under the Creative Commons Attribution (CC BY) License.

According to the Sedentary Behavior Research Network Terminology Consensus Project, SB refers to any waking behaviours that result in ≤1.5 MET energy consumption while in a sitting, reclining, or lying posture (Tremblay et al., 2017). As sleeping time is not counted as SB, most SB can generally be assumed to consist of sitting. While the energy consumption during standing may be ≤1.5 MET in some individuals (Kowalsky et al., 2021; Mansoubi et al., 2015), standing still is usually not considered as a SB because the posture itself may also be of importance. For example, due to the lack of muscle activity, sitting can result in lower extremity venous blood pooling, which, in combination with altered blood flow due to the flexed joints, result in turbulent blood flow, decreased antegrade shear stress, and endothelial dysfunction (Restaino et al., 2016). Standing also loads the musculoskeletal system different to sitting. Therefore, standing still is classified as its own category (Tremblay et al., 2017).

PA is defined as any bodily movement produced by skeletal muscles that result in energy expenditure (Caspersen et al., 1985). In the context of health promotion, PA is divided into LPA (1.5–2.9 METs), moderate-intensity PA (3.0–5.9 METs), and vigorous-intensity PA (≥6.0 METs), the latter two of which are often combined into MVPA (≥3.0 METs) (Bull et al., 2020).

The current PA guidelines by the World Health Organization (WHO) recommend that adults should participate in at least 150 minutes of moderate-intensity PA or 75 minutes of vigorous PA every week along with muscle strengthening activities twice every week (Bull et al., 2020). To increase health benefits one can double the amount of weekly PA. Physical inactivity, on the other hand, is defined as insufficient amount of PA to meet the current PA guidelines (Tremblay et al., 2017). It is important to appreciate the difference between SB and physical inactivity since the terms are sometimes incorrectly used interchangeably. On a side note, no widely adopted guidelines on daily SB duration exist today, and therefore, any common definition for a “sedentary” individual does not exist (Sedentary Behaviour Research Network, 2012).

PA evidently includes physical exercise (training). However, distinct from other PAs, physical exercise is a planned, structured, and repetitive form of PA, frequently with health- or performance-related goals (Caspersen et al., 1985). Other domains of PA include occupational, domestic, transportation, and leisure-time PA (Strath et al., 2013), although physical exercise is a subcategory of leisure-time PA. Together, PAs that are not considered physical exercise, are generally called non-exercise or, sometimes, everyday physical activities.

2.2 Measurement of physical activity behavior

Measuring PA behavior (namely PA, SB, and body postures) in health-related studies is of paramount importance when the outcome may be affected by the levels of PA or SB. In order to assess the domain, quantity, and intensity of PA or SB, several methods have been developed.

2.2.1 Self-reports

Self-reports of PA or SB assessment include questionnaires and diaries or logs, where the participant assesses themself the PA- or SB-related data. Questionnaires can be divided into three different main types (Strath et al., 2013). Global questionnaires are usually short, and they are used to grossly categorize an individual's PA into physically active or inactive. Recall questionnaires are used to quantify the PA and SB of an individual within a certain period of time (e.g., the past week or month), and they may be more detailed in terms of different domains or intensities of PA or SB. While questionnaires tend to be retrospective in nature, diaries or logs aim at being more "real-time". For example, a diary can be filled every hour or 15 minutes to capture the daily activities with better temporal precision.

For SB assessment, self-reported screen time has been sometimes used as a surrogate measure. While screen time is associated with health risks, including mortality risk (Celis-Morales et al., 2018), the association can, in part, be mediated by other factors than SB, like unhealthy snacking while watching the television. Furthermore, screen time notably underestimates total SB duration (Colley et al., 2022).

The wide availability and low cost of self-reports are among their strengths. Moreover, the data from questionnaires can be transformed into numerical data on the intensity (i.e., METs), duration, and frequency of the activity (Strath et al., 2013). Additionally, the self-report methods for PA and SB assessment may include questions on the domain (i.e., occupational or leisure) of the activity. However, these methods are susceptible to social desirability and recall bias, which may have significant effects on the estimates on the duration and intensity of PAs and SBs (Prince et al., 2008, 2020). Indeed, compared to device-based measures the self-report methods tend to underestimate SB by 1.5 h/day, on average (Prince et al., 2020). In terms of PA, the estimates from seld-reports and device-based methods do not seem to have a consistent under- or overestimation pattern; however, the correlation between the methods is generally low-to-moderate (Prince et al., 2008). Furthermore, sex, education, and age may affect the self-reported PA and SB estimates (Dyrstad et al., 2014).

2.2.2 Device-based methods

Device-based methods include motion and/or posture sensors, energy expenditure measures, physiological measures, and direct observation (Strath et al., 2013). Motion sensors, or accelerometers and inclinometers, have become increasingly used in PA research over the past decades, since they provide an estimate of the duration and intensity of PA behavior that is not as susceptible for social desirability and recall bias as the subjective methods. However, it is noteworthy that most of the device-based methods are not completely free of subjective bias as the individual may choose to wear the measurement device at selected times or on certain days, and simply knowing of being measured might alter PA behavior. In addition, the devices may not capture all types of PA behavior. Therefore, device-based methods should not be referred to as objective methods.

Energy expenditure measures (e.g., doubly labeled water or room calorimetry) and physiological measures (i.e., heart rate monitoring) along with direct observation (e.g., in a laboratory or using video taping) provide the least subjective, or the most objective, estimates of PA and, in the case of direct observation, SB (Hills et al., 2014). The shortcoming of energy expenditure measurements is the inability to estimate PA intensity and SB duration (Hills et al., 2014).

Heart rate can easily be measured in free-living conditions, and it can provide an estimate of PA intensity, duration, and frequency (Hills et al., 2014). However, as heart rate can be affected by other factors besides PA (e.g., pharmacological agents or mental stress), heart rate is best when used in conjunction with other methods (Hills et al., 2014).

Direct observation has both subjective and objective measurement qualities (Hills et al., 2014; Strath et al., 2013). It is objective in the sense that the measured individual cannot influence the interpretation of different behaviors, whereas the observer's decision to classify a behavior into certain intensity is somewhat subjective. However, direct observation is a valid tool to assess PA intensity and duration (Lyden et al., 2014). The obvious drawback of the method is very limited use in free-living conditions, albeit wearable cameras have been used (Davies et al., 2020). However, the wearable cameras are mostly used to complement accelerometer data and not for quantitative PA behavior assessment.

2.2.2.1 Step counters

Step counters, or pedometers, are one of the first devices to measure human ambulation dating back several hundred years, and their popularity has gained interest in the general population as well as research towards the end of the 20th century (Bassett et al., 2017). Step count is still used as an overall estimate of an individual's daily PA in studies assessing the relationship between PA and health (Bassett et al., 2017). Several types of step counters (e.g., mechanical, accelerometer, wrist-, hip-, pocket-, or ankle-worn) exist. Moreover, the benefits of measuring steps include the simple outcome measure (i.e., number of steps), the objectivity of the measurement, and the relative ease of measurement (Bassett et al., 2017).

However, while step count may be a good overall estimate of PA in the general population, its inability to discriminate different intensities of walking and other PAs than walking (such as bicycling or swimming) limit the detail in which step count can assess PA. Furthermore, gait abnormalities or slow walking speed may also hinder step detection (Cyarto et al., 2004). Nevertheless, many of the modern PA measurement devices provide a step count in addition to other PA and SB measures.

2.2.2.2 Accelerometers

Accelerometers are being increasingly used in PA and SB research due to their ability to quantify PA and SB duration, frequency, and intensity as well as body posture. Additionally, the recording time in some devices may be several weeks without recharging (Strath et al., 2013). However, accelerometers also have some limitations that should be acknowledged. The positioning of the device (e.g., hip, thigh, or wrist) has an influence on the estimates of PA and SB measured, and the algorithms for analysis should be selected accordingly (Janssen & Cliff, 2015). For SB measurement, the thigh has been proposed as the optimal placement (Janssen & Cliff, 2015). On the other hand, the device has to be attached to the thigh using adhesive tape which limits the possibilities to perform long term (e.g., multiple months) measurements. Moreover, some accelerometers do not tolerate water and cannot be worn during water-based activities. In addition, hip-worn accelerometers may not be able to detect upper limb activities, such as carrying or manoeuvring objects, isometric muscle work, or non-weight-bearing exercise, like bicycling (Chen & Bassett, 2005). That said, methods for identifying bicycling or stair walking have been developed, too (Skotte et al., 2014). Yet, detecting isometric muscle work is impossible with accelerometers, as the devices detect movement and isometric work does consume energy without producing significant movement.

An accelerometer works by a seismic mass that is attached to a piezoelectric sensor which reacts to acceleration and generates an output voltage that is proportional to the acceleration (Chen & Bassett, 2005). As a single piezoelectric acceleration sensor is uniaxial, i.e., it reacts to acceleration only in one direction, three acceleration sensors (so called triaxial accelerometers) are often combined to capture acceleration in all three dimensions (Chen & Bassett, 2005).

The raw acceleration data must be digitally processed in order to produce meaningful data of PA behavior. Several methods and data processing algorithms have been established. Indeed, the data processing can have a marked impact on the PA and SB estimates (Vähä-Ypyä et al., 2022), which should be acknowledged when comparing results obtained using different methods (e.g., comparing an accelerometer study to the PA guidelines).

An important factor to consider is the epoch duration that has been used in the data analysis. The epoch duration essentially determines the resolution at which the PAs and SBs are captured. Short epochs (e.g., a few seconds) capture even short bouts of PA and have a good resolution for fast changing intensity during a given activity (e.g., quickly alternating between running, walking, and standing still during sports) (Chen & Bassett, 2005). However, while longer epochs (e.g., several minutes) might not capture all short-duration behaviors, they may better reflect self-reported PA levels which the current PA guidelines are mostly based on (Vähä-Ypyä et al., 2022). Still, as the PA guidelines suggest that "every move counts", meaning that any body movement can benefit health (The World Health Organization, 2020), it is useful to study the PAs and SBs in great detail and resolution in scientific studies.

Methods for PA quantification include, for example, activity counts, Euclidean norm minus one, activity index, and mean amplitude deviation (MAD) (Sievänen & Kujala, 2017). As mentioned, the estimates vary with different methods, yet no golden standard method has been established. Nevertheless, the outcome should be transformable to a physiologically meaningful variable, like MET, using transparent algorithms (Sievänen & Kujala, 2017). Using METs (or MET-minutes/hours) as the outcome variable, the data can easily be interpreted and compared across studies in addition to easily classifying the accelerometer data into different intensity categories, such as LPA or MVPA.

For the purpose of this thesis, the MAD method is described in more detail. The MAD algorithm was published in 2015 by Vähä-Ypyä et al. (Vähä-Ypyä et al., 2015) and further validated in 2015 (Vähä-Ypyä et al., 2015). In the MAD algorithm, the raw triaxial acceleration data (in gravity units, *g*) is transformed into the resultant acceleration (r_i) using the formula:

$$r_i = \sqrt{x_i^2 + y_i^2 + z_i^2}8$$

Where x_i, y_i, and z_i are the ith measurement samples of the acceleration signal in the three dimensions (Vähä-Ypyä et al., 2015). Then, the typical distance of data points from the mean ($\bar{r}$) is calculated resulting in the MAD-value (Vähä-Ypyä et al., 2015):

$$MAD = 1/n \; |r_i - \bar{r}|$$

As a result, MAD provides an estimate of the PA intensity in milligravity (m*g*) units. The MAD value correlates strongly with measured oxygen uptake and can therefore be transformed into MET-values (Vähä-Ypyä et al., 2015). MAD cut-point of >91 m*g* is sensitive and specific for determining the intensity >3.0 MET (i.e., MVPA), and the cut-point of >414 m*g* is sensitive and specific for >6.0 MET intensity (i.e., vigorous PA) (Vähä-Ypyä et al., 2015). MAD >22.5 m*g* has been used as the cut-point for >1.5 MET intensity (i.e., LPA) (Vähä-Ypyä et al., 2018). Furthermore, step count can also be calculated using the vertical acceleration data (Vähä-Ypyä et al., 2018).

Additionally, SB duration can be estimated from accelerometer data using different algorithms. Activity counts are sometimes used as a measure of SB (e.g., <100 counts/min). However, while this does indicate that the accelerometer is moving very little, the algorithms for calculating the activity counts may vary between accelerometer brands making comparisons between studies difficult (Sievänen & Kujala, 2017). Moreover, activity counts are unable to discriminate different sedentary postures and standing.

Used in conjunction with the MAD method, SB assessment using the angle for posture estimation (APE) algorithm is a reliable method for recognizing lying, sitting, and standing (Vähä-Ypyä et al., 2018). APE is based on the incident accelerometer orientation in relation to the Earth's gravity vector. The Earth's gravity vector is set as the reference vector based on the accelerometer position while walking is detected. Then, when the MAD value is under 22.5 m*g* (i.e., ≤1.5 MET) the accelerometer's orientation in relation to the reference vector is analyzed. A deviation of ≥11.6° from the reference vector is considered sitting, reclining, or lying, and a deviation of <11.6° is considered standing (Vähä-Ypyä et al., 2018). The APE algorithm is visualized in **Figure 2**.

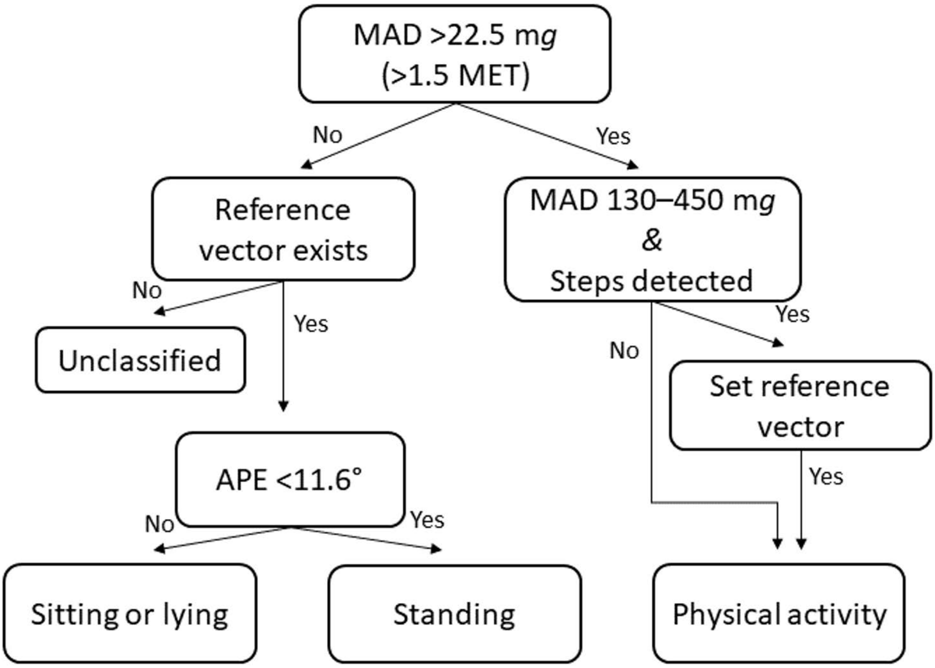


Figure 2. The angle for posture estimation algorithm. Modified from Vähä-Ypyä et al., 2018. MAD = mean amplitude deviation, MET = metabolic equivalent of task, APE = angle for posture estimation.

2.3 Randomized controlled trial

Randomized controlled trials are prospective studies that are used to assess the effectiveness (sometimes referred to as effects in a “real world” setting) or efficacy (the effects of an intervention under ideal, controlled, setting) of an intervention. In a randomized controlled trial, the eligible participants are randomly assigned to the study groups, often a group that receives the intervention and a comparator group that receives either a comparator intervention, a placebo, or no intervention (Zabor et al., 2020). The randomization is performed to reduce bias, because if participants or researchers were to select the group allocations, several human factors could interfere the interpretation of the results (e.g., the healthiest individuals seeking to the active intervention groups). With proper randomization, the groups should be balanced and similar to each other before the intervention (De Boer et al., 2015). Nevertheless, the baseline characteristics of a study sample should always be appreciated, as individuals seeking to voluntarily participate in a study are often healthier than the actual target population; this is known as the healthy participant effect or bias (Maldonado-Cañón et al., 2024).

With the similarity of groups at baseline and the prospective nature of the trial, it is assumed that the only difference between the groups during the trial is the administered intervention. Yet, possible confounders should be measured and controlled for if necessary. Therefore, randomized controlled trials are often seen superior to observational studies and even as the gold standard for causal inference (Zabor et al., 2020). However, randomized controlled trials have their limitations, too. A notable proportion of published randomized controlled trials have inadequate sample sizes (Berg et al., 2023; Tam et al., 2020), and not all research questions are ethical to investigate in a randomized setting (e.g., health effects of smoking or the effectiveness of parachute use, as humorously demonstrated by Smith & Pell (Smith & Pell, 2003)). Moreover, all participants may not adhere to the allocated intervention or control protocol, which, on the other hand, reflects a realistic clinical setting, but limits the interpretations on efficacy of the intervention.

