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The Role of Sedentary Behavior in Cardio-Preventive Research

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LIST OF ABBREVIATIONS

AHA	American Heart Association
AMR	Accelerometer measurement reactivity
CMRS	Clustered cardiometabolic risk score
CRF	Cardiorespiratory fitness
DBP	Diastolic blood pressure
DZHK	Deutsches Zentrum für Herz-Kreislauf-Forschung (Englisch: German Centre for Cardiovascular Research)
HDL-C	High-density lipoprotein cholesterol
IBEKO	'In Bewegung kommen, in Bewegung bleiben', a feasibility pilot study
ICC	Intraclass correlation
IPAQ	International Physical Activity Questionnaire
LPA	Light-intensity physical activity
MET	Metabolic equivalent of task
MVPA	Moderate-to vigorous physical activity
NHANES	National Health and Nutrition Examination Survey
NHLBI	National Heart, Lung, and Blood Institute
OLSR	Ordinary least-squares regression
PA	Physical activity
QR	Quantile regression
SB	Sedentary behavior
SBP	Systolic blood pressure
SBRN	Sedentary behavior research network
SIT-Q-7d	Last 7-d Sedentary Behavior Questionnaire
TV	Television
VO_{2peak}	Peak oxygen uptake
WC	Waist circumference

SUMMARY

Background: Sedentary behavior (SB) is a modifiable behavior with increasing prevalence worldwide. There is emerging evidence that time spend in SB and the manner in which SB is accumulated over time is associated with cardiovascular and cardiometabolic health. The requirement for SB data to be accurately measured is minimization, or at least accurate quantification of human-related sources of measurement errors such as accelerometer measurement reactivity (AMR). The present thesis was to examine SB and their associations with cardiovascular and cardiometabolic health, and to focus on challenges related to the assessment of SB. The first aim of the thesis was to identify patterns of SB describing how individuals accumulate their time spend in SB day-by-day over one week, and to examine how these patterns are associated with cardiorespiratory fitness as a marker for cardiovascular health (paper 1). The second aim of the thesis was to examine the multiple types of SB, and how this is associated with a clustered cardiometabolic risk score (CMRS; paper 2). The third aim of the thesis was to examine AMR and the reproducibility in SB and physical activity (PA) in two measurement periods, and to quantify AMR as a confounder for the estimation of the reproducibility of SB and PA data (paper 3).

Methods: The three papers were based on data of two different studies. For study 1, 1165 individuals aged 40 to 75 years were recruited in three different settings. Among these, 582 participated in a cardiovascular risk factor screening program including cardiopulmonary exercise testing. For the analyses of paper 1, 170 participants were eligible, agreed to wear an accelerometer, fulfilled the wearing regime, and completed the study period by wearing the accelerometer for seven consecutive days. Patterns in accelerometer data were classified based on time spent in SB per day applying growth mixture modeling. Model-implied class-specific peak oxygen uptake (VO_{2peak}) means were compared using adjusted equality test of means (paper 1). The underlying study of paper 2 and 3 were based on data of a pilot study aiming to investigate the feasibility of a brief tailored letter intervention to increase PA and to reduce SB during leisure time. Among the individuals who agreed to be contacted again in study 1, a random sample of those aged between 40 and 65 years was drawn. Of those, 175 attended in a cardiovascular examination program. Assessment included giving blood sample, standardized measurement of blood pressure, waist circumference, body weight, and height at baseline, and after twelve months. Further, they agreed to complete a paper-pencil questionnaire on SB (Last 7-d Sedentary Behavior Questionnaire, SIT-Q-7d) and PA (International Physical Activity Questionnaire, IPAQ), and to receive seven-day accelerometery at baseline, and after 12 months. In addition, self-administered assessments were conducted at months one, three, four, and six after baseline. Only individuals of

a random subsample (= intervention group) received up to three letters tailored to their self-reported SB and PA at months one, three, and four. For paper 2, associations between SBs and a clustered cardiometabolic risk score (CMRS) were analyzed using linear as well as quantile regression. To account for missing values at baseline, multiple imputations using chained equations were performed resulting in a total sample of 173 participants. Paper 3 comprised data of 136 individuals who participated at the baseline and twelve months assessments, and fulfilled the wearing regime. AMR was examined using latent growth modeling in each measurement period. Intraclass correlations (ICC) were calculated to examine the reproducibility of SB and PA data using two-level mixed-effects linear regression analyses.

Results: Results of paper 1 revealed four patterns of SB: 'High, stable', 'Low, increase', 'Low, decrease', and 'High, decrease'. Persons in the class 'High, stable' had significantly lower VO_{2peak} values (M = 25.0 mL/kg/min, SD = 0.6) compared to persons in the class 'Low, increase' (M = 30.5 mL/kg/min, SD = 3.6; p = 0.001), in the class 'Low, decrease' (M = 30.1 mL/kg/min, SD = 5.0; p = 0.009), and in the class High, decrease' (M = 29.6 mL/kg/min, SD = 5.9; p = 0.032), respectively. No differences among the other classes were found. In paper 2, results revealed that the only factor positively associated with a CMRS in all regression models was watching television. Depending on the regression analysis approach used, other leisure-time SBs showed inconsistent (using a computer), or no associations (reading and socializing) with a CMRS. In paper 3, results revealed that time spent in SB increased (baseline: b = 2.3 min/d; after 12 months: b = 3.8 min/d), and time spent in light PA decreased (b = 2.0 min/day; b = 3.3 min/d). However, moderate-to-vigorous PA remained unchanged. Accelerometer wear time was reduced (b = 4.6 min/d) only at baseline. The ICC coefficients ranged from 0.42 (95% CI = 0.29 - 0.57) for accelerometer wear time to 0.70 (95% CI = 0.61 - 0.78) for moderate-to-vigorous PA. None of the regression models identified a reactivity indicator as a confounder for the reproducibility of SB and PA data.

Conclusions: The present thesis highlights SB in the field of cardiovascular and cardiometabolic research that have implications for future research. Individuals sit for different purposes and durations in multiple life domains, and the time spent in SB is accumulated in different patterns over time. Therefore, research should consider the fact that SB is embedded in an individual's daily life routine, hence might have differential effects on cardiovascular and cardiometabolic health. Further, methodological aspects have to be considered when dealing with SB. In order to detect how SB is 'independently' associated to an individual's health, an accurate measurement of SB is fundamental. Therefore, human-related sources of bias such as AMR should be taken into account when either planning studies or when interpreting data drawn from analysis of SB data.

ZUSAMMENFASSUNG

Hintergrund: Sitzen ist ein modifizierbares Verhalten, das weltweit immer häufiger auftritt. Forschungsergebnisse deuten darauf hin, dass die Zeit, die man im Sitzen verbringt, und die Art und Weise, wie sich die Sitzzeiten zusammensetzen, mit der kardiovaskulären und kardiometabolischen Gesundheit einer Person zusammenhängen. Die grundlegende Voraussetzung für eine genaue Messung des Sitzens ist jedoch, dass Ursachen von Messfehlern, wie beispielsweise die Reaktivität beim Tragen eines Akzelerometers, minimiert oder zumindest hinreichend genau quantifiziert werden können. In der vorliegenden Arbeit wurden Zusammenhänge zwischen dem Sitzen und der kardiovaskulären und kardiometabolischen Gesundheit untersucht und Aspekte hervorgehoben, die genaue Messungen von Sitzverhalten beeinflussen können. Im ersten Artikel wird der Frage nachgegangen, wie viele und welche Sitzmuster bei Personen über eine Woche identifiziert werden können und ob diese mit der kardiorespiratorischen Fitness, als wesentlicher Parameter für die kardiovaskuläre Gesundheit, assoziiert sind. Im zweiten Artikel wurde die Frage untersucht, in welchen verschiedenen Sitzverhaltensweisen Personen ihre Zeit verbringen und ob dies mit einem kontinuierlichen Risikoscore der kardiometabolischen Gesundheit (CMRS) zusammenhängt. Der dritte Artikel adressiert die Frage, ob das Tragen eines Akzelerometers reaktives Verhalten hervorruft und in welchem Ausmaß sich Reaktivität über wiederholte Messungen zeigt. Zudem wurde untersucht, in welchem Ausmaß Sitzverhalten und körperliche Bewegung reproduzierbar sind und ob Reaktivität als konfundierender Faktor für die Reproduzierbarkeit von Sitz- und Bewegungsdaten quantifizierbar ist.

Methode: Die drei Artikel basieren auf Daten aus zwei Studien. Für Studie 1 wurden 1165 Personen im Alter von 40 bis 75 Jahren in drei Settings rekrutiert, von denen 582 an einem Programm zum Screening von kardiovaskulären Risikofaktoren, ein kardiopulmonaler Belastungstest eingeschlossen, teilnahmen. Von diesen waren 170 eligible Teilnehmer, das heißt sie trugen an sieben aufeinander folgenden Tagen ein Akzelerometer und erfüllten die Tragekriterien. Zur Modellierung der Veränderungen über den Tragezeitraum hinsichtlich der im Sitzen verbrachten Zeit und zur Identifizierung von dahinterliegenden Sitzmustern wurden latente Wachstumskurvenmodelle berechnet. Modell-implizierte klassenspezifische Mittelwerte für die maximale Sauerstoffaufnahme (VO_{2peak}) wurden mit Hilfe von Chi-Quadrat-Tests verglichen (Artikel 1). Die Ergebnisse des zweiten und dritten Artikels basierten auf Daten einer Machbarkeitsstudie für eine computergestützte Kurzintervention mit dem Ziel eine Steigerung der körperlichen Aktivität und eine Reduktion von Sitzzeiten während der Freizeit zu erreichen. Aus einer Zufallsstichprobe von kontaktbereiten Personen im Alter zwischen 40 und 65 Jahren aus

Studie 1, nahmen 175 Personen erneut an einem kardiovaskulären Untersuchungsprogramm teil. Dieses umfasste eine Blutprobenentnahme sowie eine standardisierte Messung des Blutdrucks, des Taillenumfangs, des Körpergewichts und der Körpergröße zu Baseline und nach 12 Monaten. Zu beiden Zeitpunkten wurden von den Teilnehmern ein Fragebogen zum Sitzverhalten (Last 7-d Sedentary Behavior Questionnaire, SIT-Q-7d) und zur körperlichen Bewegung (International Physical Activity Questionnaire, IPAQ) ausgefüllt und ein Akzelerometer an sieben aufeinander folgenden Tagen getragen. Die Fragebögen wurden zusätzlich noch nach dem ersten, dritten, vierten und sechsten Monat nach Baseline ausgefüllt. Eine per Zufall ausgewählte Gruppe von Teilnehmern erhielt im ersten, dritten und vierten Monat bis zu drei automatisiert generierte schriftliche Feedbackbriefe zu Sitzverhalten und körperlicher Bewegung. Für den zweiten Artikel wurden Assoziationen zwischen verschiedenen Sitzverhaltensweisen in der Freizeit und dem CMRS mit Hilfe einer linearen Regression sowie Quantilregression analysiert. Nach multipler Imputation für fehlende Baselinewerte, ergab sich eine Gesamtstichprobe von 173 Teilnehmern führte. Der dritte Artikel umfasst Daten von insgesamt 136 Personen, die zu Baseline und nach 12 Monaten an der Studie teilnahmen und die Tragekriterien für das Akzelerometer erfüllten. Zur Modellierung der Veränderungen über den Tragezeitraum hinsichtlich der im Sitzen verbrachten Zeit sowie des Zeitumfangs leichter und moderat bis anstrengender körperlicher Bewegung wurden latente Wachstumskurvenmodelle berechnet. Basierend auf Mehrebenenanalysen mit linearen gemischten Modellen wurden Intraclass-Korrelationen (ICC) berechnet, um die Reproduzierbarkeit der Sitz- und Bewegungsdaten einschätzen zu können.

Ergebnisse: Die Ergebnisse des ersten Artikels zeigten vier Sitzmuster: "Hoch, stabil", "Niedrig, erhöht", "Niedrig, verringert" und "Hoch, verringert". Personen der Klasse "Hoch, stabil" hatten signifikant niedrigere VO_{2peak}-Werte (M = 25.0 ml/ kg/ min, SD = 0.6) im Vergleich zu Personen der Klasse "Niedrig, erhöht" (M = 30.5 ml/ kg/ min, SD = 3.6; p = 0.001), der Klasse "Niedrig, verringert" (M = 30.1 ml/ kg/ min, SD = 5.0; p = 0.009) und solchen in der Klasse "Hoch, verringert" (M = 29.6 ml/ kg/ min, SD = 5.9; p = 0.032). Es wurden keine Unterschiede zwischen den anderen Klassen gefunden. Die Ergebnisse des zweiten Artikels weisen darauf hin, dass in allen Regressionsmodellen nur Fernsehen positiv mit einem CMRS assoziiert war. In Abhängigkeit von dem gewählten Regressionsverfahren ergaben sich für andere Sitzverhaltensweisen, die in der Freizeit gezeigt werden, hingegen inkonsistente Ergebnisse (Nutzung eines Computers) oder keine Assoziationen (Lesen und Zeit mit anderen Personen verbringen) mit einem CMRS. Die Ergebnisse des dritten Artikels zeigten, dass über beide Tragezeiträume (baseline und nach 12 Monaten) die sitzend verbrachte Zeit um 2.3 min/ Tag beziehungsweise 3.8 min/ Tag zunahm und leichte körperliche Aktivität um 2.0 min/ Tag beziehungsweise 3.3 min/ Tag abnahm. Die Tragezeit des Akzelerometers reduzierte sich nur zu Baseline um 4.6 min/ Tag. Der Umfang moderater bis anstrengender körperlicher Bewegung änderte sich weder zu Baseline noch nach 12 Monaten. Die ICC-Koeffizienten reichten von 0.42 (95% *CI* = 0.29 – 0.57) für die Tragezeit des Akzelerometers bis 0.70 (95% *CI* = 0.61 – 0.78) für moderate bis anstrengende körperlicher Aktivität. Ein Reaktivitätsindikator konnte in keinem Regressionsmodell als konfundierender Faktor für die Reproduzierbarkeit von Sitz- und Aktivitätsdaten identifiziert werden.