To reduce the risk of bias in a randomized controlled trial, the main analyses should be performed using the intention-to-treat principle, which means that all participants should be analyzed in the group they were originally allocated to, regardless of the actual received intervention (Smith et al., 2021). In addition to the intention-to-treat analysis, the participants can also be re-divided into groups based on the actual received intervention to estimate the effects of receiving the intervention. However, the benefits of randomization are lost with this approach and the results should be interpreted with caution (Smith et al., 2021).

Practical drawbacks of conducting a randomized controlled trial include high costs and time demands (Zabor et al., 2020). Therefore, a single phenomenon is often studied using different study designs, including both observational (cross-sectional and cohort studies) and interventional studies. Moreover, as all randomized controlled trials have to make choices on the inclusion criteria and details on the intervention(s), systematic reviews and meta-analyses are eventually needed to further review all relevant trials and the effects of an intervention.

2.4 Health consequences of sedentary behavior

During the 21st century, the health effects of SB has been under a lot of interest both among researchers and the general public. This has occurred due to shifts in work environments (e.g., increasing prevalence of sedentary occupations) and increases in leisure-time SBs, such as computer use outside work (Yang et al., 2019). With the advent of improved measurement technologies, like accelerometers, the quantification of SB has become increasingly convenient, which has likely contributed to the increase in SB research (Evenson et al., 2022).

Majority of the studies on SB and health have been observational studies (e.g., cross-sectional or cohort studies where the exposure, like SB, is not manipulated by the researchers), although interventional evidence on the effects of modifying SB is emerging. The interventional studies have focused on either the mechanistic and acute effects of SB, or the effects of reducing SB over a longer period of time. In this chapter, the current evidence on the health consequences of SB is presented according to the different study designs to highlight the strengths and limitations of different study designs.

In short, the current evidence suggests that SB would be detrimental to cardiovascular health and reducing SB could result in small improvements in cardiovascular risk factors. However, the detrimental effects of SB may not be independent of PA (especially moderate-to-vigorous intensity). Moreover, the interventional studies have focused on cardiovascular risk factors, while the effects of SB reduction on the structure and function of the cardiovascular system remain largely unknown.

2.4.1 Associations between sedentary behavior and mortality

Multiple meta-analyses have shown that high SB associates with increased all-cause mortality (Biswas et al., 2015; Ekelund et al., 2016, 2019, 2020; Ku et al., 2018; Patterson et al., 2018; Xu et al., 2019). While the association seems very consistent, the conclusion that high SB itself would cause increased mortality might be erroneous for two reasons. First, reverse causality cannot fully be ruled out in association studies. This means that an underlying disease or disability that causes increased mortality risk itself also causes increased SB. Additionally, poor health affecting both SB and the mortality outcome can also be a source of (potentially unmeasured) confounding, where a factor influences both the exposure and outcome if not controlled for adequately. Moreover, studies where volunteers are recruited for SB measurements are prone to selection bias, as the healthiest individuals might be most interested in participating in a health-related study. Finally, it seems that the association between SB and mortality is confounded or mediated by PA.

When the daily amount of PA is sufficient, it seems that the adverse effects of SB are attenuated (Ekelund et al., 2016, 2020; Xu et al., 2019). When PA and SB are measured with self-reports, about 60–75 minutes/day of moderate-intensity PA is sufficient for eliminating the increased mortality risk with high (i.e., >8 h/day) SB (Ekelund et al., 2016). Similarly, using self-reported data, another meta-analysis concluded that to overcome the increased mortality risk of 9 h/day of SB, about 60 min of moderate-intensity PA is needed (Xu et al., 2019). However, when PA and SB are measured using accelerometers, already 30–40 min/day of MVPA may attenuate the risk of death (Ekelund et al., 2020). Furthermore, more recent evidence suggests even less, 22 min of MVPA per day, may be sufficient at eliminating the increased risk for mortality (Sagelv et al., 2023). Rather than indicating strict thresholds for sufficient SB or PA durations, these studies show that MVPA can attenuate the risk for mortality that high SB associates with.

2.4.2 Associations between sedentary behavior, cardiovascular diseases, and related risk factors

Recent evidence suggests an increased risk for cardiovascular diseases with high SB. A meta-analysis comprising of 19 studies showed that the risk for cardiovascular diseases is 24 % higher in the most sedentary adults (self-reported SB 10.5 h/day) compared to the least sedentary individuals (SB 2.75 h/day) (Jingjie et al., 2022). Similar, albeit statistically non-significant (p=0.21), associations were observed for screen time-based studies (Jingjie et al., 2022). Another meta-analysis of 18 different studies found a similar association between self-reported SB and pooled cardiovascular diseases and cardiovascular disease related mortality risk (Liang et al., 2022). Further, a 2023 meta-analysis of 19 cohort studies concluded that (self-reported in most included studies) SB and the risk of fatal and non-fatal cardiovascular diseases follow a J-shaped dose-response curve, with the healthiest duration of daily SB being 2–3 h (Onagbiye et al., 2023). The evidence of increased cardiovascular disease risk with high SB was further strengthened by a longitudinal 7.5-year cohort study of 5951 women, reporting a hazard ratio of 1.29 (95% CI 1.10, 1.51) for heart failure with preserved ejection fraction per 1 standard deviation increase of SB (LaMonte et al., 2024).

In addition, an eight-year longitudinal study of almost 90 000 participants reported that SB associated with the risk for heart failure and cardiovascular mortality even among individuals with ≥150 min MVPA/week (Ajufo et al., 2024). Importantly, meeting the 150 min threshold (corresponding to PA guidelines) was defined using wrist-worn accelerometers and five-second epochs (Ajufo et al., 2024), which most likely does not represent meeting the PA guidelines (Vähä-Ypyä et al., 2022). Indeed, the association between heart failure and SB disappeared when a 230-min/week MVPA threshold was utilized (Ajufo et al., 2024), which suggests that the SB-related risk is not independent from MVPA.

High SB duration associates with multiple cardiovascular disease risk factors. Cross-sectionally, women with SB ≥10.3 h/day have 2.2-fold odds for having diabetes compared to women with SB ≤8.3 h/day (Bellettiere et al., 2019). Similar findings have been reported in men (George et al., 2013). A meta-analysis of 16 prospective and two cross sectional studies including both sexes and almost 800 000 participants concluded reported a 2.12-fold increased risk for diabetes with high SB (Wilmot et al., 2012).

Additionally, a meta-analysis of mostly cross-sectional studies reported a 45% increase in obesity risk in individuals with high SB (Silveira et al., 2022). Similarly, a meta-analysis of only prospective studies reported a 33% increase in combined overweight or obesity risk due to SB (Campbell et al., 2018). However, no associations between SB and the five-year change in body weight or body mass index (BMI) were observed and a one-hour increase in SB per day associated with only 0.02 mm increase in waist circumference (Campbell et al., 2018). To conclude, The Physical Activity Guidelines Advisory Committee stated that high SB associates with an increased risk for mortality and morbidity (Katzmarzyk et al., 2019).

2.4.3 Short-term intervention studies

Short-term intervention studies (i.e., hours to a few weeks) assess the acute health effects of either prolonged SB or breaking up SB. These studies provide insight to the physiology of SB and the feasibility of SB interrupting interventions. However, they are unable to assess long-term health outcomes, such as changes in organ structure or disease risk.

The Dallas Bedrest and Training Study, originally performed in the year 1966, has given valuable insights to the detrimental effects of extreme SB, i.e., three weeks of bedrest (McGuire et al., 2001; Saltin et al., 1968). In the study, the cardiovascular effects of three week's bedrest were assessed in five healthy 20 year-old men. The participants were contacted again for a 30 year follow-up in the year 1996. The three week bedrest reduced cardiorespiratory fitness, cardiac output, stroke volume, and maximal exercise BP in a magnitude comparable or larger than the effects of 30 years of aging (McGuire et al., 2001). The detrimental effects of bedrest to the cardiac muscle have been since replicated in other bedrest studies (Perhonen et al., 2001). Additionally, bedrest has other detrimental effects, such as decreased insulin sensitivity (Sonne et al., 2010).

SB interrupting studies have compared varying frequencies and durations of different activities and how they affect cardiometabolic outcomes. Often, the trials have implemented breaking up SB with light intensity activities every 30 or 60 minutes for 1–5 minutes at a time, for a duration comparable to a standard workday (i.e., 8 h). In brief, such interventions have shown some beneficial effects on blood glucose and BP compared to a control group that remained sedentary, albeit some conflicting results have been reported as well (Buffey et al., 2022; Dempsey et al., 2018; Duran et al., 2023; Paterson et al., 2022). With prolonged SB, BP tends to increase by 3.2 mmHg, on average, and this could be counteracted by regularly interrupting the SB (Paterson et al., 2022). Speculatively, the increase in BP during uninterrupted SB could lead to long term effects on the cardiovascular system if the prolonged SB is repeated on most days.

2.4.4 Long-term intervention studies

Evidence on the effects of reducing SB on cardiovascular outcomes is emerging yet still relatively scarce. Nevertheless, randomized controlled trials are the golden standard method for studying the effectiveness of an intervention and establishing a causal relationship of two associated factors (e.g., SB and cardiovascular health).

To my best knowledge, to date, three meta-analyses of longer-term SB reduction-focused interventional studies in adults have been published: one studying non-clinical populations (33 studies; Hadgraft et al., 2021), another that included only clinical populations (18 studies; Nieste et al., 2021), and a third that included only studies where SB was replaced by standing among healthy adults (9 studies; Saeidifard et al., 2020). In healthy populations, SB reduction resulted in small but statistically significant changes in body mass (-0.6 kg), waist circumference (-0.7 cm), body fat percentage (-0.3 %-points), systolic BP (-1.1 mmHg), fasting insulin (-1.4 pmol/l), and high-density lipoprotein cholesterol (+0.04 mmol/l) (Hadgraft et al., 2021). When SB was replaced by only standing interventions, small benefits in fasting blood glucose (-0.1 mmol/l) and insulin (-2.3 pmol/l), and body mass (-0.75 kg) were reported (Saeidifard et al., 2020). As expected, findings for clinical populations were mostly similar yet slightly higher in magnitude (glycated hemoglobin -0.17%, body fat percentage -0.7 %-points, waist circumference -1.5 cm) (Nieste et al., 2021). Whilst the aforementioned meta-analyses suggest that reducing SB might be beneficial for some cardiovascular risk factors, the included interventions lasted mostly less than six months with few lasting 12–36 months

(Hadgraft et al., 2021; Nieste et al., 2021; Saeidifard et al., 2020). Moreover, the interventions to replace SB differed widely across studies ranging from standing to pedaling and resistance exercise. Additionally, relatively high heterogeneity between studies was reported in all three meta-analyses, meaning that the effects were not consistent across studies (Hadgraft et al., 2021; Nieste et al., 2021; Saeidifard et al., 2020).

2.5 Metabolic syndrome

Metabolic syndrome is a cluster of modifiable cardiovascular risk factors. Varying criteria for the diagnosis of metabolic syndrome have been used. However, the current definition that is used in this thesis was proposed by Alberti et al. in 2009.

According to the definition by Alberti et al. (2009), the diagnosis of metabolic syndrome requires three or more of the following criteria for European adults: elevated waist circumference (>80 cm for women or >94 cm for men), elevated blood triglycerides (>1.7 mmol/l), reduced high-density lipoprotein cholesterol (<1.3 mmol/l for women or <1.0 mmol/l for men), elevated BP (systolic ≥130 and/or diastolic ≥85 mmHg), and elevated fasting glucose (≥5.6 mmol/l) (Alberti et al., 2009).

Globally, the individual factors of metabolic syndrome are common among adults, with prevalence rates ranging from 25% for elevated glucose to 45% for elevated waist circumference (Noubiap et al., 2022). The prevalence of metabolic syndrome has been estimated at 31% among adults, globally, but its prevalence varies according to geographic location (e.g., Europe 27% or Americas 46%) and country level income (lowest income 11% and highest 31%) (Noubiap et al., 2022). In Finland, prevalence as high as 43% has been reported using the FinHealth 2017 (*FinTerveys-tutkimus* in Finnish) survey data and the criteria by Alberti et al. (2009) (Haverinen et al., 2021). The prevalence of metabolic syndrome increases with age and is higher among men than women in all age groups except in >75 year-olds (Haverinen et al., 2021).

As metabolic syndrome comprises of several coexisting cardiovascular risk factors, it associates with high risk for cardiovascular disease. For example, metabolic syndrome increases the risk for myocardial infarction by 46%, cardiovascular death by 36%, and stroke by 44% compared to individuals without metabolic syndrome (X. Li et al., 2021).

2.5.1.1 Physical activity behavior and metabolic syndrome

The development of metabolic syndrome is closely related to diet quality and PA (Angelico et al., 2023; Lee et al., 2016). The risk for developing metabolic syndrome in the highest fitness tertile compared to the lowest fitness tertile has been shown to be 53 and 63% lower in men and women, respectively (LaMonte et al., 2005). Additionally, higher PA associates with decreased risk for major cardiovascular events and all-cause mortality in adults with established metabolic syndrome (Park et al., 2020). Furthermore, exercise training interventions improve the components of metabolic syndrome and reduce its prevalence (Joseph et al., 2019). Therefore, promoting PA is crucial for primary and secondary prevention in metabolic syndrome.

A systematic review of observational studies from 2019 reported that higher SB associated with higher risk for metabolic syndrome in nine studies, whereas five studies showed no statistically significant association (Amirfaiz & Shahril, 2019). Later studies using questionnaires (Suliga et al., 2022) and accelerometers (Jankowska et al., 2024) have further found associations between higher SB and risk of metabolic syndrome. Therefore, it seems plausible that high SB would be a risk factor for metabolic syndrome, although the confounding or mediating role of PA has not been evaluated. Moreover, to my best knowledge, no interventional studies on the effects of reducing SB on the incidence of metabolic syndrome exist.

2.6 Cardiorespiratory fitness

Cardiorespiratory fitness describes the body's ability to deliver oxygen to the skeletal muscles during PA. It can be calculated from the cardiac output and arteriovenous oxygen difference using the Fick equation:

$$VO_2\ \mathrm{max} = (stroke\ volume\ \times heart\ rate)_{max} \times [C(a-v)O_2]_{max}$$

Where VO_2max is the maximal oxygen consumption, C denotes concentration, a denotes arterial, v denotes venous, and O_2 is oxygen at maximal (max) physical effort.

Most commonly, cardiorespiratory fitness is measured as the body's capacity to use oxygen per kilogram of body mass during one minute, or maximal oxygen uptake ($\mathrm{VO_2max}$) (ml $\mathrm{O_2}$/kg/min). However, common measures include maximal oxygen consumption per minute (i.e., ml $\mathrm{O_2}$/min), and maximal oxygen consumption per kilogram of fat free body mass during one minute (ml $\mathrm{O_2/kg_{FFM}}$/min). Additionally, measures related to walking distance (i.e., six-minute walking distance) or power output can be utilized. Notably, cardiorespiratory fitness should be distinguished from physical fitness which is an umbrella term comprising of cardiorespiratory fitness, muscular strength and endurance, flexibility, and according to some definitions, body composition (Caspersen et al., 1985).

Cardiorespiratory fitness is closely associated with cardiovascular health as it is dependent on the function of the cardiopulmonary, vascular, and neuromuscular systems. Indeed, solid evidence shows that good cardiorespiratory fitness has an important role in reducing all-cause and cardiovascular mortality as well as morbidity (Al-Mallah et al., 2018; Lang et al., 2024). A meta-analysis of 160 randomized controlled trials showed that physical exercise training improves both cardiorespiratory fitness and several cardiovascular disease risk factors (e.g., lipid profile or insulin sensitivity markers) (Lin et al., 2015). Even though this itself does not imply direct causality between cardiorespiratory fitness and risk factor status, it is notable that exercise training improves both outcomes. Furthermore, good cardiorespiratory fitness is beneficial in the prevention of cardiovascular disease complications among individuals with pre-existing cardiovascular disease (Al-Mallah et al., 2018).

On a population level, the global trend over the last five decades in cardiorespiratory fitness has been declining (Ekblom-Bak et al., 2019; Harber et al., 2020; Lamoureux et al., 2019; Vaara et al., 2020). However, signs of plateau in the decline have been reported (Harber et al., 2020; Vaara et al., 2020). The decline in cardiorespiratory fitness associates with increasing cardiovascular disease incidence and mortality, and all-cause mortality (Hemmingsson et al., 2022).

Importantly, the declining trends in cardiorespiratory fitness coexist with the global increase in overweight and obesity (Hemmingsson et al., 2022; Lamoureux et al., 2019). It is worth noting that, as mentioned, cardiorespiratory fitness is most commonly scaled to body mass (i.e., ml of O_2 per kg of body mass per minute) and thus, an increase in body mass without an absolute change in oxygen uptake automatically results in seemingly lower cardiorespiratory fitness. Therefore, cardiorespiratory fitness may seem low in individuals with overweight or obesity, even if the absolute oxygen uptake capacity is high. However, in a functional sense, cardiorespiratory fitness scaled to body mass describes physical performance well, as one has to bear the body mass during everyday activities. That said, the trends in cardiorespiratory fitness do not seem to be only a consequence of increased body mass because the absolute oxygen uptake has decreased similarly (Vaara et al., 2020), and also muscular fitness has declined at least in Finland (Puolustusvoimat, 2023). Additionally, the increasing physical inactivity (Guthold et al., 2018) would strongly suggest that the decline in cardiorespiratory fitness is indeed a consequence of lower oxygen uptake capacity.