Schlussfolgerung: Die vorliegende Arbeit untersuchte das Sitzverhalten von Personen im Rahmen der kardiovaskulären und kardiometabolischen Gesundheitsforschung. Es können hieraus Implikationen sowie zukünftiger Forschungsbedarf in diesem Gebiet abgeleitet werden. In zukünftigen Studien sollte berücksichtigt werden, dass Sitzen nicht losgelöst auftritt, sondern in das alltägliche Leben eines Individuums eingebettet ist. Personen sitzen aus verschiedenen Gründen in mehreren Lebensbereichen und die im Sitzen verbrachte Zeit ist von Person zu Person und von Tag zu Tag unterschiedlich zusammengesetzt. Dies kann unterschiedliche Auswirkungen auf die kardiovaskuläre und kardiometabolische Gesundheit haben. Ferner ist eine genaue Messung von Sitzverhalten von grundlegender Bedeutung, um festzustellen, inwiefern das Sitzverhalten "unabhängig" von anderen Einflussfaktoren mit der Gesundheit eines Individuums assoziiert ist. Darüber hinaus sollten konfundierende Faktoren wie beispielsweise Reaktivität in der Planung von Studien sowie bei der Interpretation von Sitz- und Aktivitätsdaten berücksichtigt werden.

1 INTRODUCTION

1.1 'The new kid on the block'[1]: Definition and prevalence of sedentary behavior and its role in cardio-preventive research

Cardiovascular diseases as one of the major noncommunicable diseases are the leading cause of morbidity and mortality worldwide and represent an important public health problem.[1] Various cardiometabolic risk factors adversely contribute to an increased risk of cardiovascular diseases, e.g., high blood pressure, obesity, hyperglycemia, or hyperlipidemia. Regular physical activity (PA) is a widely accepted non-pharmacological strategy to improve cardiometabolic health and can therefore reduce the risk for cardiovascular diseases.[2] Particularly, moderate-to-vigorous PA (MVPA) is most beneficial for cardiovascular and cardiometabolic health.[3] As shown in figure 1, next to PA, other movement and non-movement behaviors might contribute to the risk of cardiovascular as well as cardiometabolic health.

Figure 1 Illustration of the conceptual model of sedentary behavior terminology adapted from the Sedentary Behavior Research Network (SBRN).[5]

Notes. *MET*: Metabolic equivalent of task. The metabolic equivalent task is a physiological concept intended to approximate the energy expenditure at different intensities of physical activity. The metabolic equivalent task is defined as the ratio of a work metabolic rate to a standard resting metabolic rate.[4]

Individuals spent the majority of the day in sedentary behavior (SB) and spent less time in PA on a moderate-to-vigorous intensity level. While a various health consequences were found to be associated with PA and inactivity, SB has become an emerging research topic only in the last decade. Defined by the Sedentary Behavior Research Network (SBRN), SB is any waking behavior characterized by an energy expenditure of ≤ 1.5 metabolic equivalent of task (MET), while in a

[1] Cited from Després JP. Physical Activity, Sedentary Behaviours, and Cardiovascular Health: When Will Cardiorespiratory Fitness Become a Vital Sign? Canadian Journal of Cardiology, 2016; 32; 505-513

sitting, reclining or lying posture.[5] Modern lifestyle in Western societies is characterized by high levels of SB per day, in almost all life domains such as work, commuting, and leisure and has increased in recent years.[6, 7] Data on prevalence of time spend in SB vary depending on the measurement method used. Based on objective measures like an accelerometer adults spend more than half their waking time per day in SB. Several studies showed that European and American adults averagely spend 6 to 9 hours per day (h/ d) in SB.[8, 9] In contrast, SB data based on self-reported questionnaire showed an average time spend in SB of almost equal to 5 h/ d in 20 countries worldwide.[10]

Recent evidence has linked a large amount of time spend in SB to poor cardiovascular and cardiometabolic health and all-cause as well as cardiovascular mortality.[9, 11-13] The association between SB and risk for cardiovascular disease or mortality seems to be nonlinear with increased risk at very high levels of time spend in SB.[14, 15] In addition, the manner in which SB is accumulated, e.g., in periods of prolonged and uninterrupted SB, seems to be associated with detrimental cardiovascular and cardiometabolic health effects.[11, 12, 16] Moreover, the association between SB and all-cause mortality is even more pronounced among individuals who are generally physical inactive.[17] Figure 2 displays the joint association between SB and physical activity (PA), and cardiovascular and cardiometabolic health. However, replacement of SB with light-intensity PA (LPA) or MVPA might be associated with cardiometabolic health in the long term.[18]

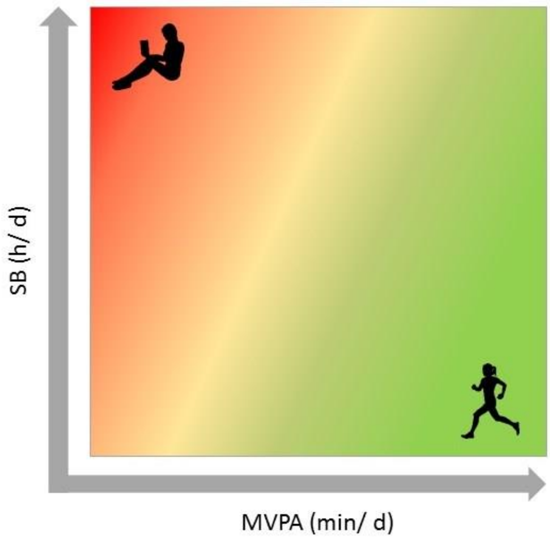


Figure 2 Illustration of the joint associations of sedentary behavior (SB), moderate-to-vigorous physical activity (MVPA), and cardiovascular and cardiometabolic health.

Notes. The figure was adapted from Katzmarzyk and colleagues (2019).[13] The red area of the figure indicates a higher risk of cardiovascular and cardiometabolic disease or mortality, and the green area indicates a lower risk of cardiovascular and cardiometabolic disease or mortality. The highest risk group is those who spend high amounts of time in SB combined with (almost) no time spend being physical active on a modest-to-vigorous level. The more active an individual is, the more likely it is that adverse cardiometabolic or cardiovascular effects of sitting can be reduced or even eliminated.[17]

While insufficient PA is a well-established risk factor for cardiovascular and cardiometabolic health,[19] there is still a debate as to whether the associations between SB and these health risk outcomes might exist independently of PA. So far, the evidence based on SB data is insufficient to define quantitative guidelines,[20] resulting in generic and non-quantitative SB guidelines in some countries, including Germany.[21]

Due to the fact that SB is complex and includes multiple domains, dimensions, and correlates,[9] methodological challenges need to be addressed in the field of cardiovascular and cardiometabolic research.[20] The present thesis addresses three aspects of SB. First, it aims to identify patterns of SB to improve the understanding of how an individual accumulates SB over time and how this is associated with cardiovascular health. Second, it intends to focus on how individuals spend their time in multiple types of SB because there is contradictory evidence as to whether and how different types of SB are associated with cardiometabolic health. Third, the thesis wants to examine how wearing a device such as an accelerometer that is subject to human-related sources of bias can influence accurate measurement and reproducibility of SB.

1.2 Patterns of sedentary behavior and cardiorespiratory fitness

Cardiorespiratory fitness (CRF) is an important marker of cardiovascular health.[22] A meta-analysis of 33 studies showed that each 1 - MET unit increase in CRF was associated with a pooled risk reduction of 13% and 15% of all-cause mortality and coronary heart event or cardiovascular event, respectively.[23] CRF is the capacity of the body to transport and utilize oxygen during PA.[24] Therefore, differences in CRF between individuals might partly explained by differences in the engagement in PA.[2] However, even less is known about how SB is associated with CRF and studies examining associations between SB and CRF showed inconsistent results. Higher levels of SB per day,[24-28] long sedentary bout duration and less breaks in SB[28, 29] were found to be associated with lower CRF. Other studies found no differences in SB between individuals with high and low levels of CRF,[30] or different associations between SB and CRF with regard to sex.[31]

How individuals accumulate their day-to-day SB over time might have different effects on cardiovascular health, even though identifying patterns of SB can help to understand who is at risk of cardiovascular health within a population in a more detailed manner.[9] Most studies examining the associations between SB and cardiovascular risk factors primarily focus on the accumulated time spent in SB, but not day-to-day patterns of SB. It is questionable whether the operationalization of SB as a one-dimensional measure and the assumption that a single regression line adequately represents SB can reflect the day-to-day variability of SB over time. Potential differences in individual patterns in which SB is accumulated and how these patterns may differentially influence the magnitude of cardiovascular risk factors remain undetected. So far, there are three studies using data of the National Health and Nutrition Examination Survey (NHANES) either identified patterns of SB based on data from accelerometers in an adult general population[32] or examined associations between patterns of SB and health-related outcomes such as age, body mass index, history of disease,[33] or all-cause mortality.[34] These outcomes seems to differ between individuals classified in distinct patterns of SB. So far, no study has included CRF as an important cardiovascular health marker and analyzed its association with day-to-day patterns of SB.

1.3 Sedentary behavior in leisure time and a clustered cardiometabolic risk score

Individuals spend their time doing various activities while sitting such as watching television (TV), using a computer, playing video games, reading, or eating. Evidence suggests that not all types of SB seem to be equal in terms of energy expenditure and their effects on vascular functions.[35] Moreover, the impact of these activities on vascular functions appear to be depend on multiple life domains they are undertaken in. Recent studies have found that leisure-time SB had stronger effects on cardiometabolic health compared to occupational SB.[36, 37] The dose-related association of high amounts of time spend watching TV, a common leisure-time activity, with an unfavorable cardiometabolic health profile is supported by various evidence (e.g.,[9, 38-42]). However, evidence in adults on the individual cardiometabolic risk profile and other leisure time activities such as using a computer, reading or socializing is more inconclusive.[40, 43-53] Compelling evidence on the impact of SB during a broader range of leisure activities on the cardiometabolic risk is lacking.

In general, evidence suggest that prolonged time spend in SB is adversely associated with a decrease in muscle and insulin sensitivity, blood flow, energy expenditure, and several other vascular functions[9, 12, 54] which are assumed to be associated with altered cardiometabolic functioning such as increased blood pressure, increased plasma glucose, increased lipoproteins, and abdominal obesity. To cluster these cardio-metabolic risk factors in the same individual appears to pose an additional risk for cardiovascular diseases.[51] Furthermore, data of a meta-analysis revealed that spending high amounts of time engaging in SB increased the odds of having the metabolic syndrome by 73% compared to spending low amounts of time engaging in SB.[55] According to the definition of the American Heart Association (AHA) and the National Heart, Lung, and Blood Institute (NHLBI) waist circumference (WC), blood pressure, plasma glucose and triglycerides, and high-density lipoprotein cholesterol (HDL-C) comprised the metabolic syndrome that is considered to be one of the major risk factors for cardiovascular disease and diabetes mellitus.[56]

In summary, SB in leisure time seems to be associated with an unfavorable cardiometabolic health profile. In order to get a deeper understanding of this association, a number of methodological challenges need to be addressed. A growing body of literature recommends using a cluster of continuous cardiometabolic risk factors instead of using a binary definition of the metabolic syndrome.[57, 58] In addition to paper 2, only one other study simultaneously examined a broader range of SBs in leisure time and their associations with a score using a cluster of continuous cardiometabolic risk factors.[40]

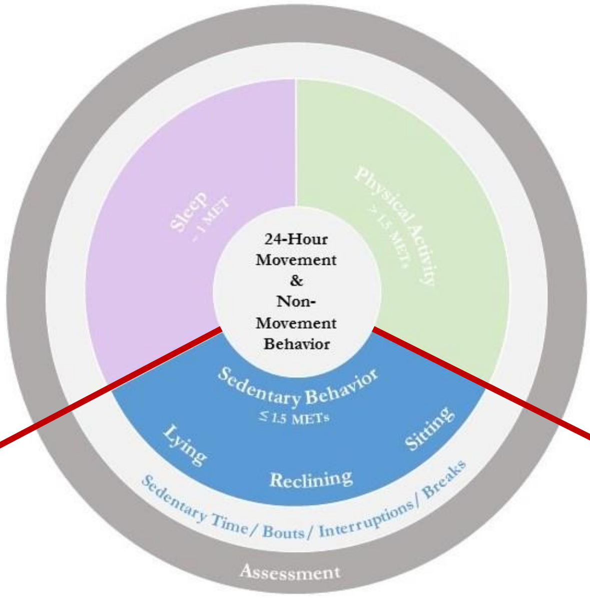
1.4 Reactivity and reproducibility: Challenges of sedentary behavior assessment

SB and PA are complex behaviors that are prone to vary over time – even on a daily basis – and to differ greatly between individuals. An accurate measurement of an individual's inherent behavioral variability is necessary to measure habitual levels of SB and PA.[59] In addition, it might provide the basis for a better understanding of studies examining the associations between SB and PA and cardiovascular and cardiometabolic health risk outcomes.[59, 60]

Accelerometry is frequently used to assess SB and PA. However, a potential source of limitations from accelerometer data is the Hawthorne effect, firstly described in the 1950s. The term refers to an individual's tendency to alter their behavior due to the awareness of being monitored. Therefore, the measurement of SB and PA with an accelerometer itself can lead to reactivity due to wearing a device.[61] AMR is mostly operationalized by the day-to-day variability of SB and PA using a 7-day accelerometer wearing protocol.[62, 63] So far, it is not known whether a 7-day period of monitoring is indeed sufficient in reflecting the mean level on the entire intensity spectrum from SB to MVPA, especially for more than one measurement period. In addition, it remains unclear how AMR might affect the reproducibility of SB and PA data. Studies examining accelerometer measurement reactivity (AMR) in adults are scarce and ambiguous.[63-69] So far, the extent of AMR occurrence at different levels of the entire spectrum of movement and non-movement (from SB to MVPA) in more than one measurement period has not been investigated.

1.5 Aims

The present thesis comprises three scientific and peer-reviewed publications that have investigated SB defined by the SBRN[5] and their associations with cardiovascular health (paper 1) and cardiometabolic health (paper 2), as well as challenges related to the assessment of SB (paper 3). Figure 3 visualizes and summarizes the aims of the three peer-reviewed papers.