On a public health perspective, the declining cardiorespiratory fitness is concerning. As poorer fitness associates with poorer health and lower physical functioning (Hemmingsson et al., 2022; Nuuttila et al., 2025), it also associates with more sickness absence days and lower work ability (Kolu et al., 2022). All of this leads to high economic burden and decreased quality of life (Chaput et al., 2023; Flesaker et al., 2021).

2.6.1.1 Measurement of cardiorespiratory fitness

Cardiorespiratory fitness can be estimated and measured using several methods. Overall, the methods can be divided into non-exercise methods and exercise testing which can be field-based or laboratory-based.

As the name suggests, non-exercise methods estimate cardiorespiratory fitness without actual exercise testing based on resting heart rate and varying demographic and health markers (Sloan et al., 2022). These methods may be best suited for population-level research when resources are limited but their application on individuals is limited.

Field tests for cardiorespiratory fitness include 12-minute running test (Cooper's test), 6-minute or 2 km walking test, 20 m shuttle run, and step tests (Cuenca-Garcia et al., 2022). Of the field tests, the maximal tests, such as the 20 m shuttle run or the 12-minute running test, seem to be most reliable for younger individuals, whereas the submaximal tests, such as the 6-minute walking or step tests, may be better suited for older adults and individuals with difficulties in performing maximal exercise like running (Cuenca-Garcia et al., 2022).

Most common laboratory-based cardiorespiratory fitness tests include maximal and submaximal bicycle ergometer and treadmill tests. Different testing protocols exist, but generally heart rate and preferrably respiratory gas exchange are measured while the external load (e.g., bicycle ergometer's resistance or treadmill speed or inclination) is gradually increased until exhaustion, a medical reason for termination (e.g., chest pain), or once a pre-determined submaximal level is achieved. Then, either by extrapolating from the achieved values in submaximal tests or judging by the measured maximal heart rate or respiratory gas exchange, maximal cardiorespiratory fitness is determined.

VO_2max is defined as plateau in oxygen uptake despite an increasing workload (Poole & Jones, 2017). However, in some cases this criterion is not achieved and secondary criteria are used to define VO_2max. These include heart rate that is ≤10 beats/minute from age-predicted maximum, blood lactate concentration of ≥8 mmol/l, or respiratory exchange ratio of >1.0–1.15 (Poole & Jones, 2017). Of note, to validate an individual's true VO_2max, the exercise testing should be performed twice: once with a graded protocol to achieve an estimate of VO_2max and then with a supramaximal (e.g., 10% above the achieved maximum) test to validate the plateau in oxygen uptake (Poole & Jones, 2017). If only a single test is performed, the result is sometimes called VO_2peak, indicating only the peak oxygen uptake achieved during a test (Poole & Jones, 2017). However, a meta-analysis of 54 studies points out that the difference between the initial incremental test and the validation test is not statistically significant ($p=0.15$) and only 0.85%, which is less than the measurement error of 2–3% (Costa et al., 2021). Therefore, while the validation does increase confidence in the VO_2max estimate, it may not be a requisite for establishing maximal cardiorespiratory fitness.

2.6.1.2 Physical activity behavior and cardiorespiratory fitness

Physical exercise training is the way to improve cardiorespiratory fitness in most individuals. This has been proven in numerous studies across different age groups and the improvement in cardiorespiratory fitness is dose-dependent (Huang et al., 2016; Lin et al., 2015). In addition to structured exercise training, habitual accelerometer-measured PA associates with cardiorespiratory fitness (Nayor et al., 2021). Thus, increasing PA and exercise training are key in stopping the global decline in cardiorespiratory fitness.

Observationally, cardiorespiratory fitness also associates negatively with SB (Nayor et al., 2021; Silva et al., 2020). However, the effects of modifying (i.e., reducing) SB on cardiorespiratory fitness remain scarcely studied. A three-year randomized controlled trial observed a 2.6 ml/min/kg increase in the intervention group, and subsequent *post hoc* analyses of the same study showed an inverse dose-response relationship between the changes in SB and cardiorespiratory fitness (Balducci et al., 2019, 2022). However, this SB-reduction study also promoted increasing MVPA although most of the SB was replaced by LPA (Balducci et al., 2022). A recent meta-analysis of randomized controlled trials on the effects of reducing SB on cardiorespiratory fitness observed a borderline significant improvement in cardiorespiratory fitness in studies that focused only on SB reduction (mean difference 2.18 [95% CI 0.01. 4.36] ml/min/kg, p=0.05) (Prince et al., 2024). The authors concluded that the evidence is very low certainty and more high quality evidence is needed (Prince et al., 2024).

2.7 Cardiovascular health

2.7.1 High blood pressure

Hypertension, or high arterial BP, is defined as resting office BP higher than 140 mmHg systolic and/or higher than 90 mmHg diastolic, according to the European Society of Cardiology/European Society of Hypertension (ESC/ESH) 2018 guidelines (Williams et al., 2018). The Finnish Current Care Guidelines are based on the ESC/ESH 2018 guidelines (Working group appointed by the Finnish Medical Society Duodecim, the Finnish Hypertension Society, 2020). However, the threshold for hypertension diagnosis is based on a BP level at which the benefits of treatment outweigh the risks, according to the ESC/ESH guidelines (Williams et al., 2018), although the risk of cardiovascular disease may increase already below the threshold. Indeed, evidence suggests that BP lowering may be beneficial for preventing cardiovascular disease regardless of baseline BP – that is, even in individuals with optimal BP (Rahimi et al., 2021). The ESC/EHS guidelines define normal BP as 120–129/80–84 mmHg (systolic/diastolic) and lower than that is considered optimal (Williams et al., 2018). These classifications remained unchanged in the ESH 2023 guidelines (Mancia et al., 2023). However, the definitions are not unequivocally accepted. The ESC/ESH guidelines differ from the American College of Cardiology/American Heart Association (ACC/AHA) 2017 guidelines, which define normal BP as <120/80 mmHg and hypertension as ≥130/80 mmHg (Whelton et al., 2018). Several reasons for the differences exist, such as differences in the health care systems and different target populations (Whelton et al., 2022). Additionally, the ACC/AHA guidelines place more emphasis on the SPRINT trial, which showed that intensive BP control (i.e., target systolic BP <120 mmHg) resulted in less cardiovascular events than standard BP control (i.e., target systolic BP <140 mmHg) (The SPRINT Research Group, 2015; Whelton et al., 2022). However, on a mean population level any reduction in BP could be seen beneficial, as the risk for cardiovascular disease increases linearly with higher BP, at least in values above 110/70 mmHg (Zheng et al., 2022). Nevertheless, to my best knowledge, a minimal clinically important difference for BP does not exist, and the guidelines recommend treating BP below a set target (i.e., <140/90 mmHg for all, and <130/80 mmHg if the treatment is well tolerated) (Williams et al., 2018).

Hypertension affects globally over 30% of the adult population (Zhou et al., 2021). Over the last three decades, the number of adults with hypertension has doubled, whilst the percentage of adults with hypertension has remained stable due to a decreasing prevalence in high-income countries and an increasing prevalence in middle- and low-income countries (Zhou et al., 2021). In Finland, the latest Healthy Finland Survey 2023 showed a hypertension prevalence of 52 and 46% among adult men and women, respectively (Laatikainen et al., 2023).

Hypertension is considered as the leading non-environmental risk factor for global disease burden (Brauer et al., 2024). Numerous studies have shown that high BP causes cardiovascular diseases and deaths, and BP lowering consistently lowers their risk following a dose-response relationship, that is, lower BP leads to lower disease and mortality risk (Baffour et al., 2023; Ettehad et al., 2016; Rahimi et al., 2021; Rapsomaniki et al., 2014; The SPRINT Research Group, 2015).

Whilst hypertension itself is nearly always symptomless, it can cause subclinical cardiovascular dysfunction before major cardiovascular disease, such as myocardial infarction or stroke. In newly diagnosed patients with hypertension and no co-morbidities, arterial stiffness is already higher than in normotensive individuals (Murray et al., 2022). Additionally, the left ventricle (LV) of the heart hypertrophies as a compensatory mechanism to minimize wall stress (Drazner, 2011), and the LV hypertrophy begins already at high-normal levels (i.e., systolic BP 124 mmHg) (Cuspidi et al., 2019). Ultimately, LV hypertrophy may lead to clinical heart failure (Velagaleti et al., 2014).

Notably, BP is usually presented as two values, systolic and diastolic BP. The former represents the BP in the arteries during cardiac systole and the latter represents the arterial BP during diastole. Large longitudinal studies suggest that both systolic and diastolic BPs associate with adverse cardiovascular health (Flint et al., 2019; Kanegae et al., 2017).

2.7.1.1 Measurement of blood pressure

BP may be measured in several ways and each of them have their own strengths, limitations, and interpretations. The only direct method to measure arterial BP is invasive intra-arterial measurement (e.g., using a radial artery catheter), which in practice is limited to hospital and laboratory use. Therefore, BP is most often measured indirectly from the brachial artery. During the non-invasive measurement, a pneumatic cuff is first inflated around the upper arm to occlude the brachial artery. Then, the pressure is gradually released and the recovery of brachial artery pulsation is observed. The observation is performed either by auscultation (e.g., using a stethoscope) or digital oscillometric technique, where the automated device senses the reflected pulse on the inflated cuff (James & Gerber, 2018). Automated oscillometric devices are commonly used for their convenience, but it should be noted that the oscillometric method does not directly observe systolic and diastolic pressures but estimates them based on mean arterial pressure (James & Gerber, 2018). The auscultatory method remains the gold standard (James & Gerber, 2018; Mancia et al., 2023) for BP measurement, yet validated automatic oscillometric devices are still preferred for clinical use as they minimize errors related to the observer's skills (Mancia et al., 2023; Williams et al., 2018).

Office BP is often higher than home BP. Thus, BP should be measured at home for the diagnosis of hypertension (Mancia et al., 2023; Williams et al., 2018). Either repeated home measurements (in the morning and the evening on 3–7 days) or 24-h ambulatory BP measurement should be performed to establish reliable information on BP (Mancia et al., 2023). High office BP with normal home BP readings is called white-coat hypertension and normal office BP with high home BP is called masked hypertension (Mancia et al., 2023).

In addition to resting or ambulatory BP measurements, BP during physical exercise can provide added prognostic value. For example, in some individuals office BP may be normal even though out-of-office BP is elevated. This is called masked hypertension, and exercise BP measurement may help in its detection (Schultz et al., 2011). Moreover, higher BP during submaximal exercise associates with higher LV mass index and arterial stiffness even when resting BP is normal (Oh et al., 2018; Sung et al., 2012), which argues for the measurement of BP during exercise in addition to resting BP. Additionally, measuring BP after exercising may be valuable, as higher BP during the recovery from maximal exercise associates with an increased risk for future myocardial infaction (Laukkanen et al., 2004).

In healthy individuals, systolic BP increases linearly with increasing workload by about 5 mmHg/MET to adapt for the increased perfusion needs in the skeletal muscles (Hedman et al., 2020). Diastolic BP remains relatively stable. High peak systolic BP during maximal exercise has been considered as a sign of poor prognosis, but in fact more recent evidence shows that low peak systolic BP associates with poor prognosis (Hedman et al., 2022). As the peak BP is closely related to the maximal exercise capacity (i.e., higher workload results in a higher BP), this finding is rational. That said, excessively high BP at submaximal workloads may be a sign of adversely high BP (Schultz et al., 2022).

2.7.1.2 Physical activity behavior and blood pressure

The current hypertension guidelines describe lifestyle changes as “fundamentally important” in preventing or delaying the diagnosis of hypertension and lowering BP in patients with established hypertension (Mancia et al., 2023; Whelton et al., 2018). In addition to weight management, dietary sodium restriction and potassium increase, moderation in alcohol consumption, and smoking cessation, the recommended lifestyle changes include regular PA. Indeed, solid meta-analytic evidence shows a dose-response relationship between higher PA and lower hypertension incidence (Huai et al., 2013; X. Liu et al., 2017). Furthermore, evidence from randomized controlled trials show that aerobic exercise effectively reduces 24-h ambulatory BP by 5/3 mmHg in adults with established hypertension (Saco-Ledo et al., 2020). Emerging evidence suggests that high SB may be associated with higher BP and an increased risk for hypertension (Lee & Wong, 2015; Li et al., 2024). Preliminary evidence from randomized controlled trials also suggest a small BP lowering effect of SB reduction in healthy adults (Hadgraft et al., 2021). However, this effect was not found in trials studying clinical populations (Nieste et al., 2021). Yet, a six-month randomized controlled trial in older adults reported a significant between-group difference of 3.5 mmHg reduction in systolic BP in favor of the intervention group that reduced daily SB (Rosenberg et al., 2024). Moreover, short-term (i.e., 1-day) studies suggest that breaking up prolonged SB may acutely reduce BP (Dempsey et al., 2018), which, in theory, could improve arterial function and ultimately BP. Nevertheless, more long-term studies on the effects of SB reduction on BP are needed.

2.7.2 Cardiac dysfunction and heart failure

Heart failure refers to insufficient cardiac output which may be caused by impaired diastolic filling of the LV (heart failure with preserved ejection fraction, HFpEF), impaired LV ejection (heart failure with reduced ejection fraction, HFrEF), or a combination of these (heart failure with mildly reduced ejection fraction, HFmrEF). Heart failure itself is a clinical syndrome of symptoms, such as dyspnea, leg edema, and fatigue that are caused by varying pathologies, like coronary artery disease, genetic disease, or hypertension.

The European heart failure guidelines (2021) emphasize the presence of symptoms when diagnosing heart failure (McDonagh et al., 2021). Interestingly, the American guidelines (2022) highlight the role of risk factors in heart failure staging by classifying the sole presence of risk factors (e.g., hypertension, metabolic syndrome, or diabetes) as stage A of heart failure (at risk for heart failure) (Heidenreich et al., 2022). Additionally, stage B (pre-heart failure) is defined as no symptoms of heart failure but presence of adverse cardiac remodelling, such as LV hypertrophy or impaired diastolic function (Heidenreich et al., 2022). The clinical stages of heart failure (C–D) involve having current or previous heart failure symptoms (C) or advanved symptoms and hospitalizations regardless of proper treatment (D) (Heidenreich et al., 2022). The most recent Finnish guidelines from 2023 also recommend the A–D grading, similar to the American guidelines (Working group appointed by the Finnish Medical Society Duodecim, the Finnish Cardiac Society, 2023). While the staging and criteria for diagnosis vary across guidelines, the progressive nature of heart failure from preclinical to clinical disease should be appreciated.

Heart failure affects 1–3% of adults worldwide and its prevalence increases strongly with age (Savarese et al., 2023). Therefore, the number of individuals with heart failure (especially HFpEF) is constantly increasing with the aging population despite the slightly decreasing incidence (i.e., the proportion of population who get the disease in a year) (Savarese et al., 2023). This, in turn, leads to increased economic burden of heart failure due to an increased need for health care (Huusko et al., 2019; Savarese et al., 2023). For example, a Swedish study estimated that the average health care related costs in the first year after heart failure diagnosis was almost 13 000 €/patient/year (Boman et al., 2021). Additionally, adults with heart failure report significant levels of disability (García-Olmos et al., 2019). Furthermore, 49% of healthy 58 year-olds progress to preclinical heart failure during a 4-year follow-up (Young et al., 2022), and within four years, over one-third of individuals with stage A heart failure progress to stage B, and 6 % at stage B progress to clinical heart failure (i.e., stage C or D). Taken together, effective strategies for the prevention of heart failure are crucial.

2.7.2.1 Measurement of cardiac structure and function

Besides risk factors and symptoms, echocardiography is a valuable tool in monitoring cardiac structure and function in preclinical (stages A and B according to the American and Finnish guidelines) and clinical (stages C and D) heart failure. The relevant echocardiographic measurements for this thesis are presented in **Table 1**. Common measures obtained by transthoracic echocardiography include LV posterior wall and septal thickness and LV end-diastolic and end-systolic diameter measured from the parasternal long axis M-mode images (Mitchell et al., 2019). LV mass can then be estimated using the end-diastolic diameter and wall thicknesses (Lang et al., 2015). Additionally, the parasternal M-mode imaging can be used to measure the left atrium and aortic root (Mitchell et al., 2019). While the parasternal long axis M-mode can be used to estimate LV volumes and ejection fraction they are not recommended as these measurements rely on assumptions of the LV geometry (Lang et al., 2015). Thus, biplane disk summation of the apical two- and four-chamber views is recommended for LV end-diastolic and end-systolic volume measurements (Lang et al., 2015; Mitchell et al., 2019). Using the LV volumes, stroke volume, ejection fraction and, with heart rate, the cardiac output can be calculated. To further evaluate LV systolic function, global longitudinal strain (GLS) may be measured from the apical two-, three-, and four-chamber views using speckle-tracking (Mitchell et al., 2019). LV GLS has been shown to predict adverse cardiac outcomes even when LV ejection fraction is normal (Verdonschot et al., 2021).

In addition to structural and systolic function measures, cardiac diastolic function can be assessed using Doppler echocardiography. From the apical four-chamber view, pulsed wave Doppler is used to measure transmitral flow, namely the peak early diastolic (E) and atrial contraction (A) flow velocities (Mitchell et al., 2019). The E/A ratio can be used as a marker of diastolic function. Moreover, tissue Doppler imaging from the same view is used to assess early mitral annulus (e') velocity, and the E/e' is commonly used as a measure of LV filling pressure (Mitchell et al., 2019).

It should be acknowledged that numerous other echocardiographic measures can be taken, for example measurements of the right ventricle and the cardiac valves (Mitchell et al., 2019). Furthermore, cardiac structure and function may be assessed by other imaging modalities, such as cardiac magnetic resonance imaging or computed tomography. However, their description is beyond the scope of this brief review as the empirical research in this thesis does not utilize such measurements. Additionally, echocardiography is the most widely used imaging modality for assessing cardiac structure and function.

Table 1. Overview of the echocardiographic measures used in this thesis.

Measure	View	Reference range*	Reference	May be clinically related with**	Other
LV posterior and septal wall thickness	PLAX, M-mode	M: posterior 6–12 mm, septum 6–12 mm; F: posterior 6–12 mm, septum 5–11 mm	(Harkness et al., 2020)	Hypertension, resistance training	
LV end-diastolic diameter	PLAX, M-mode	M: 42.0–58.4 mm; F: 37.8–52.2 mm	(Lang et al., 2015)	Hypertension, endurance training	
LV end-systolic diameter	PLAX, M-mode	M: 25.0–39.8 mm; F: 21.6–34.8 mm	(Lang et al., 2015)	Impaired contractility	
LV mass	PLAX, M-mode	M: 72–219 g (BSA-indexed 40–110 g/m^2); F: 51–173 g (33–99 g/m^2)	(Harkness et al., 2020)	Hypertension	Estimated from LV diameters and wall thicknesses
Left atrial diameter	PLAX	M: 30–40 mm; F: 27–38 mm	(Lang et al., 2015)	Impaired diastolic filling	Measurement of sole diameter is not recommended
Left atrial volume	A2CH and A4CH, biplane summation	<34 ml/m^2	(Lang et al., 2015)	Impaired diastolic filling	
LV end-diastolic volume	A2CH and A4CH, biplane summation	M: 62–150 ml; F: 46–106 ml	(Lang et al., 2015)	Endurance training	
LV end-systolic volume	A2CH and A4CH, biplane summation	M: 21–61 ml; F: 14–42 ml	(Lang et al., 2015)	Impaired contractility	May be used to calculate ejection fraction and stroke volume
LV GLS	A2CH, A3CH, and A4CH, speckle-tracking	Depends on vendor, usually –18 to –22%	(Galderisi et al., 2017)	Sensitive to subclinical LV systolic dysfunction	
Peak early diastolic transmitral flow velocity (E)	Pulsed-wave Doppler	Middle age: M: 0.47–1.04 m/s; F: 0.46–1.15 m/s	(Miyoshi et al., 2020)	Decreases with age	
Peak atrial contraction transmitral flow velocity (A)	Pulsed-wave Doppler	Middle age, E/A-ratio: M: 0.67–1.92; F: 0.66–2.08	(Miyoshi et al., 2020)	The E/A ratio is used as a sign of diastolic function; E/A-ratio decreases with age	
Early mitral annulus velocity (e')	Tissue Doppler	Middle age, lateral: M: 6.13–17.11 cm/s; F: 6.16–17.27 cm/s	(Miyoshi et al., 2020)	The E/e' ratio is used as a sign of LV filling pressure; E/e' ratio increases with age	May be measured either at the lateral or septal annulus

*Refers to a range of ±2 standard deviations from healthy population mean or 95% of healthy individuals. Exact values may differ between the reference populations. **Not an exhaustive list. LV = left ventricle, PLAX = parasternal long axis, M = male, F = female, BSA = body surface area, A2CH = apical two-chamber view, A3CH = apical three-chamber view, A4CH = apical four-chamber view, GLS = global longitudinal strain.

In addition to resting echocardiography, the imaging can also be performed during exercise testing. In HFpEF and diastolic dysfunction, the main interest during exercise echocardiography is often diastolic function (e.g., E/e’) and cardiac output (Guazzi et al., 2022). Moreover, LV myocardial strain rate (the percentage of global myocardial shortening, such as GLS) during exercise may be assessed as a measure of LV systolic function. Especially with the increasing heart rate during exercise, LV diastolic function is challenged which reflects to systolic function according to the Frank-Starling Law (i.e., the myocardial contraction is directly related to the preload) (Delicce & Makaryus, 2023). For example, peak exercise helps to reveal the impaired LV GLS in hypertensive compared to normotensive individuals (Qingfeng et al., 2022) making it a sensitive measure for subclinical cardiac dysfunction.

2.7.2.2 Physical activity behavior and cardiac structure and function

PA is beneficial in both preventing and treating cardiac dysfunction and heart failure (LaMonte & Eaton, 2021). In young adults, exercise training, among other changes, increases maximum cardiac output and LV diastolic function (Arbab-Zadeh et al., 2014). Similar endurance training-induced changes in cardiac output have been observed in healthy sedentary 71 year-olds as well, although the training did not reverse cardiac stiffening (Fujimoto et al., 2010). Importantly, the inability to reverse cardiac stiffening seems to be related to age, as similar exercise training does reverse cardiac stiffening in 53 year-olds who already have LV hypertrophy and elevated cardiac biomarkers (Hieda et al., 2021). Thus, while exercise training can be beneficial at all ages, the best cardioprotective effect is achieved by beginning the exercise already at a younger age. In addition to exercise training, higher total MVPA (which includes all domains of PA) associates with higher LV mass index and left atrial volume (Grönlund et al., 2024).

A few studies have investigated the association between SB and cardiac structure and function (Ashraf et al., 2023; Berdy et al., 2021; Gibbs et al., 2014; Ryu et al., 2018; Thangada et al., 2021). A summary of the studies is presented in **Table 2**. Only two of the five studies utilized accelerometers in SB quantification (Berdy et al., 2021; Thangada et al., 2021). The most consistent finding in these studies is the low number of statistically significant associations between SB and cardiac structure or function. Of the significant associations, LV mass index is positively associated with SB in two of the three studies investigating it (Berdy et al., 2021; Gibbs et al., 2014; Thangada et al., 2021). However, other cardiovascular disease risk factors, such as BMI and diabetes, smoking, or cholesterol, may explain the observed association as it turned non-significant in the fully adjusted models (Berdy et al., 2021; Gibbs et al., 2014). Yet, observational studies have found an increased risk for cardiovascular disease with high SB (Biswas et al., 2015; Jingjie et al., 2022) and SB reduction interventions have caused beneficial changes in risk factors for cardiac disease (Hadgraft et al., 2021; Nieste et al., 2021), which warrants further research into SB and cardiac structure and function.

Table 2. Summary of the studies on the association between sedentary behavior, physical activity, and cardiac structure or function in adults.

Author and year	Sample size	Mean age, years	SB/PA measure	Associations with SB	Associations with PA	Notes
(Ashraf et al., 2023)	228	53	Questionnaire, IPAQ	↔ Diastolic dysfunction	↓ E/e', LA volume index, pulmonary artery pressure, prevalence of diastolic dysfunction	89% had diastolic dysfunction
(Berdy et al., 2021)	1206	56	1 wk accelerometry	↑[A] LV mass index ↑[B] E/e', GLS* ↓[B] stroke volume	↑ LA volume index ↓ global circumferential strain*	A: Risk-factor adjusted model NS B: Observed only in a healthy subpopulation
(Thangada et al., 2021)	1368	49	1 wk accelerometry	↔ LV structure or function	↑ stroke volume, LV mass index, LV end-diastolic volume index	PA associations only with vigorous, not moderate PA
(Ryu et al., 2018)	57449	40	Questionnaire, IPAQ	↔ LV relaxation	↓ LV impaired relaxation ↑ LV end diastolic-volume, LV mass index, LA diameter	SB association only analyzed for prevalence of LV impaired relaxation
(Gibbs et al., 2014)	2854	50	Questionnaire, sedentary screen time	↑ LV mass index[C], mass/volume-ratio[C]	–	C: NS after BMI adjustment, associations only in whites

↑ = positive association, ↓= negative association, ↔ = no association, SB = sedentary behavior, PA = physical activity, IPAQ = International physical activity questionnaire, LA = left atrium, LV = left ventricle, GLS = global longitudinal strain, NS = non-significant, BMI = body mass index. *GLS and global circumferential strain are negative values where a higher (more positive) value represents poorer cardiac function.

3 Aims

As addressed in the previous chapters, the current research on the effects of SB on cardiovascular system's health has several limitations. Whilst observational studies suggest that SB would be detrimental to cardiovascular health, interventional evidence remains limited on the actual effects on the structure and function of the cardiovascular system. Studies using detailed cardiovascular measurements, such as imaging and exercise measurements are scarce. Furthermore, previous studies have often utilized self-reports for SB quantification, and when accelerometry has been used, the measurement has often lasted only one week at most.

This thesis investigates the role of SB in the prevention and treatment of cardiovascular risk factors and diseases. The aims of this thesis are to investigate whether a six-month intervention aimed at reducing daily SB by 1 h affects

1. cardiorespiratory fitness (Study I),
2. BP at rest or during graded maximal exercise test, or during recovery from maximal exercise (Study II), and
3. cardiac remodeling and LV function at rest and during exercise testing in adults with metabolic syndrome and physical inactivity (Study III).

4 Materials and methods

This study consists of secondary outcomes of a two-armed randomized controlled trial (named EXSIT), whose main objective was to investigate the effects of SB reduction intervention on whole-body insulin sensitivity (Sjöros et al., 2023). The study was conducted at the Turku PET Centre (Turku, Finland) between April 2017 and March 2020. It was approved by the Ethics Committee of the Hospital District of Southwest Finland (16/1801/2017) and pre-registered at Clinicaltrials.gov (NCT03101228, 05/04/2017). All participants gave their written informed consent before entering the study and the study was conducted according to the Declaration of Helsinki.

The EXSIT study consists of a four-week screening period during which the participants wore accelerometers to determine baseline SB and PA. The baseline measurements (anthropometry, exercise test, blood pressure, and echocardiography) were taken after the screening but before the six-month intervention period was commenced. The same measurements were repeated after the intervention. The participants were advised to take their medications as usual throughout the study and before all examinations.

The original articles (studies I–III) of this thesis report the intervention effects on various outcomes. Therefore, the shared methods for participants, accelerometry, intervention, and anthropometrics are presented first. The article specific methods are then described in a logical (I to III) order.

4.1 Participants

Participants for the EXSIT study were recruited from the region of Southwest Finland using bulletin board leaflets, newspaper advertisements, and a recruitment announcement on the University of Turku website. Inclusion criteria to the screening were

- Age 40–65 years
- BMI 25–40 kg/m^2

- Self-reported physical inactivity (less than 120 min/week of moderate-intensity PA based on the initial interview)
- Self-reported high SB (sitting for majority of the day).

Exclusion criteria were

- Medically treated diabetes
- History of cardiac events
- Resting systolic BP ≥160 and/or diastolic BP ≥100 mmHg
- Abundant consumption of alcohol (exceeding the Finnish national guidelines: men >23 units/week, women >12 units/week)
- Use of tobacco products or narcotics
- Diagnosed depression or bipolar disorder
- Inability to understand written Finnish
- Previous significant exposure to ionizing radiation (due to the positron emission tomography that was performed in this study; reported elsewhere (Sjöros et al., 2023))
- Any condition that could be detrimental to the study procedures or participant.

The volunteers that were eligible based on the criteria above, were interviewed on-site and their BP, waist circumference, height and weight were measured. These participants received accelerometers for four weeks to measure habitual PA and SB. During the four weeks, the participants were instructed to visit a laboratory of the Turku University Hospital at a convenient time for fasting blood samples.

To be included in the intervention period, the participants had to fulfil the additional inclusion criteria which were:

- Metabolic syndrome according to the consensus statement by Alberti et al., 2009 (as described in chapter 2.5 of this thesis). However, individuals with diagnosed diabetes or fasting blood glucose ≥7 mmol/l were excluded.
- Measured SB >10 h/day or >60% of accelerometer wear time during the four-week screening.

4.2 Accelerometry

During the screening period of the EXSIT study, all participants received a hip-worn triaxial accelerometer (UKK AM30, UKK Terveyspalvelut Oy, Tampere, Finland) to be worn for four consequtive weeks during normal living. The device was worn on the right hip using an elastic belt during waking hours except for when the device could be exposed to water. The participants were instructed to maintain normal PA and SB habits during the screening measurement.

During the intervention, all participants were given a triaxial accelerometer (Movesense, Suunto, Vantaa, Finland, with an acceleration sensor LSM6DS3, STmicroelectronics, Geneva, Switzerland) to be worn on the right hip during waking hours for the whole six-month intervention period (**Figure 3**). A hip-worn device was chosen instead of a thigh-worn one because the six-month measurement would not be feasible with a device that is taped to skin. The participants were instructed to wear the accelerometer throughout the intervention period during waking hours except for when the device could be exposed to water.

Wear time of 10–19 h/day and a minimum of seven days was considered valid, and non-wear time was defined as at least 30 minutes of less than 187.5 m*g* acceleration of each three axes. If the wear time exceeded 19 h in a day, it likely means that the participant slept wearing the device and thus, measurement exceeding 19 h/day was subtracted from measured SB.

Figure 3. Movesense accelerometer attached at the right hip. (Image: Jooa Norha)

The Movesense accelerometer recorded the acceleration data with 52 Hz sampling frequency, ±8 *g* range, and 4 m*g* resolution. The raw acceleration data was automatically stored in an online cloud server and processed at the UKK Institute later. The acceleration data was analyzed in six second epochs, and classified first into LPA (1.5–2.9 MET or MAD 22.5–91.5 m*g*), moderate-intensity PA (3.0–5.9 MET or MAD 91.5–414.5 m*g*), and vigorous-intensity PA (≥6.0 MET or MAD ≥414.5 m*g*) using the MAD algorithm (chapter 2.2.2.2) (Vähä-Ypyä et al., 2015). However, as the mean duration of vigorous-intensity PA was less than one minute per day, moderate and vigorous intensities were combined into MVPA. Moreover, daily step count was calculated using the step detection algorithm (Vähä-Ypyä et al., 2018).

When the detected PA intensity was <1.5 MET (<22.5 m*g*), the body posture was defined using the APE algorithm (chapter 2.2.2.2) (Vähä-Ypyä et al., 2018). If the accelerometer orientation (i.e., APE) was <11.6° from the reference vector, the posture was classified as standing, and if the orientation was ≥11.6° from the reference, the posture was classified as sitting or lying which were combined into SB. Additionally, the number of breaks in SB were recognized by detecting a clear vertical acceleration and subsequent standing or ≥1.5 MET activity after at least a one-minute moving average SB period (Vähä-Ypyä et al., 2018).

4.3 Intervention

After screening, the eligible volunteers (n=64) were randomized into the intervention (n=33) and control (n=31) groups. The random permuted block randomization was performed by a statistician in a 1:1 ratio using block size of 44. This block size was chosen because a subsample of 44 participants were further included in more detailed imaging, the results of which are reported elsewhere (Sjöros et al., 2023). The randomization was performed separately for men and women in SAS (version 9.4 for Windows). The group allocation for each participant was contained within a sealed envelope until all baseline measurements were performed. Due to the nature of the behavioral intervention, it was not possible to blind the participants to the group allocation.

In the intervention group, the aim was to reduce daily SB by 1 h for six months. The one-hour reduction was calculated from the individual mean during the screening measurement. The 1 h reduced from SB was guided to be reallocated to standing, LPA, and MVPA based on individual preferences. The participants were advised to continue their usual physical exercise training habits. To best facilitate substituting SB by non-exercise activities, a maximum of 20 min/day was added to MVPA. Individually tailored ways of reducing SB were discussed during a one-hour counselling session with a physiotherapist. These included, for example, the use of standing desks, walking during phone calls, choosing the stairs instead of the elevator etc. In addition to the counselling session, the participants received monthly phone calls to ensure the function of the accelerometers and adherence to the intervention. Moreover, the participants visited the research center at the midpoint of the intervention.

The control group was advised to continue their usual PA behavior during the intervention. Their SB, standing, LPA, and MVPA goals were set equal to the individually measured durations during the screening period. Similar to the intervention group, the participants in the control group received monthly phone calls and visited the research center at the midpoint of the intervention period to ensure the function of the accelerometers. After the study, the control participants were also given a SB-reduction counselling session if they wanted.

All participants were told to wear the accelerometers during the whole intervention period. The accelerometers were connected to a mobile phone application (ExSed, UKK Terveyspalvelut Oy, Tampere, Finland; **Figure 4**) that enabled the participants to monitor their daily PA behavior in relation to the individual goals.