Paper 1

The aim of paper 1 was to identify day-to-day patterns of accelerometer-based SB and to examine whether cardiorespiratory fitness differs between classes with distinct SB patterns.

This was investigated in the following paper:

Ullrich A, Baumann S, Voigt L, John U, van den Berg N, Dörr M, Ulbricht S: Patterns of accelerometer-based sedentary behavior and their association with cardiorespiratory fitness in adults. *Scandinavian journal of medicine & science in sports* 2018; 28: 2702-2709.

Paper 2

The aim of paper 2 was to examine the associations between a broader range of SBs in leisure time and a clustered cardiometabolic risk score (CMRS).

This was investigated in the following paper:

Ullrich A, Voigt L, Baumann S, Weymar F, John U, Dörr M, Ulbricht S: A cross-sectional analysis of the associations between leisure-time sedentary behaviors and clustered cardiometabolic risk. *BMC Public Health*. 2018; 18: 327.

Paper 3

The aim of paper 3 was to examine AMR and the reproducibility in accelerometer-based SB and PA in two measurement periods and to quantify AMR as a confounder for the estimation of the reproducibility of SB and PA data.

This was investigated in the following paper:

Ullrich A, Baumann S, Voigt L, John U, Ulbricht S: Reactivity and reproducibility of accelerometer-based physical activity and sedentary behavior in two measurement periods. *Scandinavian Journal of Science & Medicine in Sports* 2019; (*under review*).

Figure 3 Aims of the three papers that comprises the present thesis adapted from the SBRN.[5]

2 METHODS

The three papers[70-72] were based on data of two studies. The overall patient sample was recruited as part of the 'Herz-Kreislauf-Gesundheit in der Bevölkerung' investigating the reach of different population groups within a stepwise cardiovascular risk factor screening program.[73] Based on this sample, study 1 was conducted. In advance, a random sub-sample of individuals from the 'Herz-Kreislauf-Gesundheit in der Bevölkerung' agreed to be contacted again for future research. Based on this sample, study 2 was conducted. Study 2 entitled 'In Bewegung kommen, in Bewegung bleiben' (IBEKO, ClinicalTrials.gov: NCT02990039) is a randomized-controlled pilot study developed to assess the feasibility of a brief tailored letter intervention to increase PA and to reduce SB during leisure time. All participants of both studies gave informed written consent in accordance with the protocols approved by the clinical ethical committee of the University Medicine Greifswald (protocol number BB41/12 and protocol number BB 002/15a). Both studies were funded by the German Centre for Cardiovascular Research (German: Deutsches Zentrum für Herz-Kreislauf-Forschung, DZHK). The author's contributions to the scientific papers are summarized in table 3 (APPENDIX).

2.1 Study design, sample, and procedure

For study 1, individuals aged 40 to 75 years were recruited in general medical practices, job agencies, or via a health insurance company in northeast Germany between June 2012 and December 2013. All eligible individuals were asked to participate in a stepwise cardio-preventive health examination program. Inclusion criteria for step 1 were age (40 to 75 years), no cognitive impairments, sufficient language skills, and not being a participant of another study at the time of recruiting. Step 1 included a self-administered cardiovascular risk screening via tablet computer followed by blood pressure measurements and blood sample taking on an optional base (n = 1165). Step 2 comprised of a cardiovascular examination program including cardiopulmonary exercise testing using a cycle ergometer. Inclusion criteria for step 2 were no history of cardiovascular event (myocardial infarction, stroke), no previous vascular intervention, no diabetes mellitus, self-reported body mass index ≤ 35 kg/ m^2, no previous Methicillin-resistant Staphylococcus aureus infection, and being a resident in a predefined zip-code area. Among those who had been invited at the cardiovascular examination center at the university hospital in Greifswald (n = 706; 61 %), 582 individuals (82 %) participated in the cardiovascular examination program. In contrast to the other recruitment strategies (general medical practice and job agencies), for individuals who were recruited via a health insurance company stage 1 of the study were realized at the university hospital. Step 3 included an optional 7-day measurement of SB and PA using accelerometry. Among all invited participants (*n* = 470), 235 individuals (50 %) agreed to participate. They were instructed to wear the accelerometer attached to their right hip with an elastic band when awake for seven consecutive days, and to keep away from any water-based activities, starting the day following the cardiovascular examination program. Among those who agreed to wear the accelerometer, half of the subjects were asked to wear the accelerometer for 24 hours a day (scheme 'day and night'). The other half was instructed to wear the accelerometer after getting up in the morning, and to put it off before going to sleep (scheme 'day only'). Participants were informed that SB and PA would be recorded. Certified study staff performed all exercise tests and cardiovascular health assessments based on established standard operating procedures in the cardiovascular examination center. Figure 4 shows a flow-chart of participants addressed and analyzed as part of paper 1 to 3 and that are part of this thesis. As shown in figure 4, for the analyses conducted in paper 1 eleven of the 235 participants were excluded from analysis due to missing accelerometer data (*n* = 224). In addition, 54 participants were excluded as they did not fulfilled the accelerometer wear criteria. Wear criterion was wearing the accelerometer for seven days with one day indicating ≥ 480 minutes of accelerometer wear time. In accordance with Dyrstad and colleagues,[30] SB data were standardized by limiting the daily accelerometer wear time to the time between 6:00 am and 12:00 pm. Thus, the maximum wear time was 1080 min/ d. Thus, the final sample of paper 1 comprised 170 individuals.

For papers 2 and 3, a random sub-sample of individuals aged 40 to 65 years who agreed to be contacted again for future studies of the study already addressed in paper 1 (*n* = 1107; 95 %) was drawn. The eligibility criteria of the IBEKO study were the same as before, with one exception; in this study, people with diabetes mellitus were set to be eligible too. A total of 401 individuals were contacted and offered participation in the IBEKO study. Among those who had been offered study participation, 175 persons agreed to attend again in a cardiovascular examination program including the following measures: giving a blood sample, standardized measurement of blood pressure, waist circumference, body weight, and height at the cardiovascular examination center at baseline and after 12 months. Further, they agreed to complete a paper-pencil questionnaire on SB and PA, to wear an accelerometer for seven consecutive days, and recording a daily log of working hours over the monitoring period. Study participants were instructed to wear the accelerometer the same way already described for paper 1. After baseline assessments, participants were randomized into an assessment-only group (*n* = 85) and an intervention group (*n* = 90). Additionally, for all participants self-administered assessments regarding SB and PA were conducted at months one, three, four, and six after baseline. Only individuals of the intervention group received up to three letters tailored to their self-reported SB and PA at months one, three, and four. As seen in figure 4, for paper 2 two participants were excluded from the analyses conducted for paper 2 due to missing data on questionnaires or blood samples. Thus, the final sample of paper 2 comprised 173 participants. For paper 3, two participants at each measurement period did not provide appropriate accelerometer data (excluded: $n = 4$). In addition, data were analyzed only among those who had worn the accelerometer ≥ 10 hours per day on ≥ 5 days including at least one weekend day (excluded: $n = 24$). The final sample size of paper 3 comprised 136 participants. The IBEKO study was conducted between February 2015 and August 2016.

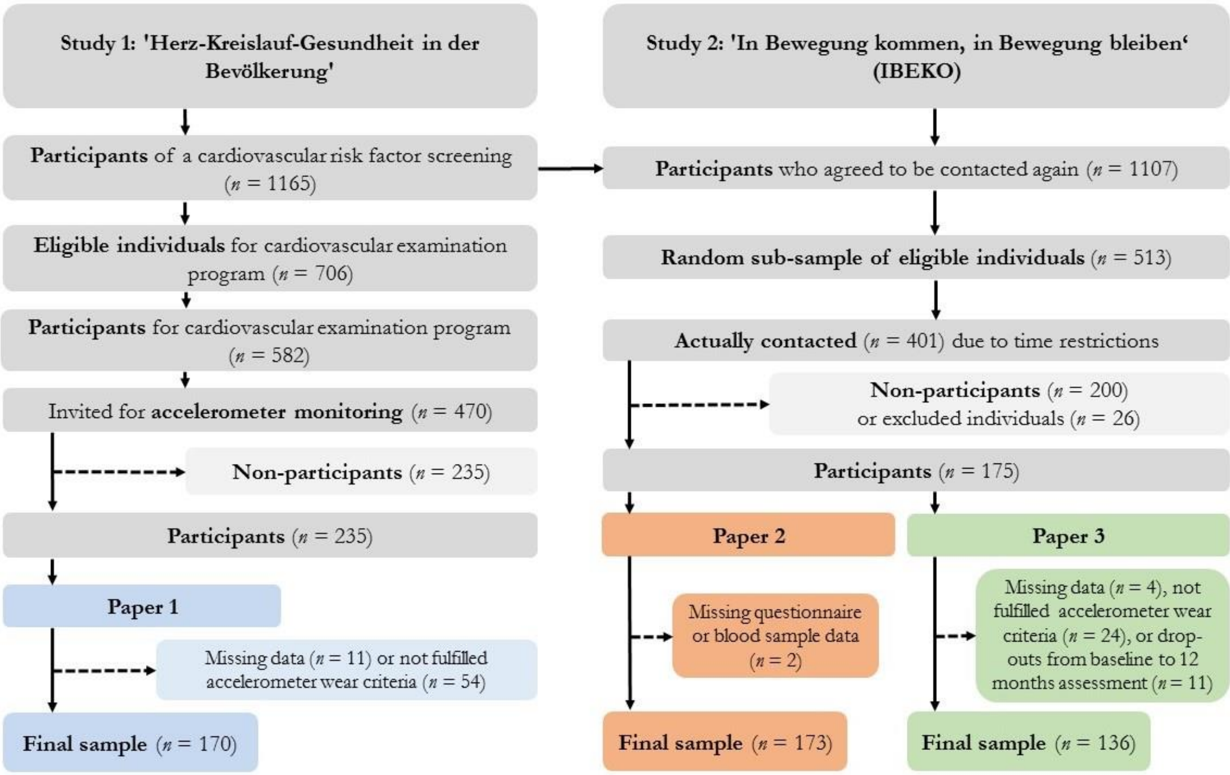


Figure 4 Colored flow of participants of paper 1 (blue), paper 2 (orange), and paper 3 (green).

Notes. The three papers were based on data of two different studies. Data of individuals of the first study 'Herz-Kreislauf-Gesundheit in der Bevölkerung' were analyzed in paper 1. In addition, a random subsample of individuals of study 1 provides the basis for recruiting participants for a feasibility study 'In Bewegung kommen, in Bewegung bleiben'. Data of this second study were analyzed in paper 2 and paper 3.

2.2 Measures

Paper 1: CRF was assessed by peak oxygen uptake (VO_{2peak}) achieved on a cycle ergometer (Ergoselect 100; Ergoline, Bitz, Germany). Following a modified Jones protocol (stepwise increase in workload of 16 W/min, starting with unloaded cycling plus the ergometer-related permanent load), the standardized cardiopulmonary exercise test was performed.[74, 75] The test was continued as symptom-limited in the absence of chest pain and electrocardiography abnormalities. Respiratory gas exchange variables were measured using a VIASYS Healthcare system (Oxycon

Pro or Rudolph's mask; VIASYS GmbH, Hoechberg, Germany). VO_{2peak} was defined as the highest ten-second average of oxygen uptake in the last minute of exercise relative to body mass (milliliters of oxygen per kilogram body weight per minute; mL/ kg/ min). Right-skewed VO_{2peak} data were square root transformed to approximate normality.

A triaxial ActiGraph Model GT3X+ accelerometer (Pensacola, FL) was used. The accelerometer was initialized at a sampling rate of 100 Hertz, and raw data was integrated into ten-second epochs. Data from the vertical axis from the accelerometers were downloaded and processed using ActiLife software (Version 6.13.3; ActiGraph). It is recommended to use cut points according to intensity threshold criteria to identify the time spent in different intensities of PA (min/ d). Therefore, values < 100 counts per min (counts/ min) were determined as SB.[76, 77] Non-wear time was calculated by the Troiano algorithm, defined as at least 60 consecutive minutes of zero activity intensity counts, with allowance for ≤ 2 counts/ min between 0 and 100.[77] SB data were square root transformed to account for their left-skewed distributions.

Sex and age (years) were obtained via a self-administrative questionnaire. Further, season of data collection (spring/ summer/ autumn/ winter) and accelerometer wear time (min/ d) were included as covariates to identify SB patterns.

Paper 2: Standardized measurements of blood pressure were conducted using a digital blood pressure monitor (705IT, Omron Corporation, Tokyo, Japan). Blood pressure was measured after a five-minute resting period three times at the right arm in a seated position. The first and the second measurements were followed by another resting period of three minutes each. The means of the second and third measurements of systolic blood pressure (SBP; mmHg) and diastolic blood pressure (DBP; mmHg) were used for further analyses. If an antihypertensive medication within the last 12 months was reported, 10 mmHg was added to the original observed value of SBP and DBP.[78] WC (cm) was measured midway between the lowest rib and the iliac crest using an inelastic tape. Non-fasting blood samples were taken and plasma triglycerides (mmol/ L), HDL-C (mmol/ L), and glucose (mmol/ L) were determined by standard procedures applied at the Institute for Clinical Chemistry and Laboratory Medicine at the University Medicine Greifswald.

These six risk factors were used to calculate the CMRS according to Knaeps and colleagues.[51] Glucose, triglycerides, and HDL-C were logarithmized ($\log_{10}$) due to their skewed distributions. Using sex-specific sample means (*M*) and standard deviations (*SD*) each cardiometabolic variable was standardized. Because the standardized HDL-C is inversely related to cardiometabolic risk, it was multiplied by −1. CMRS was created by summing the standardized values of the six cardiometabolic risk factors and dividing the sum by six to account for the number of variables included. Thus, a higher CMRS indicates a higher cardiometabolic risk.

The Last 7-d Sedentary Behavior Questionnaire (SIT-Q-7d) was used to quantify the time spent in different leisure-time SBs such as watching TV, using a computer, playing computer games, reading, doing household tasks, caring for others, pursuing hobbies, or socializing.[79] Average h/ d spend involved in these activities were calculated.