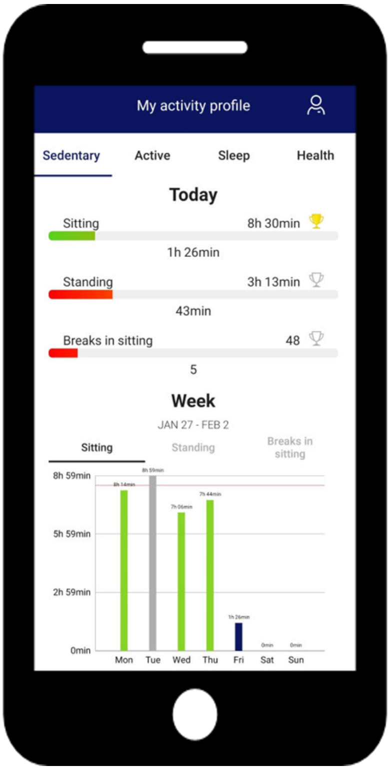


Figure 4. The ExSed application (screenshot from the application).

4.4 Anthropometrics

Body mass, fat free mass, and fat percentage were estimated using air displacement plethysmography (Bod Pod, COSMED USA Inc., Concord, CA, USA) after at least four hours of fasting (Fields et al., 2002). Waist circumference was measured midway between the lowest rib and the iliac crest using a measuring tape during normal exhalation. The waist measurement was repeated twice or until the same measurement was obtained twice. Height was measured using a wall-mounted stadiometer, and BMI was calculated as body mass (kg) / height $(m)^2$. Body surface area (BSA) was calculated according to the Du Bois formula: $0.007184 \times \text{body mass}^{0.425} \times \text{height}^{0.725}$ (Du Bois, 1916).

4.5 Exercise testing

Exercise testing was performed using a recumbent cycle ergometer (eBike EL Ergometer with Case v6.7; GE Medical Systems Inc., Milwaukee, WI, USA) and direct respiratory gas measurement (Vyntus CPX, CareFusion, Yorba Linda, CA, USA). The tests were performed between 8.30 am and 14.15 pm, with the same testing time before and after the intervention for each participant. The participants were advised to avoid strenuous PA as well as caffeine and alcohol intake for 24 h before the testing. A medical doctor supervised all exercise tests.

The exercise was initiated with an unloaded two-minute warm up after which the incremental testing started. The first load was 25 W and it was increased every three minutes by 25 W until volitional fatigue, medical reason to stop, or refusal to continue. The test was considered maximal if the respiratory exchange ratio (RER) exceeded 1.0, a plateau in oxygen uptake was achieved, or heart rate was within ±10 beats/min from the age-predicted maximum. VO_2max was determined from the respiratory gas measurements as the highest one-minute oxygen uptake. Additionally, maximal power output (Wmax) was calculated from the last completed workload plus the time at the incomplete workload: $Wmax = Wlast + (t / 180 \times 25)$, where Wlast is the last completed workload in watts and t is the number of seconds on the last, incompleted workload. Both the VO_2max and Wmax were reported as absolute ml/min and W, respectively, and scaled to whole body mass (kg_{BM}) and fat free mass (kg_{FFM}).

BP was measured by manual auscultation before the exercise test in a sitting and a lying position. During the testing, BP was measured after one minute on every workload. Finally, BP was measured one and three minutes after the test. BP at each absolute stage of the exercise test and at individually determined relative loads (i.e., percentage of max) was analyzed in addition to maximal BP and the slope of BP increase per unit of intensity (mmHg/MET).

Echocardiographic measurements of GLS were performed at each stage of the exercise test in a similar way to the resting GLS measurement (chapter 4.7).

4.6 Resting blood pressure

Resting BP was measured in a quiet room using a digital oscillometric sphygmomanometer (Apteq AE701f, Rossmax International Ltd, Taipei, Taiwan). As recommended by the 2021 European Society of Hypertension practice guidelines, an appropriately sized brachial cuff was used (Stergiou et al., 2021). The measurement was obtained after at least a 10-minute seated rest with the arm supported, mid upper arm at heart level. Two to three measurements were taken and the mean of these readings was used. The participants self-reported BP medication status (yes/no), and they were advised to take the medications as usual. Abstaining from strenuous PA as well as alcohol and caffeine intake for 24 h before the BP measurement was advised.

4.7 Resting echocardiography

Standard trans-thoracic echocardiographic variables were measured at rest before the exercise test (Vivid E9, GE Vingmed Ultrasound AS, Horten, Norway). One-lead electrocardiography was recorded for the cardiac measurements. LV end-diastolic diameter and LV wall thickness (posterior wall, septum), and LA diameter were measured at end-diastole. Relative wall thickness was calculated using the formula LV posterior wall thickness (mm) × 2 / LV end-diastolic diameter (mm). LV mass was estimated using the American Society of Echocardiography formula $0.8 \times 1.04 \times [(\text{septum thickness} + \text{LV end-diastolic diameter} + \text{posterior wall thickness})^3 - \text{LV end-diastolic diameter}^3] + 0.6$, where all diameters and thicknesses are in centimeters (Lang et al., 2015). LV mass was additionally indexed to BSA. LV end-diastolic and end-systolic volumes were calculated using the biplane disc summation method, and ejection fraction and cardiac output were calculated. GLS was measured using the speckle tracking method. LA end-systolic volume index was estimated using the biplane area-length method, and by indexing it to BSA.

For diastolic function assessment, pulsed wave Doppler images were obtained for E and A, and lateral e'. Septal e’ was missing from most participants because its measurement was not standard practice at Turku University Hospital clinical physiology department at the time. Therefore, only lateral e’ was used in this study. The ratios of E/A and E/e' were calculated.

The image analysis was performed offline using the Echopac plugin in ViewPoint (version 6.12, GE Healthcare, Solingen, Germany).

4.8 Statistical methods

The baseline data is presented as mean (standard deviation, SD) and the intervention data as model-based mean (95% confidence interval, CI) if not otherwise stated. The changes during the intervention period were analyzed using linear mixed models for repeated measurements with the intention-to-treat principle. The outcome of interest was used as the dependent variable and the independent variables included group (between-subject factor), time (within-subject factor), and group × time (interaction term). Further, sex was included as an independent variable to control for potential confounding by sex (Ji et al., 2024). In Study II, BP medication was further included as a covariate due to its potential as an effect modifier (i.e., independent effect on BP and persumably no effect on SB). When analyzing the changes in BP during the exercise test at submaximal loads, the exercise intensity (e.g., % of max or absolute watts) was included as an additional within-subject variable. Multiple comparisons were adjusted using the Tukey-Kramer method. Either compound symmetry or unstructured covariance structure was used, choosing the appropriate one based on the Akaike information criterion. The normal distribution of the residuals was judged visually.

Adherence to the intervention was assessed as the proportion of days with successful ≥1 h reduction in SB. Due to the skewed distribution, this was reported as median (quartile 1 (Q1), quartile 3 (Q3)). The between-group difference in successful SB reduction days was assessed using the Mann-Whitney U test in JMP Pro (version 17.0, SAS Institute Inc., Cary, NC, USA).

Statistical significance was set at $p<0.05$ (two-tailed). The linear models were analyzed in SAS (version 9.4, SAS Institute Inc., Cary, NC, USA). The sample size (n=64) was based on power calculations for the main outcome of the whole trial, which was whole-body insulin sensitivity (Sjöros et al., 2023). No *a priori* power calculations for any of the cardiovascular outcomes were performed. Moreover, I abstained from *post hoc* power calculations as these are not recommended (Dziak et al., 2020).

4.8.1 Additional analyses

Two kinds of additional analyses were conducted. The whole study sample was re-divided into two groups based on the actual measured changes in SB or PA in a *per protocol* fashion. The participants were grouped into less sedentary (SB reduction of ≥3%-points of accelerometer wear time, n=34) and continuously sedentary (SB reduction <3%-points or increase in SB, n=30) groups. Additionally, the participants were grouped according to the change in total PA (MVPA+LPA) into a more active (PA increase of ≥3%-points, n=33) and a less active (PA increase of <3 %-points or decrease in PA, n=31) group. The participants with missing accelerometer data (n=8) were included according to their original group allocation. The 3%-point threshold represents 27 min/day with 15 h/day of accelerometer measurement. This was chosen because it resulted in relatively even-sized groups and it represents a practical duration (i.e., half an hour). Linear mixed models identical to the main analyses were used using the *post hoc* group divisions.

Second, the changes in SB, standing, PA, and anthropometrics as well as the changes in the outcome variables were calculated among all participants, regardless of original group allocation. The correlations between the changes were analyzed using Pearson's correlation. Further, in Study II, the correlations were adjusted for the change in BMI using Pearson's partial correlation. The correlation analyses were performed in IBM SPSS Statistics (version 28.0, IBM, Armonk, NY, USA).

5 Results

Initially, 263 volunteers were assessed for eligibility to participate in the EXSIT study. Based on an initial interview, 151 volunteers underwent the four-week screening, after which 64 eligible participants were randomized into the intervention (n=33) and control (n=31) groups. The study flow chart is presented in **Figure 5**.

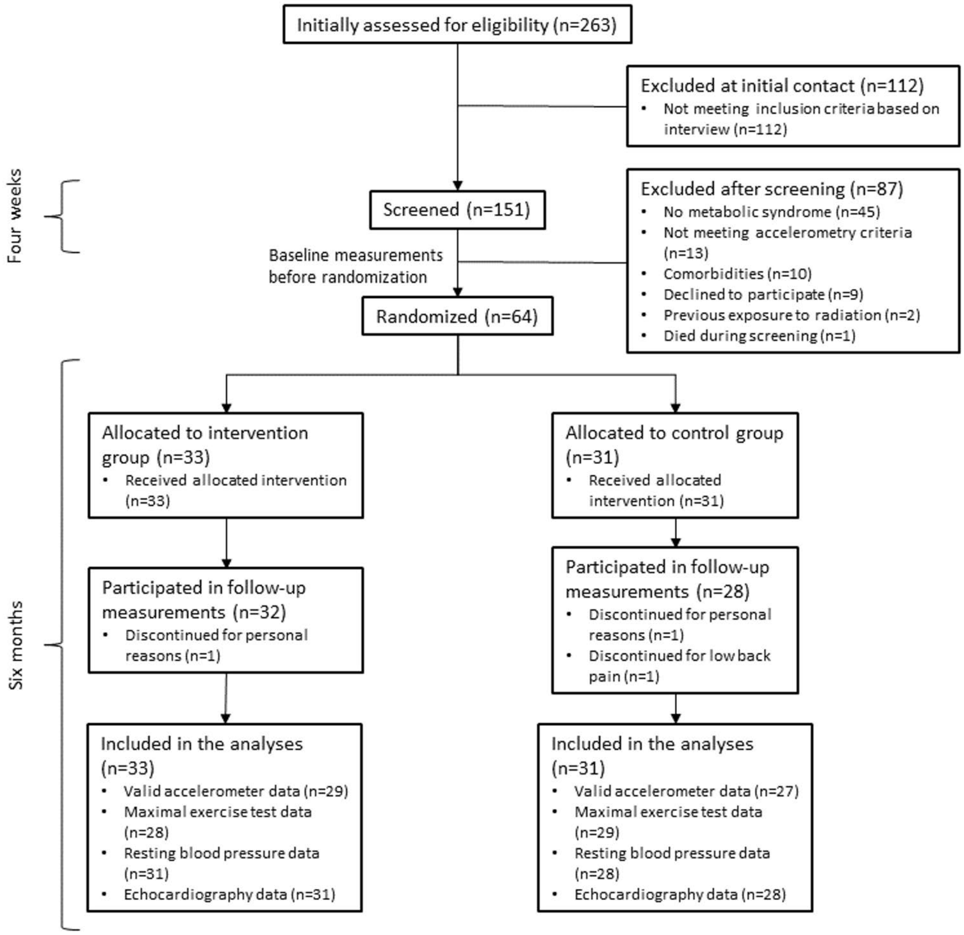


Figure 5. Study flow chart. Modified from Studies I–III.

5.1 Baseline characteristics

Fifty-eight percent of the participants were female. The mean age of the participants was 58 (SD 7) years and mean BMI was 31.6 (SD 4.3) kg/m^2. During the screening their mean SB was 10.0 (SD 1.0) h/day, standing 1.8 (SD 0.6) h/day, LPA 1.7 (SD 0.4) h/day, MVPA 1.0 (SD 0.3) h/day, and step count 5149 (SD 1825) steps/day. Mean accelerometer wear time during screening was 14.5 (SD 1.0) h/day and the number of valid accelerometry days during the screening was 26 (SD 4) days. The baseline characteristics in each group are presented in **Table 3**.

Table 3. Baseline characteristics of the participants in the intervention and control groups. Presented as mean (SD) if not otherwise stated.

	Intervention (n=33)	**Control (n=31)**
Sex, n of females (%)	20 (60.6)	17 (54.8)
Age, years	59.3 (6.01)	57.2 (7.5)
Body mass, kg	92.4 (16.6)	94.1 (15.8)
BMI, kg/m^2	31.5 (4.0)	31.7 (4.6)
Waist circumference, cm	111.1 (11.6)	110.7 (11.1)
Body fat, %	43.1 (8.0)	43.1 (8.0)
Fat free mass, kg	52.6 (11.9)	53.2 (9.8)
VO_2max, ml/min/kg$_{BM}$	22.65 (5.05)	22.76 (4.33)
VO_2max, ml/min/kg$_{FFM}$	40.02 (5.89)	39.91 (6.36)
Maximal power output, W	128 (33)	132 (30)
Sedentary behavior, h/day	10.02 (0.92)	10.06 (1.11)
Standing time, h/day	1.81 (0.61)	1.76 (0.57)
LPA, h/day	1.67 (0.40)	1.81 (0.48)
MVPA, h/day	0.96 (0.31)	0.97 (0.34)
Step count, n/day	5203 (1910)	5091 (1760)
Sedentary breaks, n/day	28 (8)	29 (8)

BMI = body mass index, VO_2max = maximal oxygen uptake, BM = body mass, FFM = fat free mass, LPA = light physical activity, MVPA = moderate-to-vigorous intensity physical activity. Modified from Studies I–III.

5.2 Accelerometry results of the intervention

The accelerometry results of this study have been originally published elsewhere (Sjöros et al., 2023), and thus will only be overviewed here. Four participants in each group had no valid accelerometry data during the intervention period due to technical issues. The intervention group reduced their SB by 40 min/day and increased their MVPA by 20 min/day, and the control group did not change their SB or MVPA (Sjöros et al., 2023). Daily step count increased in both groups but the change was significantly greater in the intervention group (increases of 3300 versus 1600 steps/day, p=0.001) (Sjöros et al., 2023). LPA increased by 10 min/day but the change was similar in both groups (Sjöros et al., 2023). Finally, standing time did not change statistically significantly (Sjöros et al., 2023).

The median percentage of days with successful ≥1 h reduction in SB was 39 (Q1 24, Q3 52) % in the intervention group and 27 (Q1 18, Q3 36) % in the control group (p=0.010).

5.3 Study I: Cardiorespiratory fitness

Baseline VO_2max was 22.65 (SD 5.05) and 22.76 (SD 4.33) $ml/min/kg_{BM}$ in the intervention and control groups, respectively. At baseline, maximal power output was 128 (SD 33) and 132 (SD 30) W in the intervention and control group, respectively. Maximal RER at baseline was 1.13 (SD 0.07) and 1.11 (SD 0.05) in the intervention and control group, respectively.

No statistically significant intervention effects on VO_2max (absolute or scaled to body mass or fat free mass) were observed. Maximal power output (absolute and scaled to body mass and fat free mass) increased among all participants (time $p<0.025$). However, the change in maximal power output was different between groups only when scaled to fat free mass (group × time p=0.036): power output remained unchanged in the control group and increased in the intervention group. Intervention results on VO_2max and maximal power output are presented in **Figure 6**.