Sex, age (years), living in a current partnership (yes/ no), and employment status (employed/unemployed) were used as covariates. The domain of leisure-time PA in MET-hours per week (MET-h/ week) and the time spent traveling in a motor vehicle in min/d (one item) were assessed using the International Physical Activity Questionnaire (IPAQ) and calculated according to the IPAQ protocol.[80] The leisure-time domain included walking, PA on a moderate-intensity level and on a vigorous-intensity level. Leisure-time SB and PA variables were square root transformed to account for their right-skewed distributions.

Paper 3: SB and PA were assessed using a tri-axial ActiGraph Model GT3X+ accelerometer. Initialization, software usage, and definition of non-wear time was similar to paper 1. Time spent in SB, LPA, MVPA, and wearing the accelerometer was determined by min/d. Values < 100 counts/ min were determined as SB, values between 100 and 2019 counts/min as LPA, and values $\geq$ 2020 counts/min as MVPA.[76, 77] SB, LPA, and accelerometer wear time were approximately normally distributed. To account for their right-skewed distributions, MVPA data were square root transformed.

Sex, age (years), and years of school education (< 10 years/ 10 to 11 years/ $\geq$ 12 years) were assessed by a self-administrative questionnaire. Study group (assessment-only group/ intervention group), time (baseline/ after 12 months), recruitment site (general practice/ job center/ health insurance), first day of measurement (weekday/ weekend day), season of data collection (winter/ spring/ summer), and the average number of working hours on each day (h/ d) the accelerometer was worn were included as covariates.

2.3 Statistical analysis

For all analyses, *p*-values below 0.05 were considered statistically significant. For paper 1 and 3, Mplus version 7.31 and 7.316 [81] and for paper 2 and 3, STATA v.14.1 and STATA v. 14.2 software (Stata Corporation, College Station, TX)[82] were used to analyze the data.

Paper 1: To identify a number of classes of individuals with distinct SB patterns, a growth mixture modeling approach was applied.[83] A maximum likelihood estimator with robust standard errors was used. Seven observed indicators represented time spent in SB on each of the seven days of the measurement week. Latent growth factors based on these indicators were used to model trajectories of SB over the week. The observed indicators were regressed on the growth factors using linear regression. The shape of the growth curves was determined by time scores defined in the measurement model of the growth factors and matched with the observed day number of the measurement week. To specify nonlinear growth curves, an overall change function was fitted to the sample by adding linear, quadratic, and cubic slopes of time scores to the models. Rescaled Likelihood Ratio Tests were used to test whether higher order functions of time scores and free growth factor variances were required.[81] To determine the optimal number of trajectory classes, a forward procedure was performed. Various model fit criteria were used to assess the model fit: the Akaike Information Criterion and the adjusted Bayesian Information Criterion, with lower values indicating a better model fit. Furthermore, class sizes, entropy with values ≥ 0.80 indicating adequate classification, and the Bootstrapped Likelihood Ratio Test were also considered. Models with one to five classes were explored. The latent class variable was regressed on sex, age, and season of data collection. To predict SB at the corresponding day of measurement, accelerometer wear time was included as time-varying covariate. A measurement-error weighted approach for stepwise latent class modeling[84] was used to analyze the association between the patterns of SB and CRF. Class-specific mean values of VO_{2peak} were compared by using adjusted equality tests of means (Chi-square tests, χ^2).

Paper 2: To account for missing data, multiple imputation using chained equations (m = 20 imputed datasets) were performed. The six cardiometabolic risk factors, the predictor variables, socio-demographic covariates, PA covariates, and auxiliary variables (e.g., body mass index, total cholesterol, glycated hemoglobin) were considered for imputation models. In the imputation procedure, the predictive mean matching method was used to account for skewed variables.[85] For analyzing associations of leisure-time SB with CMRS, ordinary least-squares regression (OLSR) was applied. In regard of heteroscedasticity, robust standard errors estimations were used. Furthermore, quantile regression (QR) was applied because this method is not influenced by outliers in the distribution of the outcome variable and might explore the association of different leisure-time SBs across the entire distribution of the CMRS.[86] Associations of SB variables at the 25th, 50th, and 75th percentiles of CMRS were analyzed. In model 1, adjustments were made for socio-demographics and for time spent in the other leisure-time SBs. In model 2, additional adjustments were made for time spent physically active in leisure time and for time spent traveling in motor vehicles.

Paper 3: To examine AMR for both measurement periods, latent growth models were used.[83] In line with paper 1, time spent in SB, LPA, MVPA, and wearing the accelerometer on each of the seven days of measurement was represented by seven growth factors. The indicators were regressed on latent growth factors representing trajectories of outcomes over a week. A maximum likelihood estimator with robust standard errors was used. The shape of the growth curves was determined by time scores defined in the measurement model of the growth factors and matched with the observed day of the measurement week. Rescaled Likelihood Ratio Tests were used to test whether higher order functions of time scores and free growth factor variances were required.[81] To predict the outcomes at the corresponding day of measurement, accelerometer wear time and working hours were included as time-varying covariates if appropriate. Non-zero time trends in the outcomes over the days of measurement would imply reactivity. In the models, the slope factor was freely estimated and treated as a reactivity indicator reflecting the individual average change in outcome over time. Therefore, the factor scores of outcomes were saved and included as a reactivity indicator in further analysis.

Means for each outcome of the seven days of measurement were calculated. Two-level mixed-effects linear regression analyses were performed to assess changes in accelerometer-based outcomes from baseline to 12 months apart. All models were adjusted for sex, age, education, study group, time, recruitment site, first day of measurement, and season of data collection. In addition, the individual average value of accelerometer wear time, the reactivity indicator of accelerometer wear time, the reactivity indicator of the respective SB and PA outcome, and a combination of these factors were included as potential covariates step-by-step. Intraclass correlation (ICC) coefficients were used to decide which model for each outcome was most appropriate. The ICC coefficient is classified as follows: less than 0.40 indicates poor, between 0.40 and 0.75 fair to good, and 0.75 or more excellent reproducibility.[87]

3 RESULTS

Baseline sample characteristics of the three papers

Baseline sociodemographic variables and variables related to data collection of the samples of paper 1, 2, and 3 are displayed in table 1. Further descriptive characteristics of each paper are shown in the following sections and in the corresponding publications, respectively.

Table 1. Baseline descriptive characteristics of the study samples of the three papers

	Paper 1 (*n* = 170)		**Paper 2 (*n* = 173)**		**Paper 3 (*n* = 136)**	
Sociodemographic variables						
Age, years	56.4	(9.5)	54.4	(6.2)	54.6	(6.3)
Gender						
Female	97	(57.1)	111	(64.2)	89	(65.4)
School education, years						
< 10	21	(12.4)			7	(5.2)
10-11	111	(65.3)			95	(70.4)
> 11	38	(22.3)			33	(24.4)
Employed			138	(81.2)		
Working hours, h/ d					4.1	(3.0)
Current partnership, yes			124	(71.7)		
Variables related to data collection						
Setting						
General practice	58	(34.1)			54	(39.7)
Job center	28	(16.5)			24	(17.6)
Health insurance company	84	(49.4)			58	(42.7)
Season						
Spring	15	(8.8)			118	(86.8)
Summer	32	(18.8)			9	(6.6)
Autumn	114	(67.1)			-	-
Winter	9	(5.3)			9	(6.6)
First day of measurement						
Weekday					113	(83.1)

Notes. Data are presented as $M \pm SD$ for continuous variables and as *n* (%) for categorical variables. The colored-coded areas indicate the corresponding colors for each paper as shown in figure 4.

3.1 Paper 1: Patterns of sedentary behavior and cardiorespiratory fitness

Sample characteristics

On average, participants wore the accelerometer for 933.5 min/d (*SD* = 103.6) and spent 677.8 min/d (*SD* = 108.3) in SB. The mean of VO_{2peak} was 26.9 mL/ kg/ min (*SD* = 6.4).

Patterns of sedentary behavior and their association with cardiorespiratory fitness

With regard to the model fit criteria and entropy, the four-class model was selected. As shown in figure 5, participants in the class 1 showed stable amounts of SB across the week (labeled 'High, stable') with a mean of 724.9 min/ d spent in SB. Participants in the class 2, the class 3, and the class 4 showed varying SB across the week. Participants in the class 2 (labeled 'Low, increase') were characterized by a lower amount of SB on weekdays compared to weekends with a mean of 622.2 min/ d. Participants in the class 3 (labeled 'Low, decrease') were characterized by less sitting throughout the week with a mean of 540.2 min/ d. Participants in the class 4 (labeled 'High, decrease') were characterized by a higher amount of SB on weekdays compared to weekends with a mean of 694.8 min/d.

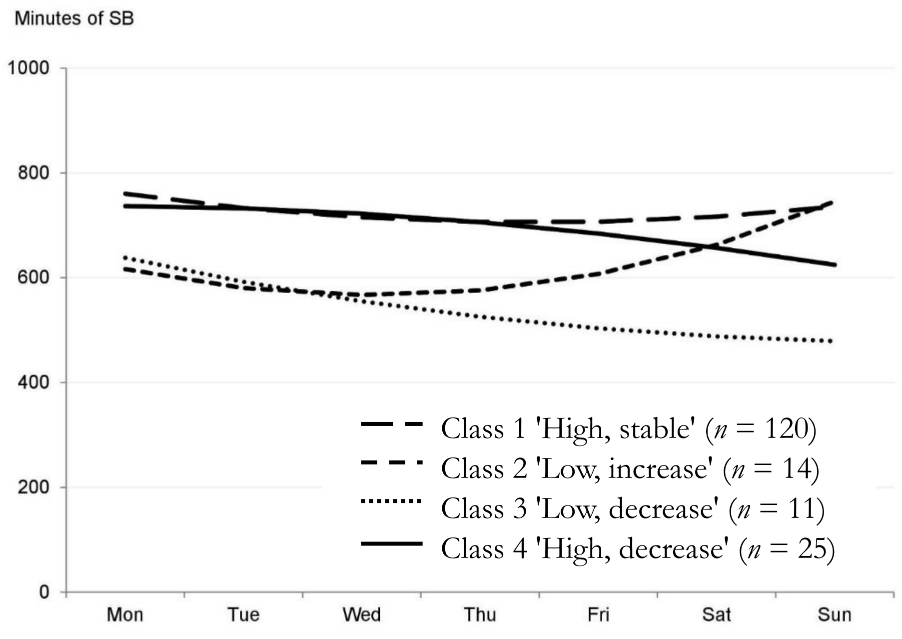


Figure 5 Results of latent growth modeling for a four class solution of sedentary behavior patterns.

Notes. *SB*: Sedentary behavior. Class sizes for model-implied mean trajectories of time spent in sedentary behavior over seven consecutive days of measurement. Latent class models with quadratic growth curves. Intercept and linear slope variances were freely estimated. Variances of quadratic slopes were fixed to zero. Linear slope variances were not held equal across classes. For illustration and reasons of interpretability, SB data were back-transformed.

The adjusted equality test of means across classes revealed a significant overall difference with a value of $\chi 2 = 17.5$ ($p < 0.001$). Post-hoc tests showed that individuals in the class 'High, stable' had significantly lower VO_{2peak} values ($M = 25.0$ mL/ kg/ min, $SD = 0.6$) compared to persons in the class 'Low, increase' ($M = 30.5$ mL/ kg/ min, $SD = 3.6$; $p = 0.001$), in the class 'Low, decrease' ($M = 30.1$ mL/ kg/ min, $SD = 5.0$; $p = 0.009$), and in the class 'High, decrease' ($M = 29.6$ mL/ kg/ min, $SD = 5.9$; $p = 0.032$), respectively. No differences among the other classes were found.

3.2 Paper 2: Sedentary behaviors in leisure time and a clustered cardiometabolic risk score

Sample characteristics

In median, participants spent 2.5 h/ d (interquartile range, *IQR*: 1.8 - 3.5) watching TV, 0.4 h/ d (*IQR*: 0.1 - 1.0) using a computer, 0.5 h/ d (*IQR*: 0.4 - 1.0) reading, and 0.4 h/ d (*IQR*: 0.0 - 1.0) socializing during leisure time. The median PA during leisure time was 15.6 MET-h/week (*IQR*: 3.3 - 33.1) and participants spent 30 min/ d (*IQR*: 10 - 60) traveling in motor vehicles. The mean CMRS was -0.0 ($SD = 0.6$) with a minimum value of -1.3 and a maximum value of 1.6.

Associations between sedentary behaviors in leisure time and a clustered cardiometabolic risk score

Results of OLSR and OR analysis are displayed in table 2. OLSR analysis revealed that there was a positive association between watching TV and CMRS (model 1: $b = 0.27$, $p = 0.029$); model 2: $b = 0.30$, $p = 0.021$). QR analysis revealed that watching TV was positively associated with the 25th (model 1: $b = 0.35$, $p = 0.015$; model 2: $b = 0.34$, $p = 0.008$), the 50th (model 1: $b = 0.32$, $p = 0.039$; model 2: $b = 0.37$, $p = 0.015$), and the 75th percentiles (model 2: $b = 0.32$, $p = 0.041$) of CMRS. The 50th (model 1: $b = -0.43$, $p = 0.019$) and the 75th percentiles (model 1: $b = -0.71$, $p = 0.015$) of CMRS revealed a negative association with using a computer. In model 2, these significant associations disappeared (model 2, 50th percentile: $b = -0.28$, $p = 0.277$; model 2, 75th percentile: $b = -0.55$, $p = 0.052$). There were no statistically significant associations between reading or socializing and CMRS. Similar results were found for OLSR and QR analyses using complete cases of the leisure-time SB variables (see additional files of the corresponding paper 2).