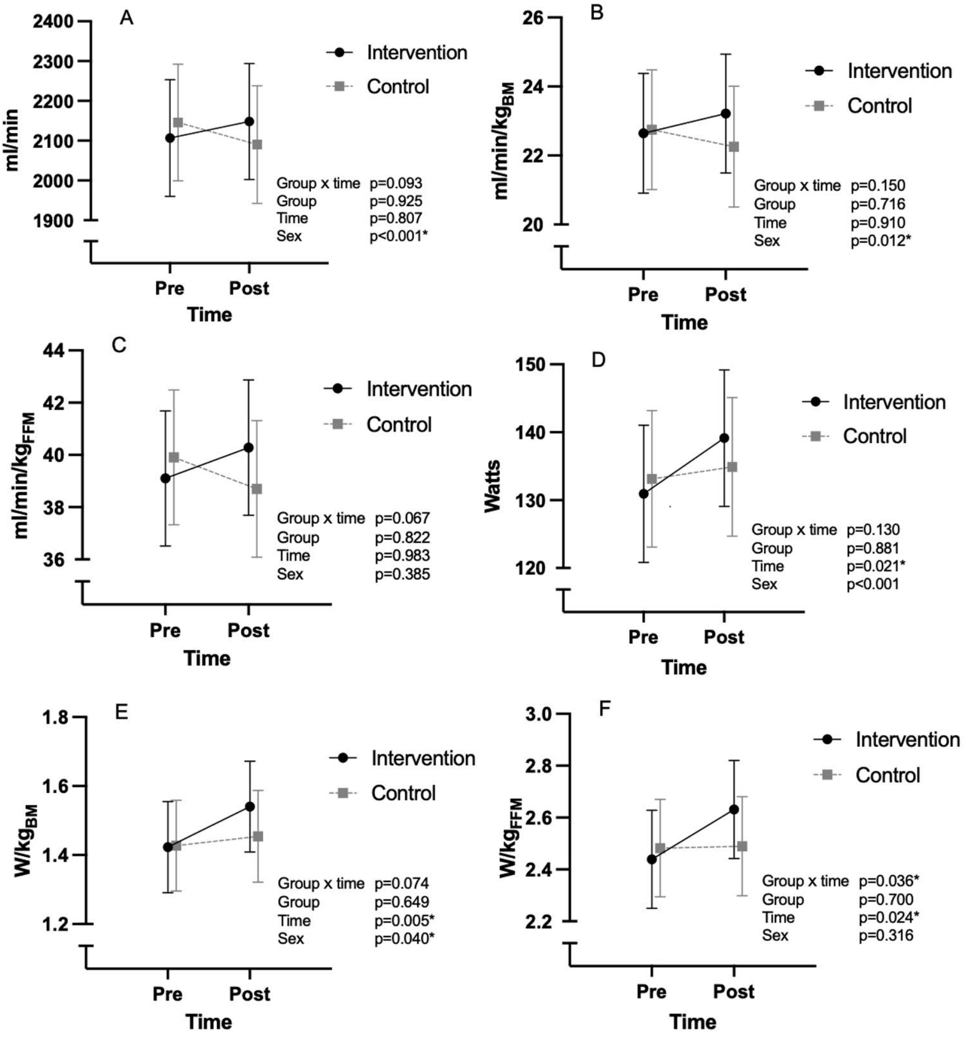


Figure 6. Maximal oxygen uptake (VO_2max) A) without scaling, B) scaled to body mass, C) scaled to fat-free mass, and maximal power output (watts) D) without scaling, E) scaled to body mass, and F) scaled to fat-free mass in the intervention and control groups before and after the six-month intervention. BM = body mass; FFM = fat-free mass. Values are model based means, and error bars denote 95% CIs. Solid line represents the intervention group and dashed line represents the control group. *Statistically significant ($p<0.05$). From Study I.

5.3.1 Additional analyses

The changes in the total daily step count correlated positively with the changes in VO_2max scaled to body mass (r=0.31, p=0.030) and to fat free mass (r=0.30, p=0.042). Furthermore, the change in standing time correlated negatively with all

VO_2max measures (r = −0.33 to −0.40, $p<0.05$ for all). The correlation results are presented in **Table 4**.

Table 4. Pearson's correlation coefficients for changes (Δ) in cardiorespiratory fitness and accelerometry outcomes, which are presented as percentage of accelerometer wear time.

	Δ SB, %	**Δ Standing, %**	**Δ LPA, %**	**Δ MVPA, %**	**Δ Steps/day**	**Δ SB breaks/day**
Δ Maximal power output	0.00	-0.14	0.12	0.10	0.18	-0.02
Δ Wmax/kgBM	-0.03	-0.12	0.17	0.11	0.20	0.02
Δ Wmax/kgFFM	-0.05	-0.15	0.24	0.12	0.23	0.00
Δ VO_2max, ml/min	0.15	-0.40*	0.03	0.23	0.28	0.08
Δ VO_2max, ml/min/kgBM	0.08	-0.33*	0.09	0.24	0.31*	0.13
Δ VO_2max, ml/min/kgFFM	0.10	-0.40*	0.17	0.21	0.30*	0.10

SB = sedentary behavior, LPA = light physical activity, MVPA = moderate-to-vigorous intensity physical activity, VO_2max = maximal oxygen uptake, Wmax = maximal power output, BM = body mass, FFM = fat free mass. *p<0.05. From Study I.

5.4 Study II: Blood pressure

Of the 64 participants, 16 (49%) and 17 (55%) used BP medication in the intervention and control group, respectively. Three participants had a change in BP medication during the intervention period (one participant in the control group initiated candesartan treatment for migraine, one participant in the control group increased the dose of losartan, and one participant in the intervention group changed from amlodipine+valsartan to candesartan). The most common medication group was angiotensin receptor blockers (24/33 participants on BP medication).

At baseline, resting BP (systolic/diastolic) was 146/89 (SD 15/8) and 139/88 (SD 16/9) mmHg in the intervention and control group, respectively. Corresponding maximal BP for each group was 218/95 (SD 22/12) and 214/88 (SD 23/12) mmHg. Systolic BP recovery at one and three minutes after the exercise test was –11 (SD 15) and –48 (SD 21) mmHg in the intervention group, respectively, and –13 (SD 20) and –53 (SD 21) mmHg in the control group.

Resting systolic and diastolic BP decreased in both groups during the intervention period (time p=0.017 for systolic and 0.042 for diastolic) without differences between groups (group × time p>0.1 for both). No statistically significant changes in any other BP variables were observed. However, maximal diastolic BP and systolic BP throughout the graded exercise test were lower in the control group throughout the study (group p=0.030 and 0.027, respectively). The intervention results for resting and exercise BP are presented in **Figure 7** and **Figure 8**.

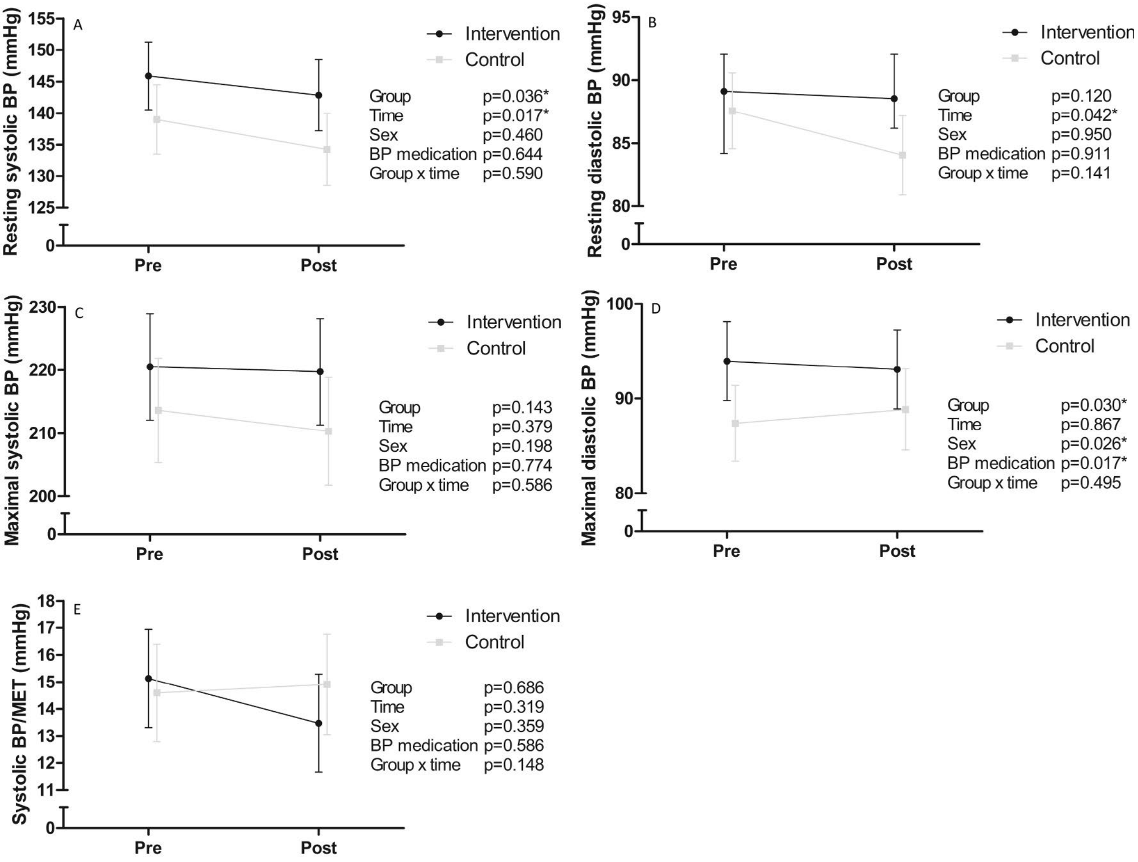
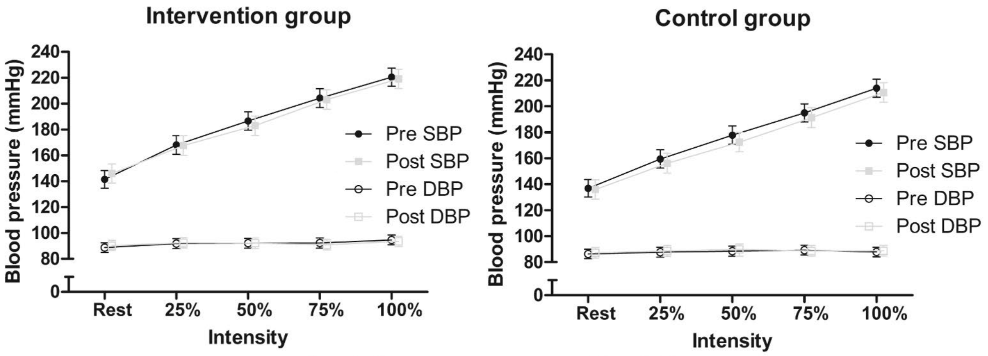


Figure 7. Intervention effects on A) systolic, B) diastolic, C) maximal systolic, D) maximal diastolic blood pressure, and E) systolic blood pressure/metabolic equivalent slope in the intervention (black dots) and control (grey squares) groups before (pre) and after (post) the intervention. Estimates are model-based least squares means and error bars represent 95% confidence intervals. BP = blood pressure, MET= metabolic equivalent of task. *p<0.05. From Study II



Systolic BP		Diastolic BP	
Group	p=0.027*	Group	p=0.068
Time	p=0.313	Time	p=0.794
Intensity	p<0.001*	Intensity	p=0.017*
Sex	p=0.599	Sex	p=0.119
BP medication	p=0.175	BP medication	p=0.141
Group x intensity x time	p=0.907	Group x intensity x time	p=0.911

Figure 8. Systolic and diastolic blood pressure at rest before the exercise test, and at 25%, 50%, 75%, and 100% of maximal power output in the intervention (left panel) and control (right panel) groups before (black circles) and after (grey squares) the intervention. Estimates are model-based least squares means and error bars represent 95% confidence intervals. SBP = systolic blood pressure, DBP = diastolic blood pressure, BP = blood pressure. *p<0.05. From Study II.

5.4.1 Additional analyses

When the main analyses were repeated with the participants re-divided into groups according to the measured change in time spent in SB, the results remained practically identical to the main results. However, when dividing the group based on the change in total PA, diastolic BP during submaximal intensity exercise tended to decrease in the more active group, whereas the change was smaller or even opposite in the less active group, albeit statistically significant changes at a specific intensity level were present for neither group (group × intensity × time p=0.025; all pairwise comparisons p>0.05). Furthermore, systolic BP during the exercise test trended towards a decrease in the more active group. However, the changes in systolic BP during the exercise test were not statistically significant (group × intensity × time p=0.075).

In the whole study group, the change in standing time associated positively with the change in systolic BP/MET-slope (r=0.29, p=0.043), and the association remained statistically significant when adjusting for the change in BMI (r=0.36, p=0.014). No other significant associations between changes in accelerometer outcomes and resting, maximal, or recovery BP were found (data not shown).

When investigating the associations between the changes in the accelerometer variables and BP at submaximal relative (% of maximal power output) and absolute (W) exercise intensities, the changes in LPA and MVPA associated with the changes in BP at relative intensities of 25 and 50% of maximal power output. Corresponding findings were present for absolute exercise intensities. Furthermore, the changes in daily steps, standing time, and SB correlated with the changes in some of the submaximal BPs. A heat map of the non-adjusted correlations is presented in **Figure 9**. When adjusting for the change in BMI, correlations remained similar to the non-adjusted correlations (data not shown).

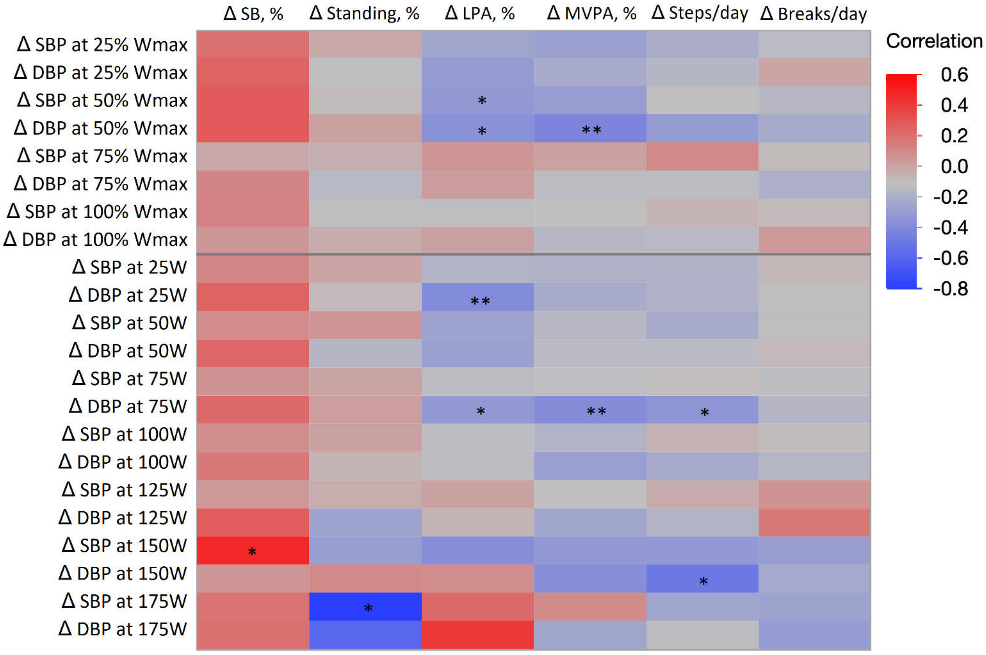


Figure 9. Heat map of Pearson's correlations of changes (Δ) in the whole study group in the accelerometry and blood pressure variables during exercise test at relative intensities (i.e., percentage of maximal power output) and at absolute workloads (W). Accelerometry variables were analyzed as proportions of daily accelerometer wear time. SBP = systolic blood pressure, DBP = diastolic blood pressure, % Wmax = percentage of maximal power output, SB = sedentary behaviour, LPA = light physical activity, MVPA = moderate-to-vigorous physical activity. *p<0.05, **p<0.01. From Study II.

5.5 Study III: Cardiac structure and function

At baseline, mean LV posterior wall thickness was 8.6 (SD 1.4) and 8.6 (SD 1.1) mm in the intervention and control group, respectively. In the corresponding groups, LV end-diastolic diameters were 52.9 (SD 5.5) and 51.8 (SD 4.1) mm and LV mass indices were 80.9 (SD 19.3) and 78.0 (SD 13.3) g/m^2, respectively. Participants in the intervention group had lateral E/e' of 7.6 (SD 1.9) and GLS of -18.0 (SD 2.9) %, while participants in the control group had the corresponding values of 7.4 (SD 1.7) and -18.9 (SD 2.2) %, respectively. All participants had LV ejection fraction of ≥55%.

No statistically significant changes in any variables related to cardiac structure, diastolic or systolic function at rest or during exercise were observed. The intervention results on cardiac parameters are presented in **Figure 10**, **Figure 11**, and **Table 5**.