Table 2. Results of linear and quantile regression analysis (*n* = 173)

	OLSR	QR25	QR50	QR75
CMRS[a,c]	*b* [95% CI]	*b* [95% CI]	*b* [95% CI]	*b* [95% CI]
Watching TV				
Model 1[c]	0.27*	0.35*	0.32*	0.26
	[0.03; 0.52]	[0.07; 0.63]	[0.02; 0.62]	[-0.09; 0.62]
Model 2[d]	0.30*	0.34*	0.37*	0.32*
	[0.05; 0.56]	[0.09; 0.59]	[0.07; 0.66]	[0.01; 0.63]
Using a computer				
Model 1[c]	-0.35	-0.15	-0.43*	-0.71*
	[-0.70; 0.00]	[-0.67; 0.18]	[-0.79; -0.07]	[-1.27; -0.14]
Model 2[d]	-0.26	-0.26	-0.28	-0.55
	[-0.65; 0.13]	[-0.66; 0.13]	[-0.81; 0.24]	[-1.10; 0.01]
Reading				
Model 1[c]	-0.07	-0.18	-0.21	0.06
	[-0.57; 0.42]	[-0.71; 0.35]	[-0.95; 0.53]	[-0.72; 0.83]
Model 2[d]	-0.17	-0.36	-0.33	-0.04
	[-0.68; 0.34]	[-0.84; 0.13]	[-1.17; 0.50]	[-0.77; 0.70]
Socializing				
Model 1[c]	-0.08	0.07	-0.09	-0.26
	[-0.38; 0.21]	[-0.33; 0.48]	[-0.44; 0.26]	[-0.72; 0.19]
Model 2[d]	-0.06	0.08	-0.07	-0.20
	[-0.37; 0.24]	[-0.23; 0.38]	[-0.46; 0.31]	[-0.64; 0.24]

Notes. *OLSR:* ordinary least squares regression; *QR:* quantile regression; *b:* unstandardized regression coefficient; *CI*: confidence interval; *TV*: television. [a] Presented are multiple imputed data using chained equations (*m* = 20 imputed datasets) to account for missing values. [b] Based on robust standard errors; * $p < 0.05$. [c] Model 1: Adjusted for socio-demographic (sex, age, current partnership, and employment) and other leisure-time sedentary behavior variables. [d] Model 2: Adjusted for socio-demographic (sex, age, current partnership, and employment), leisure-time physical activity, traveling in motor vehicles, and other leisure-time sedentary behavior variables.

3.3 Paper 3: Reactivity and reproducibility of sedentary behavior and physical activity

Sample characteristics

At baseline, the average accelerometer wear time was 880.8 min/ d (*SD* = 85.9) and after 12 months, 864.8 min/ d (*SD* = 93.6), the average SB was 602.6 min/ d (*SD* = 96.6) and 593.8 min/ d (*SD* = 99.2), the average LPA was 230.9 min/ d (*SD* = 60.1) and 227.5 min/ d (*SD* = 57.9), and the average MVPA was 47.3 min/ d (*SD* = 24.4) and 43.5 min/ d (*SD* = 23.0), respectively.

Accelerometer measurement reactivity

At baseline, participants increased time spent in SB by 2.3 min/ d and after 12 months, by 3.8 min/ d and reduced time spent in LPA by 2.0 min/ d and by 3.3 min/ d, respectively. Neither at baseline nor after 12 months participants significantly changed time they spent in MVPA. Participants significantly reduced the accelerometer wear time by 4.6 min/ d at baseline. After 12 months, participants did not significantly change accelerometer wear time. Results of AMR were displayed in figure 6. The reactivity indicators of accelerometer wear time ($p < 0.001$), SB ($p = 0.008$), and LPA ($p = 0.006$) significantly differed from baseline to 12 months apart.

Reproducibility of sedentary behavior, physical activity, and accelerometer wear time

The ICC coefficients (95% CI) were between 0.41 (*CI*: 0.28 - 0.56) for accelerometer wear time and 0.70 (*CI*: 0.61 - 0.78) for LPA. The regression model adjusted for the average value of accelerometer wear time was most appropriate for SB (*ICC* = 0.68), for LPA (*ICC* = 0.68), and for MVPA (*ICC* = 0.70). For accelerometer wear time, none of the additional adjustments were appropriate (*ICC* = 0.42).

The time spent in SB, LPA, MVPA, and accelerometer wear time did not significantly decline or increase between the two measurement periods. The average value of accelerometer wear time was a significant confounder in all SB and PA regression models ($p < 0.001$). Detailed results of baseline and after 12 months parameter estimates for latent growth models of SB, LPA, MVPA, and accelerometer wear time, ICC coefficients, and results of two-level mixed-effects linear regression analyses are shown in the corresponding paper (paper 3).

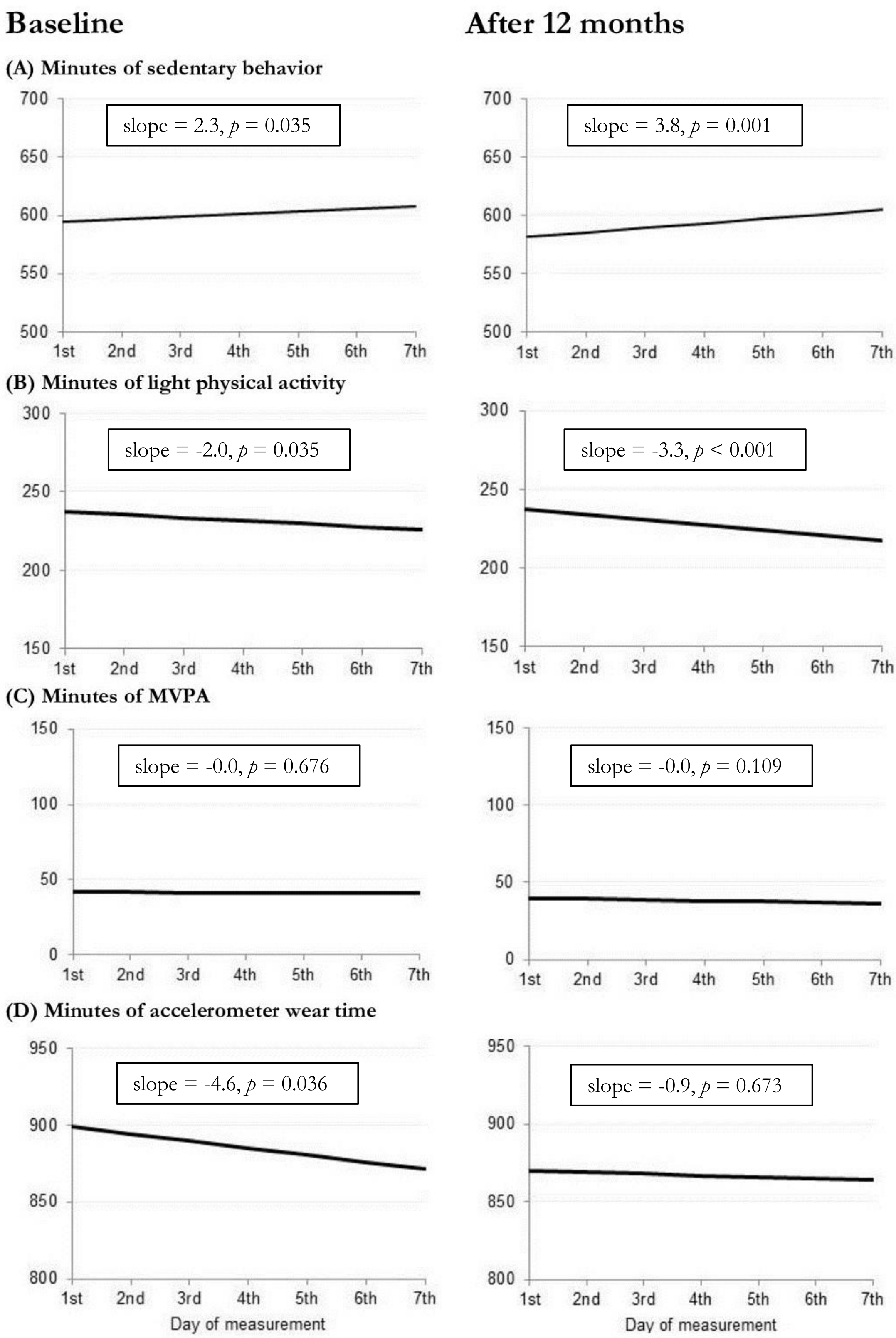


Figure 6 Estimated average linear growth curves for minutes spent in sedentary behavior (A), light physical activity (B), moderate-to-vigorous physical activity (MVPA) (C), and wearing the accelerometer (D) at baseline and after 12 months. Adjusted for accelerometer wear time and working hours if appropriate.

4 DISCUSSION

The aim of the present thesis was to examine SB and their associations with cardiovascular and cardiometabolic health and to focus on challenges related to the assessment of SB. Data revealed three main findings.

a. Four classes of trajectories (classes 1 to 4) of SB could be identified. Trajectories represent the participant's individual course of change based on accelerometer data over the period of one week. Individuals in the class 'High, stable' had significantly lower VO_{2peak} values compared to persons in the class 'Low, increase', in the class 'Low, decrease', and in the class 'High, decrease', respectively. No differences among the other classes were found.
b. Watching TV was unfavorably associated with cardiometabolic health measured by the CMRS. For other leisure-time SBs, findings on associations with cardiometabolic health were either inconsistent (using a computer) depending on the confounder included in the regression model or revealed no associations at all (reading and socializing).
c. AMR differentially influence SB and PA in two measurement periods depending on the intensity level of PA. It seems to have a similar impact on SB and LPA on repeated measurements, whereas MVPA does not appear to be affected by AMR. Further, AMR could not be identified as a crucial confounder for the reproducibility, whereas accelerometer wear time was found to be an important contributing factor regarding the data analyses of accelerometer-based SB and PA data.

4.1 General discussion

Patterns of sedentary behavior and cardiorespiratory fitness

The results of paper 1 revealed four classes of trajectories based on individual patterns of change on participants who spent their time in different day-to-day patterns of SB over a week. In line with previous research, identified patterns of SB included individuals that could be classified as showing stable high levels of SB ('High, stable'), varying patterns of SB on weekdays compared to weekends ('Low, increase' and 'High, decrease'), and relatively low levels of SB ('Low, decrease') throughout the week.[32] These patterns of SB are comparable with those known from PA research. Individuals classified as 'Weekend couch potato' are characterized by higher PA on weekdays compared to weekends which corresponds to the class 'Low, increase'.[32] A pattern known as 'Weekend warriors' is characterized by one or two sessions of high total volume of PA per week mostly during the weekend and less on weekdays which corresponds to the class 'High, decrease' and 'Low, decrease'.[88] The data on patterns of SB also revealed that both low SB and increased variability of SB during the week might be associated with higher levels of CRF. In line with the present findings, evidence suggests a more favorable association between belonging to the 'Weekend warrior' activity pattern and cardiovascular as well as cardiometabolic health profile compared to physically inactive individuals.[88-90] Particularly, modest amounts of PA in leisure time seems to provide substantial benefits for cardiovascular mortality.[91] In addition, CRF did not differ among the classes 'Low, increase', 'High, decrease', and 'Low, decrease'. Even though no causal attributions can be derived from interpreting observational patterns of SB, the findings suggest that these patterns might be associated with a better CRF whereas only high and stable levels of SB result in low CRF. In short, everything might be better for an individual's CRF than prolonged time spend in SB over the week. This is also conform with previous research showing that a total amount of high levels of time spent in SB, fewer number of breaks in SB, and longer bout durations of SB were associated with low CRF.[24-29]

Most of the included individuals were part of the 'High, stable' pattern spending an average of 67% of their observed time in SB. As visualized in figure 2, reducing daily time spent in SB, e.g., by breaking up prolonged periods of SB and replacing them with LPA, may have a beneficial impact on cardiovascular health.[25, 92] Furthermore, recent evidence suggests that individuals with a stable pattern of high amount of SB over time have the highest risk of cardiovascular mortality compared to those who show sustained low levels of SB or variability in SB over time.[13] Therefore, in future research on cardiovascular health prevention might consider particularly addressing these individuals with stable high patterns of SB by combining SB and PA interventions in order to improve cardiovascular outcomes.

Patterns of SB seem to differ between weekdays and weekend days. Evidence suggests that high levels of occupational SB may decrease the odds of being categorized in a group of less sit individuals.[93] Further, it should be noted that the time individuals spend sitting at work, the kind of work they do, and the mode used to get to work (e.g., driving by car or bike), may influence SB in leisure time.[94] Especially, prolonged time spent sitting in cars seems to be adversely associated with a cardiometabolic risk profile.[95] To distinguish between accelerometer-based SB at the workplace and SB in leisure time, data of working hours (assessed by self-reported protocol or log) should be considered as potential confounder to identify patterns of SB in different life domains.

Moreover, studies have shown that socioeconomic (e.g., employment, education, household income), sociodemographic (e.g., age, sex), behavioral (e.g., MVPA, smoking), individual (e.g., body mass index, history of disease), environmental (e.g., urban versus rural, safety), and seasonal factors were associated with certain SB and PA patterns.[33, 89, 94, 96-100] Therefore, there is a great need to better understand these risk factors with regard to SB and to understand their combined effects on individual's health.[9]

Sedentary behavior in leisure time and a clustered cardiometabolic risk

The results of paper 2 suggest that different SBs during leisure time may differ regarding their impact on cardiometabolic health. The data confirmed results of previous cross-sectional studies that higher amount of time spent watching TV is associated with cardiometabolic risk factors and an unfavorable cardiometabolic health profile.[40-49] Recently, data published showed that watching TV was the primary driver of the association between SB and cardiometabolic risk and that the association remained statistically significant even after adjusting for other SBs like using a computer or reading.[40] Further, favorable changes in screen-based SB (e.g., watching TV, using a computer) may positively affect clustered cardiometabolic health over a time span of five to ten years.[38, 39, 51] The present data added to the literature that regardless of the individuals cardiometabolic health profile (favorable versus unfavorable), data of all percentile groups of CMRS indicated that prolonged watching TV had similar negative cardiometabolic effects.