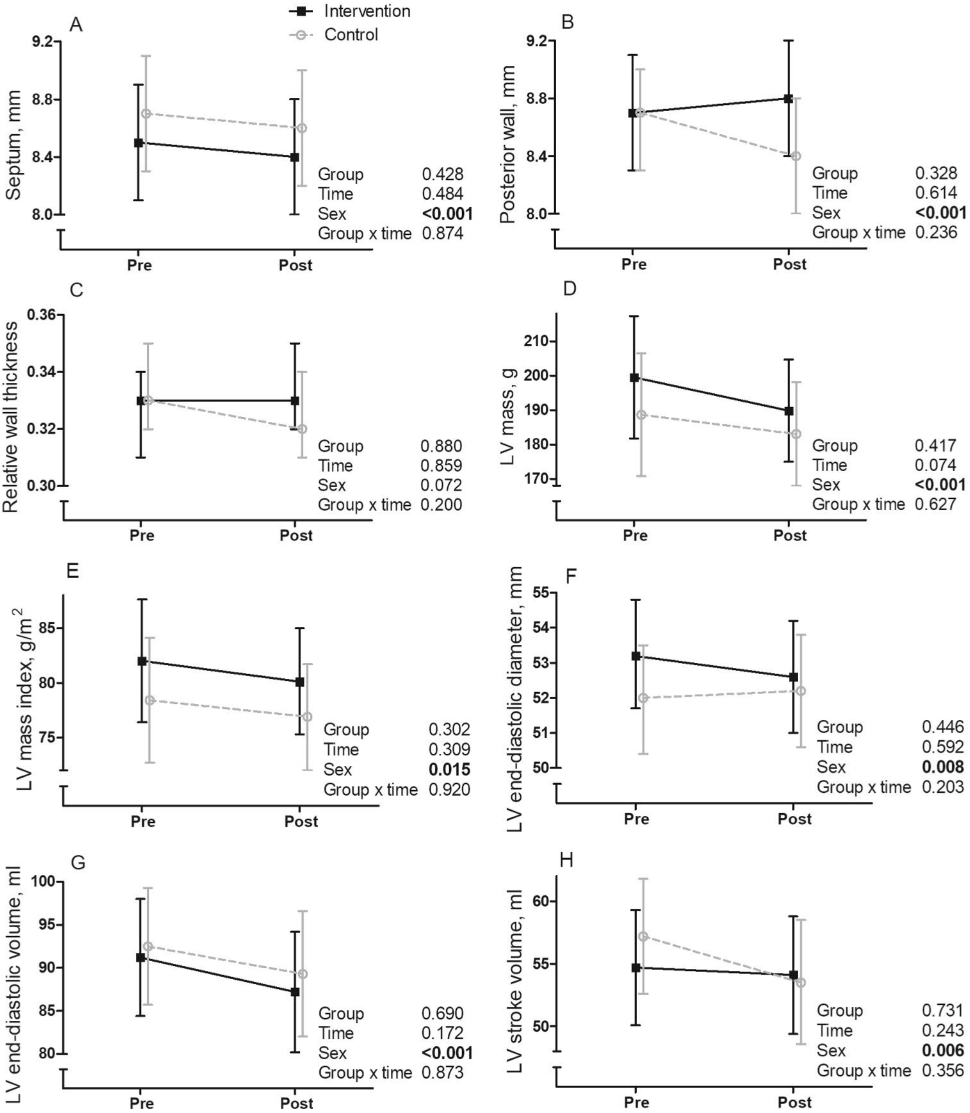


Figure 10. Intervention effects on A) septal thickness, B) posterior wall thickness, C) relative wall thickness, D) left ventricular (LV) mass, E) LV mass index, F) LV end-diastolic diameter, G) LV end-diastolic volume, and H) LV stroke volume. Black solid lines represent the intervention group and gray dotted lines represent the control group. Estimates are model-based least squares means and error bars represent 95% confidence intervals. From Study III.

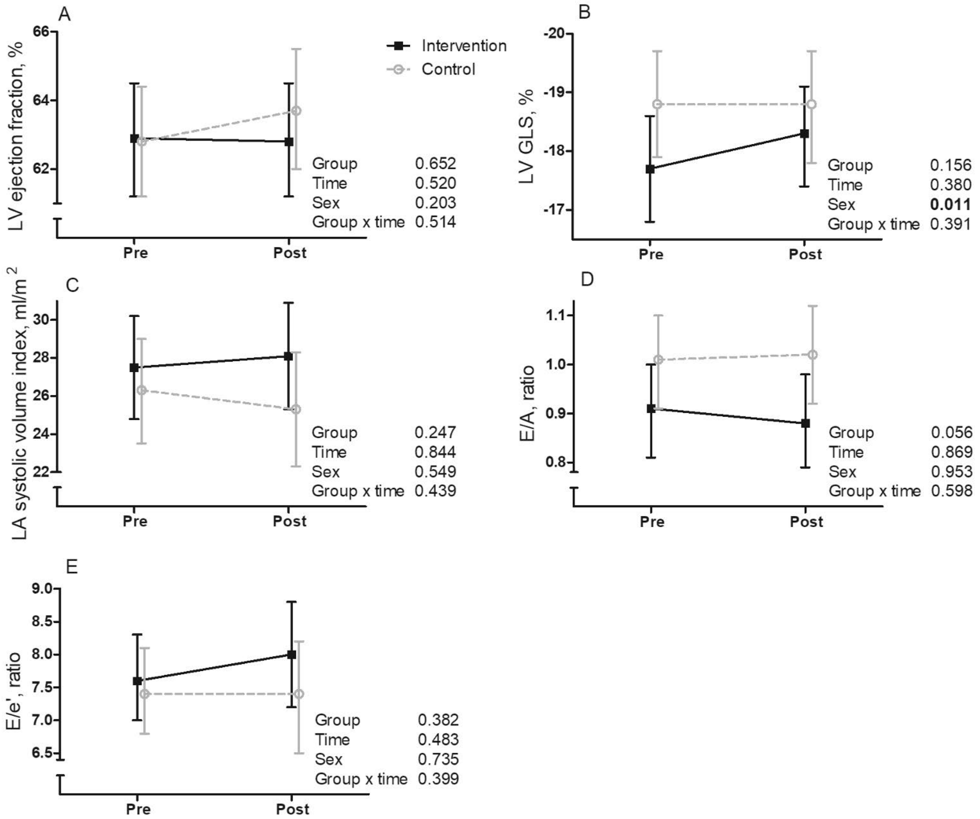


Figure 11. Intervention effects on A) left ventricular (LV) ejection fraction, B) LV global longitudinal strain, C) left atrial (LA) systolic volume index, D) E/A ratio, and E) E/e' ratio. Black solid lines represent the intervention group and gray dotted lines represent the control group. Estimates are model-based least squares means and error bars represent 95% confidence intervals. From Study III.

5.5.1 Additional analyses

When the main analyses were repeated with the participants re-divided into groups according to the measured change in SB, statistically significant group × time effects on LV end-diastolic diameter and LV mass index were observed (p=0.020 and 0.045, respectively; **Figure 12**). The LV end-diastolic diameter and mass index remained unchanged in the continuously sedentary group and decreased in the less sedentary group. Moreover, a similar, albeit not statistically significant, trend in LV mass was observed (group × time p=0.078). During the exercise test, GLS at 25, 100, and 125 W improved in the less sedentary participants compared to the continuously sedentary group (group × time p<0.05; **Table 5**)

The change in LPA correlated inversely with the change in LV mass index (r=-0.32, p=0.026) and the change in GLS at 75 W (r=-0.39, p=0.039). Additionally, the change in standing time correlated positively with the change in E/e'-ratio (r=0.28, p=0.048) and negatively with the change in GLS at 100 and 125 W (r=-0.56 and -0.54, p=0.008 and 0.048, respectively). Furthermore, the change in step count correlated negatively with the change in GLS at 25 and 50 W (r=-0.41 and -0.46, p=0.024 and 0.012, respectively). Finally, the changes in body adiposity markers (body fat percentage and body weight) correlated positively with the changes in posterior wall and septal thickness, relative wall thickness, and LV mass and mass index.

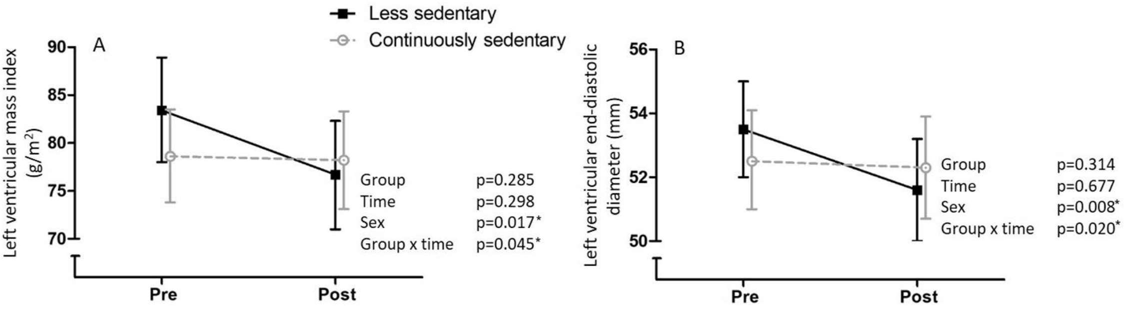


Figure 12. Additional analysis results on A) left ventricular mass index and B) left ventricular end-diastolic diameter. Black solid lines represent the participants who successfully reduced sedentary behavior by at least 3 %-points and gray dotted lines represent the participants who either increased their sedentary time or decreased it by less than 3%-points. Estimates are model-based least squares means and error bars represent 95% confidence intervals. *p<0.05. From Study III.

Table 5. Effects of reducing sedentary behavior on global longitudinal strain (GLS) during exercise testing according to the original group allocation and in the additional analysis groups. In the additional group results, the intervention group represents participants who successfully reduced sedentary behavior and control represents participants with no sedentary behavior reduction. Sex was significant (p<0.05) in all models except for the GLS 25 W and 125 W with the original group allocation, and 25 W, 100 W, and 125 W in the additional analysis. *p<0.05. Modified from Study III.

	Pre	Post	Pre	Post	Group × time p-value
	Intervention		Control		
GLS 25 W					
Original groups	-17.8 (-16.6, -19.1)	-19.5 (-18.2, -20.8)	-18.8 (-17.4, -20.1)	-18.8 (-17.3, -20.2)	0.131
n	25	21	19	17	
Additional groups	-17.6 (-16.4, -18.8)	-19.5 (-18.2, -20.8)	-19.1 (-17.7, -20.4)	-18.7 (-17.3, -20.1)	0.032*
n	25	21	19	17	
GLS 50 W					
Original groups	-17.7 (-16.4, -19.0)	-19.1 (-17.7, -20.6)	-18.9 (-17.2, -20.5)	-19.0 (-17.4, -20.6)	0.277
n	26	21	16	16	
Additional groups	-17.5 (-16.2, -18.9)	-19.1 (-17.7, -20.5)	-19.0 (-17.5, -20.6)	-19.0 (-17.4, -20.6)	0.151
n	25	21	17	16	
GLS 75 W					
Original groups	-19.0 (-17.7, -20.2)	-19.3 (-18.0, -20.5)	-18.5 (-17.1, -19.9)	-18.8 (-17.4, -20.2)	0.993
n	22	21	16	17	
Additional groups	-18.4 (-17.3, -19.6)	-19.0 (-17.8, -20.3)	-19.4 (-17.9, -20.9)	-19.1 (-17.7, -20.5)	0.419
n	24	21	14	17	
GLS 100 W					
Original groups	-17.8 (-16.3, -19.4)	-18.7 (-17.2, -20.2)	-18.6 (-17.1, -20.0)	-18.7 (-17.1, -20.3)	0.470
n	16	18	17	14	
Additional groups	-17.1 (-15.7, -18.5)	-18.8 (-17.4, -20.3)	-19.4 (-17.9, -20.9)	-18.8 (-17.3, -20.2)	0.015*
n	17	16	15	16	
GLS 125 W					
Original groups	-15.7 (-13.9, -17.4)	-17.8 (-16.0, -19.5)	-17.8 (-15.7, -20.0)	-18.0 (-15.6, -20.4)	0.172
n	15	15	10	7	
Additional groups	-15.0 (-13.5, -16.6)	-17.7 (-16.0, -19.4)	-19.1 (-17.1, -21.2)	-19.0 (-17.0, -20.9)	0.029*
n	16	12	9	10	

6 Discussion

In this thesis (Studies I–III), I present the effects of a six-month SB reducing intervention on cardiovascular health measures. The main finding of all three studies is that a six-month intervention aimed at reducing daily SB by 1 h without increasing physical exercise is not sufficient in improving cardiovascular health, as measured by cardiorespiratory fitness, blood pressure, and echocardiography, in physically inactive adults with metabolic syndrome. However, the additional analyses, regardless of original group allocation, suggest that successful SB reduction and an increase in PA may provide benefit for the cardiovascular system.

When interpreting the results of this study, it should be borne in mind that while the results are some of the first randomized controlled evidence on SB reduction and cardiovascular health, they are only generalizable to similar participants and interventions (e.g., aim of 1 h/day SB reduction with activity monitoring in adults with metabolic syndrome). Thus, this study provides novel evidence that SB reduction may not be sufficient at significantly improving cardiovascular health, but the study does not definitively rule out the possibility that other types of SB interventions (e.g., larger SB reduction, longer duration intervention, or among different populations) could be beneficial. That said, when one reduces SB the duration of other behaviors will increase and the behaviors replacing SB may have distinct health effects (Chastin et al., 2019; Mansoubi et al., 2014; Ross et al., 2024). Consequently, different SB reduction interventions may provide different health effects.

6.1 Cardiorespiratory fitness

In this study, the intervention planned for reducing daily SB did not affect cardiorespiratory fitness. Even though previous cross-sectional evidence suggests that SB associates with cardiorespiratory fitness (Silva et al., 2020), the interventional evidence is somewhat less convincing for causality between SB and cardiorespiratory fitness (Prince et al., 2024). While a recent meta-analysis reported that SB reduction interventions resulted in a statistically significant improvement in cardiorespiratory fitness (mean difference between intervention and control groups 2.18 [95% CI 0.01, 4.36] ml/min/kg_{BM}) (Prince et al., 2024), the finding was partly driven by a study where SB was not actually reduced, nor was cardiorespiratory fitness increased, but a between-group difference after the intervention was observed, affecting the meta-analysis results (Larisch et al., 2021). Furthermore, heterogeneity due to varying target populations in the included studies was present in the meta-analysis ($I^2 = 44\%$) (Prince et al., 2024), which limits the generalizability of the results.

However, in the additional analyses I did observe improved cardiorespiratory fitness when daily step count was increased. As all participants in this study increased their steps, it is possible that the increased step count diluted any between-group differences in cardiorespiratory fitness, because daily step count does positively associate with cardiorespiratory fitness (Nayor et al., 2021). Moreover, as cardiorespiratory fitness tended to improve in the intervention group and remain unchanged in the control group, the lack of statistically significant intervention effects may be partly due to inadequate study power. However, when maximal power output was scaled to fat free mass, the change between groups reached statistical significance, which is likely due to less confounding factors when body composition was taken into account.

6.2 Blood pressure

The intervention that aimed at reducing daily SB did not affect BP in any of the measured conditions. However, the additional analyses suggest that increasing habitual LPA, MVPA or a combination of them (as observed in the total PA-based group analyses) may lead to decreased BP during submaximal-intensity PA.

Interestingly, contrary to the present findings, a recent six-month randomized controlled trial of 283 older adults (mean age 69 years) found that the SB-reducing intervention group decreased their systolic BP by 3.5 mmHg more than the control group (Rosenberg et al., 2024). Moreover, the intervention group reduced SB by only 31 min/day, and most of it was replaced by standing. However, the participants in that study were ten years older than the participants in our study which may explain the differences in the results. On the contrary, a randomized controlled trial of 271 adults (mean age 45 years) reported similar results to the present study, whereby a 1.15 h/day SB reduction for three months did not influence office or ambulatory BP (Barone Gibbs et al., 2024).

All BP medications were advised to be taken as usual during the study and all possible modifications to medications were done as the participants' own physicians would recommend. Due to the heterogenous doses and medication groups, the BP medication was evaluated only as a dichotomous yes/no variable. Moreover, only one participant (in the control group) intiated BP medication during the intervention, and this was done for migraine prevention instead of hypertension. However, one participant in the control group increased their BP medication dose and one participant in the intervention group changed from dual therapy to monotherapy during the intervention period. In theory, these changes in the medications could have diluted any intervention effects. Yet, as most participants continued their medication unchanged, it is unlikely that the three participants with medication changes would have significantly affected the results.

Resting systolic and diastolic BP decreased slightly among all participants from baseline to postintervention (time $p<0.05$ for both). A plausible explanation for this could be the increase in step count in both groups (+3300 in the intervention group and +1600 in the control group), although the changes in step count did not correlate with the changes in resting BP. Interestingly, a meta-regression study calculated that a 1000-step increase per day would lead to approximately 2 mmHg decrease in systolic BP (Igarashi et al., 2018), which is in line with the observed mean decrease of 4 mmHg in systolic BP and mean increase of 2470 steps/day among all participants in this study. Another plausible explanation could be the familiarization to the study center at the end of the study, which could, speculatively, reduce anxiety during the BP measurement and consequently decrease BP. In addition, other unmeasured factors, such as sleep (Lo et al., 2018), may have influenced the results.

The finding from the additional analyses indicated that increased light-to-moderate intensity activity correlates with decreased BP at similar intensities during physical exercise testing. This suggests that even if resting BP does not change, the hemodynamic reactivity to PA may be reduced. Indeed, a study of 24 participants with chronic kidney disease suggests that individuals who are more physically active have a less steep slope in the increase of BP with increasing PA intensity during free living (Agarwal & Light, 2008). While this may be explained by better physical capacity in more active individuals, I saw this correlation also with relative intensities (i.e., 50% of maximum capacity). Moreover, BP during light-to-moderate intensity exercise associates with LV mass index and arterial stiffness regardless of resting BP (Oh et al., 2018; Sung et al., 2012). Therefore, an interesting perspective for future research would be to study the hemodynamic reactivity (i.e., the increment of BP increase with increasing PA intensity) and its relation to habitual PA and SB in individuals with metabolic syndrome.

6.3 Cardiac structure and function

No intervention effects on cardiac structure or function were observed in this study. However, in the additional analyses with group divisions according to the measured change in SB, I observed that participants with successful SB reduction had a decreased LV mass index and end-diastolic volume, as well as improved GLS during three of the five analyzed exercise intensities. Among all participants, increased LPA also associated with a decreased LV mass index suggesting that increasing LPA could have potential in the prevention of LV hypertrophy. However, it should be noted that only three participants (one female in the control group and one female and one male in the intervention group) could be classified as having LV hypertrophy.

Previous evidence on SB and cardiac structure and function is based entirely on cross-sectional and observational studies (Berdy et al., 2021; Gibbs et al., 2014; Thangada et al., 2021). The results have been somewhat inconclusive. However, SB seems to associate with higher LV mass (Berdy et al., 2021; Gibbs et al., 2014). Moreover, high SB associates with the risk of incident heart failure (Ajufo et al., 2024), and increased LV mass is a risk factor for heart failure (De Simone et al., 2008). Similar findings have also been reported previously in adolescents (Agbaje, 2023; Haapala et al., 2024). These findings, combined with the additional analysis finding from the present interventional study, would suggest that reducing SB could have the potential to prevent the LV mass increase that associates with an elevated risk for cardiac events (Hoang et al., 2015). However, further research is warranted to confirm the finding.

A possible explanation for the LV mass index decrease in those who successfully reduced SB in the additional analysis and the correlation between increased LPA and decreased LV mass index among all participants could come from Study II. There, in the additional analyses I observed that increased LPA correlated with lower BP during light-to-moderate intensity exercise. This is in line with the previous finding that lower BP at such exercise intensities associates with a lower LV mass index (Oh et al., 2018). This could be a consequence of lower afterload during daily PAs, as individuals who have lower BP at low-intensity exercise also tend to have lower arterial stiffness (Sung et al., 2012).

Remarkably, body size is an important factor to consider when analyzing cardiac parameters (Bello et al., 2016). However, BSA remained similar in both groups (group × time p=0.101 in the SB-based additional group analysis; data not shown) and the results did not markedly change when the analyses were adjusted for body mass (data not shown). Therefore, changes in body size do not seem to be responsible for the observed changes in LV size or function during exercise in the additional analyses. However, as body mass (–1.3 kg) and BMI (–0.4 kg/m^2) decreased slightly in the less sedentary group, it is possible that the improved body composition played an additional beneficial role along with the change in PA behavior.

6.4 Sedentary behavior reduction and cardiovascular health

Taken together, a six-month intervention that aims at reducing daily SB by 1 h did not influence the health of the cardiovascular system. This conclusion is also in line with other findings from the same intervention, where no main intervention effects on cardiometabolic risk factors were observed (e.g., whole body or skeletal muscle insulin sensitivity (Sjöros et al., 2023; Sjöros et al., 2023)). However, even though previous interventional studies focusing on SB reduction have reported beneficial changes in cardiovascular risk factors, the magnitude of the improvements has been notably small (Hadgraft et al., 2021; Nieste et al., 2021). Moreover, before this study, the intervention effects on the cardiovascular system's structure and function have been missing. Nevertheless, some limitations of the present study need to be addressed.

First, detecting small changes requires a large sample size. This study was powered for whole-body insulin sensitivity which required only 24 participants per group (Sjöros et al., 2023). However, a total of 64 participants were recruited to allow for possible dropouts and technical issues. Yet, this may not be sufficient for the present measures. Specifically, cardiorespiratory fitness seemed to trend towards an improvement in the intervention group compared to the control, and thus, a larger sample size may have changed the results. For BP measures, a study protocol for a SB reduction study stated that a total of 300 participants would be needed to detect significant differences in BP (Barone Gibbs et al., 2021). However, in this study no BP trends were observed and therefore the lack of intervention effects on BP may not be a sole sample size issue. For the cardiac measures, mostly no trends were observed, although, for example the changes in LV mass and GLS seemed to favor the intervention group slightly. Still, as pointed out by Wood et al., interpreting near-significant results as trends towards statistical significance is not without issues (Wood et al., 2014), which argues for more research with adequate sample sizes.

Second, it is possible that even if previous studies suggest that SB reduction could lead to improved cardiovascular risk profile, the changes in risk factors (e.g., waist circumference or BP) may precede any structural or functional changes within the cardiovascular system. Therefore, a six-month study could be too short for the structural and functional adaptations to occur.

Finally, the previously reported benefits of SB reduction have been notably small in magnitude (e.g., 0.6 kg reduction in body mass or 0.7 cm reduction in waist circumference) (Hadgraft et al., 2021). Even though the direction is favorable, it may not be clinically significant or large enough to induce structural or functional changes (Horn et al., 2022; Verweij et al., 2013). Moreover, the permanence of the benefits beyond the intervention's duration remains unknown.

Consequently, more intense PA with a possibly higher dose is needed to change the structure and function of the cardiovascular system. Even though the absolute volume of SB reduction is generally quite high when compared to, for example, the PA guidelines (e.g., an average SB reduction of 40 min every day in this study compared to the recommended moderate-intensity PA of 30 min five days per week), the intensity may play an important role. In fact, observational evidence suggests that PA intensity may be more important than volume for cardiovascular disease mortality reduction (Schwendinger et al., 2025).

The benefits of physical exercise training on cardiovascular health have been well documented (Isath et al., 2023), and my additional analyses further support the role of habitual PA in cardiovascular health. Notably, all participants in this study were self-reportedly physically inactive (as per the inclusion criteria) and no physical exercise training was encouraged. Therefore, it is reasonable to assume that the observed changes in measured PA were primarily non-exercise activities. The correlation analyses suggest that increased (non-exercise) PA and decreased SB correlates with, for example, improved cardiorespiratory fitness, BP and GLS during physical exercise, and LV mass index.

Importantly, the participants were advised to use accelerometers throughout the study to monitor daily PA behavior. Therefore, the measured changes in PA behavior should be considered more robust than if accelerometry was performed only for one week before and after the intervention. However, it is not possible to distinguish different domains of PA behavior (e.g., occupational, transportation, or leisure-time) using only accelerometers. Consequently, it is possible that some participants also started new PA habits that could be considered physical exercise training, like taking a walk. Moreover, the domain of the PA behavior may be significant for its health effects. For example, high occupational PA has been associated with an increased risk for cardiovascular events, which is opposite to the association between high leisure-time PA and lower risk for cardiovascular events (Holtermann et al., 2021). Future studies should therefore consider including diaries or other methods for assessing the domain for PA behaviors.

Interestingly, in the additional correlation analyses, an increase in standing time seemed to associate with some adverse changes in the cardiovascular measures (e.g., systolic BP/MET slope, VO_2max, and diastolic filling pressure). Two plausible mechanisms may explain this. First, the health responses to PA behavior may vary depending on the health-related outcome. For example, fasting fat oxidation or thigh muscle insulin sensitivity may be better with higher daily standing, as indicated by cross-sectional analyses (Garthwaite et al., 2023, 2024). Moreover, increasing standing in an interventional setting may improve fasting blood glucose and body adiposity (Saeidifard et al., 2020). However, the standing posture may be detrimental for the cardiovascular system, as it leads to lower limb blood pooling which causes increases in vascular tone and cardiac output. This, in turn, can lead to higher BP, as observed by the more unfavorable 24-h diastolic BP profile among individuals who spend more time standing, especially at work (Norha et al., 2024). Over time, this could lead to adverse changes in the cardiovascular system.

The second possible explanation for the seemingly unhealthy consequences of increased standing in this study relates to the reallocation of behaviors. If an individual replaces PA with standing, the increased standing would occur as harmful in the correlation analysis. However, this correlation would most likely be due to the decreased PA rather than the increased standing per se. This, however, remains speculative as no replacement modelling or compositional data analyses were performed. Yet, it seems plausible that standing could potentially decrease PA. For example, if an individual changes sitting for standing at work, they might feel physically fatigued after the workday and choose to rest instead of exercising.

In addition to the association between SB and detrimental health outcomes in previous research, another motivation for SB reduction besides health is that reducing SB might be more feasible or preferred than physical exercise by individuals who are physically inactive (Greenwood-Hickman et al., 2016). However, based on the results of the current study, the limited cardiovascular benefits should be acknowledged, especially if the motivation for reducing SB is health improvement. Yet, health improvement itself should be encouraged even if the way for it might be reducing SB, as some may prefer (Greenwood-Hickman et al., 2016). It is possible that achieving a positive behavior change empowers an individual to accumulate further beneficial health behaviors. Moreover, a SB-reducing intervention could be beneficial for some subjective outcomes, such as back pain (Norha et al., 2024) or perceived vitality (not published yet), as has been observed in the EXSIT study.

Key strengths of this study are the robust randomized controlled trial setting and the six-month intervention duration. Moreover, the use of accelerometers throughout the study, and the detailed cardiovascular measurements (graded maximal exercise test with respiratory gas exchange measurements, BP measurements at rest and during and after submaximal and maximal exercise, and echocardiography at rest and during graded exercise testing) allow for detailed assessment of the function and structure of the cardiovascular system.

On the other hand, all measurements may be prone to errors and biases. For example, individual factors, such as higher self-efficacy, being male, or higher body adiposity, can increase the odds of fulfilling only the secondary criteria (e.g., perceived exhaustion) instead of the oxygen uptake plateau criterion in the maximal cardiorespiratory fitness test (Magnan et al., 2013). Several factors, such as preceeding PA, water ingestion, measurement environment, clothing, and body posture, can cause errors of up to 33 mmHg in office BP measurements (Liu et al.,

2022) – although these factors were controlled for according to the guidelines in the present study (Stergiou et al., 2021). Assessing LV structure and function using echocardiography is convenient, especially during exercise testing, but the intraobserver variability for some measures may be notable. As an example, the intraobserver correlations between two-dimensional LV volumes are 0.89–0.94 but for LV ejection fraction the correlation is only 0.81, which can mean at highest almost 10% variability in LV measurements (Lyng Lindgren et al., 2022). In addition to adequate measure-specific (e.g., observer experience, environmental factors) actions, adequate sample sizes are needed in future studies to improve the precision of the estimates.

The intervention in this study relied mostly on the one-hour counselling session before the intervention period and self-monitoring of PA behavior during the intervention. Yet, previous evidence suggests that multicomponent interventions targeting the physical environment and the workplace could be most effective in reducing SB (Lam et al., 2022; Nieste et al., 2021). Nevertheless, the magnitude of SB reduction was remarkably similar to previous intervention studies (Chastin et al., 2021), which suggests that the intervention itself was as successful as previous SB-reducing interventions.

Notably, the participants in this study were at risk for cardiovascular diseases as they were physically inactive, overweight or obese and had metabolic syndrome. The rationale for choosing such a target population was that health improvements are more likely in at-risk individuals or individuals with a pre-existing disease than in healthy participants (Nyberg et al., 2025). However, as the participants in this study were volunteers, it is likely that the study sample overrepresents the individuals within the target population who are already most interested in their health. Therefore, generalizability to all individuals even within the inclusion criteria may be limited. Furthermore, socioeconomic status or occupation of the participants was not formally collected, which should be considered as a limitation.

6.5 Future research directions

This study can be used to improve the design of future randomized controlled trials on the cardiovascular effects of SB. First, adequate study power and sample size should be calculated based on the chosen cardiovascular outcomes, and the estimates from this study may serve as a basis for the calculations. Second, if a study aims to investigate the effect of SB independent of physical exercise training, the intervention should be clearly directed towards increasing non-exercise PA, unlike in many previous studies (Hadgraft et al., 2021). To accomplish and monitor this, I would recommend including a questionnaire or diary-based measure of PA domains in addition to the accelerometers. The inclusion of more qualitative data on the PA domain could help to differentiate work and leisure-related PA which may have distinct health effects (Holtermann et al., 2021). Future studies should also consider including more real-time monitoring of the participants' PA and guide the participants towards their allocated behavior to avoid increases in PA in the control group, as was observed with steps in this study.

Third, the effects of reducing SB on BP should be further investigated in different age groups. This and one another study with younger participants (Barone Gibbs et al., 2024) did not observe effects on BP whereas a study among older adults did see improvements in the SB-reducing intervention group (Rosenberg et al., 2024). Moreover, as performed in this study, BP should be measured in different conditions, such as during an exercise test or using an ambulatory measurement, as these can provide added value to only resting measurements (Schultz et al., 2022) and they would allow to study BP reactivity to PA which would be an interesting future direction.

Fourth, more interventional studies on the effects of SB reduction and cardiac structure are needed. My finding of improved LV mass index with successful SB reduction is based only on additional analyses and therefore needs to be confirmed. To reduce measurement error, future studies should consider using magnetic resonance imaging instead, or preferrably in conjunction with (exercise) echocardiography (Bottini et al., 1995).

7 Conclusion

The results of this study suggest that a six-month intervention aimed at reducing daily SB by 1 h does not affect cardiorespiratory fitness, BP under different physiological conditions, or cardiac structure or function in adults with metabolic syndrome, overweight or obesity and physical inactivity. However, successfully reducing SB or increasing PA may lead to improved cardiorespiratory fitness, lower BP during submaximal exercise, decreased LV mass index, and improved LV function during exercise. Future studies should be adequately powered to confirm the results of the current study.

To conclude, while successful SB reduction may provide some health benefits, it is likely that increasing PA, especially MVPA, is most beneficial for cardiovascular health.

Acknowledgements

The data collection and experiments for this thesis were conducted at the Turku PET Centre and the department of Clinical Physiology and Nuclear Medicine at the Turku University Hospital and the University of Turku between 2017 and 2020. The study was conducted within the Finnish Centre of Excellence in Cardiovascular and Metabolic Diseases supported by the Academy of Finland, the University of Turku, Turku University Hospital, and Åbo Akademi University.

This work was financially supported by grants from the Finnish Cultural Foundation, the Päivikki and Sakari Sohlberg foundation, the Hospital District of Southwest Finland, and the TYKS foundation. The doctoral programme in clinical research has also financially supported my conference attendances and given me the privilege of doing research on a salaried position.

I want to express my gratitude to the supervisors of this thesis, Associate Professors Ilkka Heinonen and Kari Kalliokoski. I am thankful for the opportunity to be able to work with the high-quality data and expertise that you have been able to provide. Under your supervision and guidance, I have grown tremendously as a researcher and my thinking about physical activity behavior, physiology, metabolism, and science in general has evolved significantly. Your support has always been easily available, which is of uttermost importance to an early-career scientist.

I want to thank Associate Professors Sari Aaltonen and Ann-Katrin Grotle for the insightful comments and discussions during the review process of this thesis. Your input notably improved the quality of the thesis. I am honored to have Professor Mikko Tulppo having agreed to act as the opponent for this thesis. I look forward to the discussions. What I love in academia is that all work is subject to relevant criticism and discussion, which is essential for developing scientific reasoning, and is ultimately at the core of all science.

My sincere thanks to chief physicians Professor Juhani Knuuti and Associate Professor Maria Saarenhovi for providing the excellent facilities to conduct this research and for giving great insights when the knowledge and opinions of cardiovascular experts have been needed. Additionally, thank you Professor Jukka

Kemppainen for being a part of the follow-up committee of my doctoral studies. Your practical tips in navigating the academic world have been useful.

A huge thank you goes also to my closest co-workers, Dr Tanja Sjöros, Dr Taru Garthwaite, and MSc (PhD by the time of publishing this) Saara Laine. In addition to guiding me with any practical issues and teaching me all about the EXSIT data, your company and presence has made this journey of PhD research fun and enjoyable. I also want to thank you for conducting the measurements and interventions in a rigorous manner which ensured high quality and robust data for my analyses.

I also want to thank the collaborators of the EXSIT study. The physical activity and accelerometry experts from the UKK Institute, Professor Tommi Vasankari, Dr Harri Sievänen, and MScEng Henri Vähä-Ypyä, have made sure to give precise and relevant comments on my manuscripts. Moreover, you have helped me to think of the results in a broader context. Without a doubt, the role of the UKK Institute has been vital for this study. I want to thank you, MD Petri Kallio, especially for the echocardiographic assessments and your expertise in interpreting the results. I also want to thank Professor Kirsi Laitinen and Dr Noora Houttu for the help you have given with the body composition measurements and all of my manuscripts. Very importantly, I want to express my gratitude to statistician Eliisa Löyttyniemi for always being helpful with any statistical issues that I had.

Without the 64 volunteers that participated in this study I would not have a doctoral thesis. Therefore, I am greatly thankful for each and every one of you for voluntarily sacrificing a significant amount of time and effort to participate. High quality science would not exist without willing volunteers.

Finally, I want to thank everyone who has supported any part of this research over the years. These include, but are not limited to, the staff at the Turku PET Centre, who tremendously helped with the data collection and administration, and Tiia Koivula, who has been a close co-worker and great company on our unforgettable conference trips all around the world.

Thank you to my whole family and all friends who have been highly supportive throughout my journey all the way from my physiotherapy studies in Turku to my master's studies in Jyväskylä and finally PhD research in Turku.

Last but not least, I want to acknowledge my beloved wife Kaisa. From celebrating an academic achievement (e.g., sharing the champagne) to getting my thoughts away from work, or helping to expand my world-view beyond a medical researcher's perspective, your presence and support have been immensely valuable at all times. And of course, you have to be acknowledged for the unique cross-stitch cover art on this thesis (and our home).

27.3.2025
Jooa Norha

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TURUN
YLIOPISTO
UNIVERSITY
OF TURKU

Painosalama, Turku, Finland 2025

ISBN 978-952-02-0132-6 (PRINT)
ISBN 978-952-02-0133-3 (PDF)
ISSN 0355-9483 (Print)
ISSN 2343-3213 (Online)