There are some attempts explaining why the association between unfavorable cardiometabolic health and time spent watching TV appears stronger than other SBs. Time spent watching TV may last longer without interruptions resulting in lower levels of metabolic energy expenditure.[101] Generally, time spent watching TV was found to be associated with several determinants of poor health outcomes, e.g., an increased intake of food with high energy density, or overall unhealthy dietary habits,[102, 103] alcohol consumption,[104] smoking,[104, 105] lower socioeconomic status,[106] and impaired mental health.[107] Moreover, accuracy to recall across contexts may vary as it might be easier to remember how long someone had watched TV than how much time they had spent in other SBs.[108] Therefore, the special role of watching TV has been discussed as a proxy for SB. In contrast, due to the overlap of watching TV and other unhealthy behaviors, it has been stated that watching TV itself does not reflect on the harmful health effects of SB.[20] Irrespective of the mechanisms underlying the unfavorable association between of watching TV on cardiometabolic health, watching TV has been firmly established as an adverse contributor to SB.

Other leisure-time SBs investigating in paper 2, however, showed inconsistent associations (using a computer) depending on the confounder included in the regression model or no associations (reading and socializing) with the CMRS. These findings are in line with previous studies that examined associations between time spent in other SBs than watching TV and individual cardiometabolic factors or a cardiometabolic risk scores.[39, 40, 43-49, 51, 52, 109] It has been argued that the less time spent in other leisure-time SBs was shorter and might therefore be an explanation for this. On the contrary, according to the results of the quantile regression analyses of paper 2, time spent sedentary while using a computer seemed to be negatively associated with CMRS among individuals in the medium and in the highest cardiometabolic risk group. Meaning that individuals with more time spent using a computer had a more favorable cardiometabolic profile, particularly in the group of individuals achieving a CMRS value of more than 50 % or 75 % of the observed sample of participants, respectively. After adjusting for leisure-time PA and time spent traveling in motor vehicles, the statistically significant association disappeared whereas the negative direction of the association remained. In contrast to these findings, the few studies examining using a computer and individual cardiometabolic factors and a cardiometabolic risk score reported a positive association indicating that less time spent using a computer seems to be associated with a more favorable cardiometabolic health profile.[40, 44, 49] Thus, different SBs may not influence the magnitude and direction of the association with clustered cardiometabolic risk in the same manner. Further research is needed in order to identify groups at risk and to examine how it relates to SB.

Reactivity and reproducibility of sedentary behavior and physical activity

In line with previous research, the data of paper 3 confirmed that individuals alter their behavior in the presence of an accelerometer.[63, 64, 66, 68, 69] In addition, the data revealed that AMR differentially influenced SB and PA in two measurement periods depending on the intensity level of PA. As shown by Baumann and colleagues analyzing the same sample of participants, individuals wearing an accelerometer appeared to replace SB with LPA.[68] Evidence of recent studies could show that LPA included standing and walking at a light pace, and therefore SB and LPA are highly correlated.[101, 110] Further, AMR seems to have had a similar impact on SB and LPA on repeated measurements, whereas MVPA does not appear to be affected by AMR. This might be because MVPA is performed less often and requires more planning than LPA. Thus, it has been argued that MVPA is less predictable on a day-to-day basis and requires more monitoring days to determine reproducible habitual behavior.[60, 111] This seems to be in contrast to the findings of paper 3 showing that the data of MVPA was the most reproducible of all outcomes because the ICC coefficient was proved to be the highest value of all other observed ICC coefficients. Hereby, the intra- and inter-individual variability in SB and PA depends on the characteristics of the study sample and therefore, might have influenced the ICC coefficient.[112]

Even though the results of paper 3 indicate the adequacy of a 7-day accelerometry monitoring to reproducibly measure SB and PA, it also highlights the importance of the accelerometer wear time. The value for the ICC coefficient of accelerometer wear time was the lowest of all outcomes. In terms of AMR, the systematic changes of accelerometer wear time differed in the magnitude between the repeated measurements. In this regard, providing clear instructions to constantly wear the device to provide valid data at each measurement time point seems to be of great importance for the compliance of participants over time.[113] As shown in previous studies, accelerometer wear time should be considered as a crucial confounder in data analysis of accelerometer data.[112, 114] However, AMR operationalized by a reactivity indicator could not be identified as a relevant confounder for the reproducibility of SB and PA data. The quantification of AMR by the slope factor as a reactivity indicator might just be one of several other ways to consider AMR in data analysis of SB and PA. Notwithstanding, data revealed that individuals change their behavior in the presence of an accelerometer. Therefore, future studies are required to identify other ways to quantify AMR to consider it as a confounder in SB and PA data analysis or to interpret conclusions drawn from data analysis.

4.2 Limitations

There are a number of limitations that have to be considered when interpreting the results of this thesis. First, the generalizability of the results of the papers may be limited due to selection bias. The proportion of individuals who declined to participate was around 50 % in both studies. Individuals who are more interested in their health or motivated to change their behavior are also more likely to participate in studies or interventions.[115] Further, results of recent studies in the sample of participants of study 1 or study 2 showed that females, current smokers, and lower educated individuals were less likely to participate.[116, 117] Thus, the findings of the papers may be biased. Second, different measurement methods to assess SB were applied across the three papers. According to the definition by the SBRN (figure 1), SB includes an energy expenditure component (≤ 1.5 METs) and a postural component (sitting, reclining, or lying).[5, 13] The hip-worn accelerometer (ActiGraph) that was used to analyze SB in the context of cardiovascular health research in paper 1 and 3 cannot differentiate well enough between sitting and standing still because movement is determined by acceleration rather than body posture.[118] Event though it might be important to consider all behaviors across the energy expenditure spectrum, the assessment of the energy expenditure component is underrepresented in the data of paper 1 and 3.[101] Further, an accelerometer cannot accurately capture types of activities, such as bicycling, and it cannot be used to assess activities, such as swimming. Therefore, the magnitude of SB may have been overestimated. In paper 2, self-reported questionnaire data were used to analyze SB. While the assessment of self-reported data might be sensitive to recall bias and social desirability, it also provides information on the contexts where SBs occured.[9] Both measurement methods of SB have advantages and disadvantages. Thus, researchers must be aware of sources of error related to each method to increase the validity and reproducibility of data.[119] A useful combination of both measurement methods is recommended in order to receive the most comprehensive SB information.[120] Third, the underlying studies were not originally designed for measuring associations between SB and health or AMR. Hence, the results may suffer from a lack of power to identify generalizable results. In order to account for this problem, relevant confounders such as PA, sociodemographic, or variables related to data collection such as season, were considered for data analysis. Other confounding variables such as sleep duration, drinking and eating habits, environmental, or work-related variables, however, were not. Fourth, data of paper 1 and 2 was based on cross-sectional analyses. Thus, no conclusions about causal inference between SB and cardiovascular and cardiometabolic health can be drawn.

4.3 Implications and future directions

Due to the complex nature of SB with multiple domains, dimensions, and correlates, future studies should address the methodological challenges[121] while the feasibility of measurements, especially regarding the burden certain measurement pose for study participants, should be considered. The acceptance of measurement methods among individuals of the target group as well as of the measurement regime should be examined due to participation rate and compliance.[111, 112, 122]

An accurate measurement of SB is essential to examine associations with health outcomes, to design and evaluate effective behavior change interventions, and to inform a large proportion of the population who is at risk of cardiovascular and cardiometabolic diseases.[119, 123] SB is embedded in a temporal, social, environmental, and individual context. Therefore, overall time spend in SB should be assessed thoroughly as well as information on life domains such as occupational or leisure, and multiple types of SB such as watching TV or socializing. As shown in figure 1, SB is one group of activities throughout a day. Next to SB, PA intensities and sleep behavior should also be assessed in future research. Spent time in one group of activities means that no other activity can be conducted.[18] Therefore, analytical methods are required to handle multibehavioral data within 24 hours of one day.[20] First studies using the approach of compositional isotemporal substitutions models showed that the substitution of SB with sleep, standing, LPA, or MVPA respectively is associated with health benefits.[18, 40, 124-128] Those effects were most pronounced among less active or less physically fit adults. Therefore, interventions should target all behaviors and particularly encourage individuals who are classified as high sedentary and low active to replace SB with LPA.[8, 22, 126] Irrespective of the fact that replacing SB with MVPA is most beneficial for cardiovascular and cardiometabolic health,[13] individuals spend little time in PA on a moderate-to-vigorous level per day. Thus, substitution of SB with LPA might be a more-feasible behavioral modification strategy to archive health benefits and to initiate other behavioral changes.[18, 22, 129]

An important piece in completing the translational puzzle from research to public health recommendations regarding SB is missing. Currently, the evidence is insufficient to define quantitative guidelines.[20] In order to ensure high quality of SB data without neglecting individuals effort to comply with the measurement regime, future research has to generate consensus on the definition, measurement, and analysis of SB data. Further research is needed to examine how many days of monitoring SB are required to accurately assess SB and to identify most appropriate measurement methods.[111, 130] In addition, measurement periods in terms of duration and frequency as well as numbers of methods used to assess SB should be balanced to identify potential intervention effects. As shown in previous research, individuals alter their behavior due to simply wearing a device, AMR can interact with interventions by masking or diminishing their effects.[61, 64] SB research should consider these aspects and focus on generating more high-quality evidence on the impact of SB on health outcomes in the long term.[20, 121] Until then, it seems appropriate to advise the public to 'sit less AND move more at any intensity level' to improve cardiovascular and cardiometabolic health.[20, 131]

4.4 Conclusions

In conclusion, the present thesis highlights the importance of SB in the field of cardiovascular and cardiometabolic research. Individuals are sitting for different purposes and durations in multiple life domains. Time spent in SB is accumulated in different patterns over time resulting in various implications for cardiovascular and cardiometabolic health. SB might prove to be an essential and independent contributor to health behavior that should be considered when addressing health behavior changes in general, and particularly, cardiovascular and cardiometabolic health. Thereby, an adequate assessment of SB is essential when considering associations between SB and individual's health, independently from other health behaviors. Human-related sources of bias such as AMR should be taken into account when either planning studies or when interpreting data drawn from analysis of SB data.

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APPENDIX

Scientific papers

The author's contribution to the scientific papers

Eidesstattliche Erklärung

List of publications

Scientific papers

Ullrich A, Baumann S, Voigt L, John U, van den Berg N, Dörr M, Ulbricht S: Patterns of accelerometer-based sedentary behavior and their association with cardiorespiratory fitness in adults. *Scandinavian journal of medicine & science in sports* 2018, 28:2702-9.

Ullrich A, Voigt L, Baumann S, Weymar F, John U, Dörr M, Ulbricht S: A cross-sectional analysis of the associations between leisure-time sedentary behaviors and clustered cardiometabolic risk. *BMC Public Health* 2018, 18:327.

Ullrich A, Baumann S, Voigt L, John U, Ulbricht S: Reactivity and reproducibility of accelerometer-based physical activity and sedentary behavior in two measurement periods. *Scandinavian Journal of Science & Medicine in Sports* 2019; (*under review*).

Paper 1

Ullrich A, Baumann S, Voigt L, John U, van den Berg N, Dörr M, Ulbricht S: Patterns of accelerometer-based sedentary behavior and their association with cardiorespiratory fitness in adults. *Scandinavian journal of medicine & science in sports* 2018, 28:2702-9.

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ORIGINAL ARTICLE

WILEY

Patterns of accelerometer-based sedentary behavior and their association with cardiorespiratory fitness in adults

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We aimed to identify patterns of sedentary behavior (SB) and examined whether cardiorespiratory fitness differs between classes with distinct patterns of SB. One hundred and seventy participants (57% women, mean age = 56.4 years) received accelerometry monitoring for 7 days. Prior to accelerometry assessment, cardiorespiratory fitness was assessed by peak oxygen uptake (VO_{2peak}). VO_{2peak} was directly measured during a symptom-limited cardiopulmonary exercise testing on a cycle ergometer. Patterns in accelerometer data were classified based on time spent in SB per day using growth mixture modeling. Model-implied class-specific VO_{2peak} means were compared using adjusted equality test of means. Growth mixture modeling revealed four patterns of SB: "High, stable" (n = 120, M = 724.9 min/d), "Low, increase" (n = 14, M = 622.2 min/d), "Low, decrease" (n = 11, M = 540.2 min/d), and "High, decrease" (n = 25, M = 694.8 min/d). Persons in class "High, stable" had significantly lower VO_{2peak} values (M = 25.0 mL/kg/min, SD = 0.6) compared to persons in class "Low, increase" (M = 30.5 mL/kg/min, SD = 3.6; P = 0.001), in class "Low, decrease" (M = 30.1 mL/kg/min, SD = 5.0; P = 0.009), and in class "High, decrease" (M = 29.6 mL/kg/min, SD = 5.9; P = 0.032). No differences among the other classes were found. We identified four classes of individuals with distinct patterns of SB and showed that VO_{2peak} partially differs between classes. Especially, individuals with stable high SB levels throughout the week might be addressed in public health recommendations and interventions.

KEYWORDS
fitness, latent class analysis, objective measure, sedentary patterns

1 | INTRODUCTION

Sedentary behavior (SB) as a modifiable risk factor for cardiovascular disease and all-cause mortality, independent of physical activity levels,[1] has emerged as an important public health problem.[2] Recent studies in adults showed that higher levels of sitting time per day were associated with lower cardiorespiratory fitness (CRF).[3,4] Further, sedentary breaks and average sedentary bout duration were found to be associated with CRF.[5] Results from other studies that evaluated the association between SB and CRF using objective measures or self-reported measures of SB were inconsistent.[6-8]

Low levels of CRF are known to be one of the leading risk factors of cardiovascular health.[9,10] A meta-analysis of 33 studies showed that each one metabolic equivalent unit increase in CRF was associated with a 13% and 15% reduction in all-cause mortality and cardiovascular events, respectively.[9] Reducing the amount of daily sedentary time, for example, by breaking up prolonged sedentary time and replacing it with low-intensity activities such as standing may have considerable implications for cardiovascular health.[3,11]

According to Young et al,[2] identifying patterns of SB can help to understand who is at risk of cardiovascular health within a population and is therefore a key research issue. General descriptions, such as the average duration of sedentary time in minutes per day, were often used to measure SB. However, the operationalization of SB as a one-dimensional measure and the assumption that a single regression line adequately represents the association of SB and CRF ignore potential differences in patterns in which sitting time is accumulated and how these patterns may influence the magnitude of CRF. A growth mixture modeling approach is a data-driven reduction process to identify homogeneous classes based on similar characteristics and patterns of a behavior like sitting. Thus, using growth mixture modeling can help to represent the multidimensionality of SB data more accurately.

So far, three studies have identified five to seven patterns of accelerometer-based SB in an adult general population using latent class analysis[12] and examined their associations with health-related outcomes.[13,14] Adults classified in the most sedentary class were older, had a higher body mass index and a history of chronic disease,[14] and were at higher risk of all-cause mortality[13] compared with people in the least sedentary class. All studies are based on the data of the National Health and Nutrition Examination Survey (NHANES). To our knowledge, no study has included CRF as a health-related outcome and analyzed its association with day-to-day patterns of SB.

In the present explorative study, we aimed to identify accelerometer-based patterns of SB by using a growth mixture modeling approach in apparently healthy adults. Further, we examined if CRF differs between groups with distinct patterns of SB.

2 | METHODS

2.1 | Participants and procedure

Persons aged 40-75 years were recruited in general medical practices, job agencies, or via a statutory health insurance company between June 2012 and December 2013 in northeast Germany. All participants provided informed written consent prior to participation. The study was approved by the clinical ethical committee of the University Medicine Greifswald, Germany (protocol number BB41/12).

Sample selection was conducted stepwise.[15,16] A total of 1165 individuals participated in a self-administered computerized cardiovascular risk screening (step 1). Of these, 706 participants (61%) were eligible for a subsequent examination program addressing cardiovascular health (step 2). Eligibility criteria were: no history of cardiovascular event (myocardial infarction, stroke), no previous vascular intervention, no diabetes mellitus as well as self-reported body mass index ≤ 35 kg/m^2, no previous Methicillin-resistant Staphylococcus aureus infection, and resident in a predefined zip-code area. Among those who had been invited, 582 individuals (82%) participated in the cardiovascular examination program including cardiopulmonary exercise testing using a cycle ergometer. Accelerometry was offered as an optional assessment (step 3). Among all invited people (n = 470), 235 individuals (50%) agreed to receive accelerometry monitoring. Study participants were instructed to wear the accelerometer on their hip with an elastic band for seven consecutive days outside of any water-based activities, starting the day following the cardiovascular health examination program. Among those who agreed to wear the accelerometer, half of the subjects were asked to wear the accelerometer for 24 hours a day (scheme "day and night"). The other half was instructed to wear the accelerometer after getting up in the morning and to put it off before going to sleep (scheme "day only").[17] Participants were informed that physical activity would be recorded for 7 days. Eleven participants were excluded from analysis due to missing accelerometer data (n = 224).

2.2 | Measures

2.2.1 | Cardiorespiratory fitness

CRF reflects the functional ability of the cardiorespiratory system of an individual.[10] It was assessed by peak oxygen uptake (VO_{2peak}) achieved on a cycle ergometer (Ergoselect 100; Ergoline, Bitz, Germany) via standardized cardiopulmonary exercise testing according to a modified Jones protocol (stepwise increase in work load of 16 W/min, starting with unloaded cycling plus the ergometer-related permanent load).[18,19] All tests were continued as symptom-limited (volitional exertion, dyspnoea, or fatigue) in the absence of chest pain and electrocardiography abnormalities. Prior to the test, patients were encouraged to reach maximal exhaustion, while during exercise no further motivational interventions were utilized. Respiratory gas exchange variables were measured continuously using a VIASYS Healthcare system (Oxycon Pro or Rudolph's mask; VIASYS GmbH, Hoechberg, Germany). Unfortunately, additional variables to quantify physical exertion like lactate levels were not available. VO_{2peak} was defined as the highest ten-second average of oxygen uptake in the last minute of exercise relative to body mass (mL/kg/min; milliliters of oxygen per kilogram body weight per minute). All exercise tests were performed by certified study staff based on established standard operating procedures.[19]

2.2.2 | Accelerometer-based sedentary behavior

To assess SB, a triaxial ActiGraph Model GT3X+ accelerometer (Pensacola, FL) was used. The accelerometer was initialized at a sampling rate of 100 Hertz, and raw data were integrated into 10-second epochs to capture more accurate data. ActiGraph accelerometer captured acceleration using counts as the output metric.[12] To interpret counts, it is recommended to use cut points according to different intensity-threshold criteria. In our study, data from the vertical axis were used and SB was defined by values <100 counts per min.[20] For analysis of SB, data from the accelerometers were downloaded and processed using ActiLife software (Version 6.13.3; ActiGraph). Time spent in SB was determined by min/d.

For standardization, the data were limited to daily accelerometer wear time between 6:00 AM and 12:00 PM according to Dyrstad et al,[6] resulting in a maximum wear time of 1080 min/d. In addition, to account for valid SB patterns during the week as well as on weekends, we analyzed data only among those who have worn the accelerometer for 7 days, with 1 day indicating ≥480 minutes of accelerometer wear time.[12] Thus, the final sample comprised 170 participants.

2.2.3 | Covariates

Sex and age were obtained by a self-administrative questionnaire. Accelerometer-based SB patterns have shown to be associated with season[21] and accelerometer wear time.[12] Thus, season (spring/summer/autumn/winter) and wear time (min/d) were included as covariates. Non-wear time was calculated by the Troiano algorithm, defined as at least 60 consecutive minutes of zero activity intensity counts, with allowance for ≤2 minutes of counts between 0 and 100.[22]

2.3 | Statistical analyses

To identify a number of distinct classes of individuals who tend to accumulate their minutes of accelerometer-based SB in a similar pattern, a growth mixture modeling approach[23] was chosen. A maximum likelihood estimator with robust standard errors was used. Time spent in SB on each of the 7 days of the measurement week was represented by 7 observed indicators. Latent growth factors based on these indicators were used to model trajectories of SB over the course of a week. SB data was square root transformed to account for their left-skewed distributions. The observed indicators were regressed on the growth factors using linear regression. The shape of the growth curves was determined by time scores defined in the measurement model of the growth factors and matched with the observed day number of the measurement week. To specify nonlinear growth curves, quadratic and cubic slopes of time scores were added to the models. Rescaled Likelihood Ratio Tests[24] were used to test whether higher order functions of time scores and free growth factor variances were required.

With the growth mixture modeling approach, unobserved classes underlying the growth factors are represented by a categorical latent variable. To determine the optimal number of trajectory classes that adequately represent the heterogeneity in the population, a forward procedure[25] was performed. The procedure was guided by various model fit criteria: (a) the Akaike Information Criterion (AIC[26]) and (b) the adjusted Bayesian Information Criterion (aBIC[27]) that balance fit and parsimony of a model, with lower values indicating a better model fit. Furthermore, (c) class sizes,[28] (d) entropy

TABLE 1 Descriptive characteristics of the study sample (n = 170)

	M/%	SD
Sociodemographic variables		
Age, years	56.4	9.5
Sex		
Female	57.1	
Education		
<10 y	12.4	
10-11 y	65.3	
>11 y	22.3	
Accelerometer variables		
Wearing time, min/d	933.5	103.6
Sedentary behavior, min/d	677.8	108.3
Monday, min/d	682.9	125.3
Tuesday, min/d	679.1	129.8
Wednesday, min/d	676.8	136.8
Thursday, min/d	679.5	121.6
Friday, min/d	679.5	129.4
Saturday, min/d	663.6	147.8
Sunday, min/d	683.5	142.6
Cardiorespiratory fitness		
VO_{2peak}, mL/kg/min	26.9	6.4
Other variables		
Recruitment setting		
General practice	34.1	
Job center	16.5	
Health insurance company	49.4	
Season		
Spring	8.8	
Summer	18.8	
Autumn	67.1	
Winter	5.3	

M, mean; SD, standard deviation; VO_{2peak}, peak oxygen uptake.

with values ≥0.80 indicating adequate classification,[29] and (e) the Bootstrapped Likelihood Ratio Test (BLRT) were considered. BLRT has been shown to be a consistent indicator of the optimal number of classes. Models with one to five classes were explored.

To increase the probability of finding the optimal number of classes, the latent class variable was regressed on sex, age, and season of data collection. Accelerometer wear time was included as time-varying covariate that was specified to predict SB at the corresponding day of measurement.

To analyze the association between class membership of participants based on patterns of SB and CRF as the continuous distal outcome, a measurement-error weighted approach for stepwise latent class modeling[30] was used. Right-skewed VO_{2peak} data were square root transformed to approximate normality. Class-specific mean values of VO_{2peak} were compared by using adjusted equality test of means (chi-square tests). Our study has an explorative rather than a confirmatory character. Accordingly, no power calculation was conducted. *P*-values below 0.05 were considered statistically significant. Statistical analyses were performed using Mplus version 7.31.[24]

3 | RESULTS

3.1 | Characteristics of participants

Descriptive characteristics of the study sample are shown in Table 1. Analysis of included (n = 170) and excluded participants (n = 54) showed no differences in sociodemographic, setting, or season variables and CRF. On average, participants wore the accelerometer for 933.5 min/d and

TABLE 2 Models with one to five classes: Model fit indices (AIC, aBIC), entropy, and class sizes for model-implied mean trajectories of time spent in sedentary behavior over 7 consecutive days of measurement

	One-class solution	Two-class solution	Three-class solution	Four-class solution	Five-class solution
AIC	4006	3964	3957	3948	3948
aBIC	4005	3962	3955	3946	3947
Entropy	1.00	0.89	0.80	0.82	0.76
C1, n (%)	170 (100)	154 (91)	26 (15)	120 (71)	56 (33)
C2, n (%)		16 (9)	13 (8)	14 (8)	77 (45)
C3, n (%)			131 (77)	11 (6)	10 (6)
C4, n (%)				25 (15)	18 (11)
C5, n (%)					9 (5)

aBIC, adjusted Bayesian Information Criterion; AIC, Akaike Information Criterion; C, Class.
Latent class models with quadratic growth curves. Intercept and linear slope variances were freely estimated. Variances of quadratic slopes were fixed to zero. Linear slope variances were not held equal across classes.

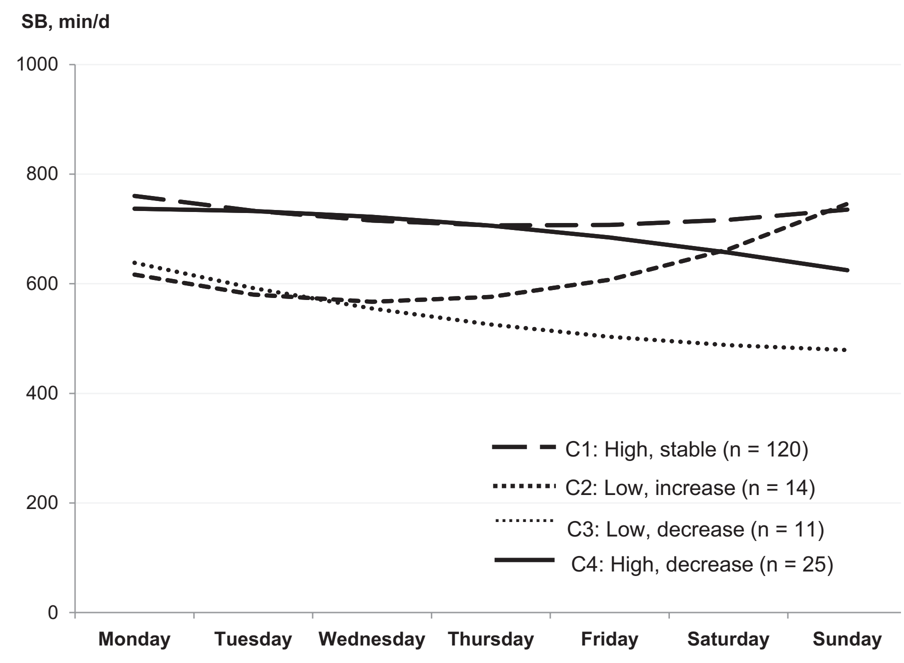

FIGURE 1 Four-class solution: Class sizes for model-implied mean trajectories of time spent in sedentary behavior over seven consecutive days of measurement. Latent class models with quadratic growth curves. Intercept and linear slope variances were freely estimated. Variances of quadratic slopes were fixed to zero. Linear slope variances were not held equal across classes. For illustration and reasons of interpretability, SB data were back-transformed. C, Class; SB, Sedentary behavior

TABLE 3 Four latent classes derived from accelerometer data (n = 170): Class sizes (n/%), model-implied mean values of sedentary behavior (min/d) over 7 consecutive days of measurement, model-implied means and standard deviations of peak oxygen uptake (mL/kg/min), chi-square, and *P*-values of class differences according to peak oxygen uptake

	n	%	Monday, min/d	Tuesday, min/d	Wednesday, min/d	Thursday, min/d
Class 1—High, stable	120	71	760.3	732.9	715.1	706.6
Class 1 vs 2						
Class 1 vs 3						
Class 1 vs 4						
Class 2—Low, increase	14	8	616.4	580.4	567.1	575.9
Class 2 vs 3						
Class 2 vs 4						
Class 3—Low, decrease	11	6	638.0	592.3	555.0	525.6
Class 3 vs 4						
Class 4—High, decrease	25	15	736.7	732.5	722.2	706.1

For illustration and reasons of interpretability, sedentary behavior, and peak oxygen uptake (VO_{2peak}), data were back-transformed.
M, Mean; SD, Standard deviation; VO_{2peak}, Peak oxygen uptake.
[a]Based on robust standard errors.

spent 677.8 min/d in SB. The mean of VO_{2peak} was 26.9 mL/kg/min.

3.2 | Identified sedentary behavior patterns

Models with one to five classes were explored (Table 2). Based on model fit criteria (AIC, aBIC, class sizes, and BLRT) and entropy, we decided to select the four-class model for further analysis.

As shown in Figure 1 and Table 3, participants in class 1 showed stable amounts of SB across the week (labeled "High, stable"). This class had the largest proportion of participants with a mean of 724.9 min/d spent in SB. Participants in class 2, class 3, and class 4 showed SB that varies across the week. Persons in class 2 (labeled "Low, increase") were characterized by increasing values of SB with the highest values on weekends. They spent on average 622.2 min/d in SB. The SB pattern observed in the minority of participants (class 3) was labeled "Low, decrease." Persons in this class spent on average 540.2 min/d in SB and were characterized by low values of SB at the beginning of the week and decreasing values with the lowest values on weekends. The mean of SB of participants in class 4 (labeled "High, decrease") was 694.8 min/d, and persons in this class were characterized by decreasing values of SB with the lowest values on weekends.

3.3 | Differences in cardiorespiratory fitness between sedentary behavior patterns

Table 3 shows model-implied means and standard deviations of VO_{2peak} for the four classes. The adjusted equality test of means across classes revealed a significant overall difference with a value of $\chi^2 = 17.5$ ($P < 0.001$). Post-hoc tests showed that persons in class "High, stable" had significantly lower VO_{2peak} values compared to persons in class "Low, increase," in class "Low, decrease," and in class "High, decrease." No differences between the mean values of VO_{2peak} among the other classes were found (Table 3).

4 | DISCUSSION

There are two main findings of our study. First, we identified four distinct subgroups of individuals who showed different day-to-day patterns of accelerometer-based SB over a week. Second, persons in class "High, stable" had significantly lower mean values of VO_{2peak} compared to individuals in the other three classes.

Our results are in line with previous studies that examined associations between the total amounts of time spent in SB or SB pattern variables and CRF.[3-5,7] Other studies found that there were no differences in SB between participants with high CRF and participants with low CRF assessed by maximal oxygen uptake,[6] no association between SB and CRF among moderately or vigorously physically active participants,[7] or no additionally explained significant variance in VO_{2peak} by SB.[8] To our knowledge, this is the first study that analyzed whether CRF differs between classes of accelerometer-based patterns of SB using growth mixture modeling. Using patterns of SB improves the understanding of how SB accumulates over time and how this is associated with CRF. Thus, the present study adds to the literature by showing that persons with stable high levels of SB throughout the week

Friday, min/d	Saturday, min/d	Sunday, min/d	Overall, min/d	VO_{2peak}, $M \pm SD$	Chi-square values	P-values[a]
707.0	716.6	735.4	724.9	25.0 ± 0.6		
					10.8	0.001
					6.7	0.009
					4.6	0.032
607.1	662.7	745.6	622.2	30.5 ± 3.6		
					0.0	0.884
					0.1	0.735
503.3	487.9	479.0	540.2	30.1 ± 5.0		
					0.0	0.857
684.2	657.0	624.7	694.8	29.6 ± 5.9		

had lower CRF compared to individuals with other patterns of SB across the week. CRF did not differ among those other classes.

In the present study, we identified SB patterns similar to those found in previous research.[12] Our results showed that a large proportion of study participants were classified into a pattern of SB that represents relatively stable high levels of SB throughout the week. Persons in this most sedentary class called "High, stable" spent on average 67% of the observed time in SB. In comparison with this class, individuals in the other classes showed SB that varies across the week. Accelerometer-based patterns of SB emerged that were characterized by a higher amount of SB on weekends compared to weekdays. This "Low, increase" class is comparable to a pattern known as "Weekend couch potato."[12] Individuals in class "High, decrease" and in class "Low, decrease" were characterized by a lower amount of SB on weekends compared to weekdays. This SB pattern is comparable to a physical activity pattern known as "Weekend warrior."[31]

Our findings on the number of identified classes of accelerometer-based SB in an apparently healthy adult population using the growth mixture modeling approach are slightly different from previous studies.[12-14] In contrast to the NHANES studies that identified five to seven patterns of accelerometer-based SB, we decided to select the four-class model.

Interpreting the results, it should be taken into account that the derived SB patterns might be driven by specific types of SB, such as occupational SB. As shown among nationally representative adult samples from 32 European countries, occupational SB may explain lower odds of being in less sedentary latent classes.[32] Occupational and leisure-time SB may have different health effects due to different patterns of sitting accumulation (eg, duration and repetitiveness) or the context in which SB occurs.[14,33] Furthermore, recent studies have found that leisure-time SB had stronger effects on cardiorespiratory and cardiometabolic health compared to occupational SB.[33,34] To distinguish between accelerometer-based SB at the workplace and SB in leisure-time, future studies should capture self-reported records of daily working hours and use these data as an additional confounder to identify patterns of SB. How much time individuals spend sitting at the workplace and what kind of work they do can furthermore be taken into account as it may influence SB in their leisure-time. Moreover, the usual manner individuals get to work should be considered in future studies. Especially, prolonged time spent sitting in cars has shown to be associated with a more adverse cardiometabolic risk profile.[35]

The present study has five limitations that merit discussion. First, the proportion of people who declined to participate in accelerometry was high (50%) and a selection bias is likely. A previous study investigating non-participation in accelerometry in our sample found that, for example, women were more likely to decline participation than men.[16] Thus, our findings may not be generalizable to the population as a whole. Second, we used hip-worn accelerometers that may not accurately capture all types of physical activity, such as bicycling, or miss other activities, such as swimming. Further, inactivity (eg, sleeping) after 6:00 AM or before 12:00 PM was considered to be sedentary time. Therefore, the magnitude of SB may have been overestimated in our study. Third, the sample size and, thus, some of the derived classes are small. This might have limited the detection of further patterns of SB. Fourth, study participants agreed to accelerometry monitoring for seven consecutive days, but it is still unclear whether this period is sufficient to accurately assess patterns of SB.[13] In addition, participants were informed that physical activity would be recorded over the measurement period. The administration of accelerometry may have introduced reactivity among the study participants.[36] Reactive effects could be minimized by using a longer monitoring period. Therefore, the findings of our study should be verified using a larger sample of adults, a longer accelerometer wearing time, and stratification by sociodemographic variables, such as age or sex. Finally, to examine whether SB is a stable behavior, studies are needed that measure SB at more than one point in time.

In conclusion, we identified four groups of individuals with distinct day-to-day patterns of SB and showed that CRF partially differs between these classes. Our study highlights the importance of decreasing the amount of time spent in SB, especially among individuals with stable high sedentary times throughout the week. Therefore, these individuals should be addressed in guideline recommendations and interventions that focus on reducing sitting time.

5 | PERSPECTIVES

Our findings may have important implications for future studies. Although there is evidence that both SB and CRF are associated with poor cardiovascular health, no public health recommendations regarding these two risk factors exist.[10,11] Our results showed that the magnitude of CRF partially differs between classes with distinct patterns of SB. Especially, individuals with stable high SB levels throughout the week might be addressed in public health recommendations and interventions.

Still, the problem remains that no conclusions about causality can be drawn. It needs to be clarified whether higher levels of sitting time cause lower cardiorespiratory fitness or vice versa. However, our data support the need for further studies in this field.

Evidence suggests a continuous dose-response association between sedentary time levels and the risk of cardiovascular disease. Significant risk for cardiovascular disease was observed within high levels of sedentary time (>10 h/d).[37] According to the data of SB throughout the week in three of our four classes (class 1:12 h/d; class 2:10.4 h/d; class 4:11.6 h/d), further studies should examine whether individuals in the classes differ regarding the risk of cardiovascular disease and cardiovascular mortality or regarding other cardiometabolic risk factors.

Furthermore, a population-based study of physical activity and SB patterns highlighted the important role of socioeconomic factors rather than personal factors, such as sex, age, marital status, smoking status, or body mass index.[38] Therefore, there is a great need to identify other modifiable risk factors for SB, from psychological characteristics through to environmental factors.[2]

In our study, we measured SB using accelerometry. Compared with device-derived measures, self-report questionnaires are known to be sensitive to recall bias and social desirability. On the other hand, questionnaires capture different aspects of SB because they provide information on the context.[2] For future studies, a combined use of questionnaires and accelerometers is recommended in order to receive the most comprehensive SB information.[39] Keeping in mind that SB includes multiple domains, dimensions, and correlates, there remain many methodological challenges of measuring SB.[40]

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Paper 2

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RESEARCH ARTICLE Open Access

A cross-sectional analysis of the associations between leisure-time sedentary behaviors and clustered cardiometabolic risk

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Abstract

Background: The aim of this study was to conduct a comprehensive investigation of the association between different types of leisure-time sedentary behavior (watching television, using a computer, reading and socializing) and clustered cardiometabolic risk in apparently healthy adults aged 40 to 65 years.

Methods: One hundred seventy-three participants from the general population (64% women; mean age = 54.4 years) consented to attend a cardiovascular examination program and to complete a questionnaire on leisure-time sedentary behaviors. Waist circumference, blood pressure, glucose, triglycerides, and high-density lipoprotein cholesterol of non-fasting blood samples were assessed, and a clustered cardiometabolic risk score [CMRS] was calculated. Data were collected between February and July 2015. Associations between leisure-time sedentary behaviors and CMRS were analyzed using linear and quantile regression, adjusted for socio-demographic variables and other types of leisure-time sedentary behavior (model 1) and additionally, adjusted for leisure-time physical activity and traveling in motor vehicles (model 2).

Results: Linear regression revealed that there was a positive association between watching television and CMRS (model 1: b = 0.27 [CI: 0.03; 0.52]; model 2: b = 0.30 [CI: 0.05; 0.56]). In addition, quantile regression analysis revealed that using a computer was negatively associated with the 50th (model 1: b = − 0.43 [CI: -0.79; − 0.07]) and the 75th percentiles (model 1: b = − 0.71 [CI: -1.27; − 0.14]) of CMRS. Reading and socializing were not associated with CMRS.

Conclusions: Watching television was positively associated with a clustered cardiometabolic risk score, while time spent using a computer revealed inconsistent findings. Our results give reason to consider different types of behaviors in which individuals are sedentary and the associations between these behaviors and cardiometabolic risk, supporting the need for behavior-specific assessments as well as public health recommendations to maintain or enhance adults' health.

Trial registration: Clinical trial registration number: NCT02990039, Retrospectively registered (December 12, 2016).

Keywords: Sedentary behavior, Cardiometabolic risk, Linear regression, Quantile regression, Metabolic syndrome, Multiple imputation

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Background

Sedentary behavior [SB], defined as any waking behavior characterized by an energy expenditure ≤ 1.5 metabolic equivalents while in a sitting or reclining posture [1], is highly prevalent [2]. Prevalence has increased as utilization of media technologies in leisure time has increased. Physical activity [PA] has decreased, both at work and in leisure time [3]. There is emerging evidence that changes in patterns of PA and SB are independently related to factors of cardiometabolic health including the metabolic syndrome [2, 4]. Meta-analysis data revealed that spending high amounts of time engaging in SB increased the odds of having the metabolic syndrome by 73% compared to spending low amounts of time engaging in SB [4].

The association between leisure-time SB and factors of cardiometabolic health depends on the type of SB and the age of individuals [5]. Many studies have focused on television [TV] time or time spent using a computer and their associations with cardiovascular health [2, 6]. Few studies have analyzed associations between other SBs such as reading or socializing in leisure time and cardiometabolic risk factors [7–12]. Time spent watching TV was found to be positively associated with obesity [10], type II diabetes [7], overweight [8, 9], or individual cardiometabolic biomarkers [10–12]. The evidence for using a computer in leisure time is inconsistent [7–12]. No associations have been found between other SBs such as reading or socializing in leisure time and cardiometabolic risk factors [7, 8].

A growing body of literature recommends using a cluster of continuous cardiometabolic risk factors instead of a binary definition of the metabolic syndrome [13, 14]. The reasons include (i) cardiovascular risk increases progressively with an increasing number of metabolic syndrome risk factors, and (ii) using a continuous risk score increases statistical power [14].

Current evidence has suggested that a greater increase in overall sedentary time is associated with a greater increase in clustered cardiometabolic risk in adults at high risk of developing type II diabetes [15] or in a population-based sample [16]. Nevertheless, to the best of our knowledge, no study has examined a broader range of screen-based and other leisure-time SBs and their associations with clustered cardiometabolic risk. One study has analyzed associations between SBs in leisure time and two clustered cardiometabolic risk scores over a 2-year follow-up period among adults at increased cardiometabolic risk [17]. A risk score of developing type II diabetes (Atherosclerosis Risk in Communities study) and a score of developing fatal cardiovascular disease (Systematic Coronary Risk Evaluation) was used. The findings suggested no associations between time spent watching TV, using a computer, or reading and individual cardiometabolic risk factors or clustered cardiometabolic risk scores [17].

Given the ubiquitous nature of prolonged SB in leisure time, a deeper understanding is needed about whether behaviors are associated with clustered cardiometabolic risk in order to develop adequate prevention strategies. The present study aimed to examine associations between leisure-time SBs (watching TV, using the computer, and playing computer games, reading, doing household tasks, caring for others, pursuing hobbies, and socializing) and clustered cardiometabolic risk in apparently healthy adults.

Methods

Selection of participants

Participants were recruited from a sample of 1165 individuals aged 40 to 75 years who had been recruited in general medical practices, job agencies, or via a health insurance company between June 2012 and December 2013 [18], and gave consent to be contacted again (95%). Of those, 513 persons fulfilled the following eligibility criteria: no history of cardiovascular event (myocardial infarction, stroke) or vascular intervention, age ≥ 40 and ≤ 65 years, self-reported body mass index ≤ 35 kg/m^2, and residency in a pre-defined zip-code area. A total of 401 persons were contacted and offered participation in a study that aimed to assess the feasibility of a tailored counselling letter intervention to increase PA and to reduce sedentary time.

Among those who had been offered study participation, 175 persons gave written informed consent and agreed to attend a cardiovascular examination program including the following: giving a blood sample, standardized measurement of blood pressure, waist circumference, body weight, and height at the study examination center, and completing a paper-pencil questionnaire on PA and leisure-time SB. Data were collected between February and July 2015. Two participants were excluded from analysis due to missing questionnaire or blood sample data. Our final sample comprised 173 adults (Fig. 1).

The study was approved by the clinical ethical committee of the University Medicine Greifswald (protocol number BB 002/15a).

Measures

Clustered cardiometabolic risk score

According to the definition of the American Heart Association and the National Heart, Lung, and Blood Institute [19], six cardiometabolic risk factors were assessed: waist circumference [WC], systolic blood pressure [SBP], diastolic blood pressure [DBP], glucose, plasma triglycerides, and high-density lipoprotein cholesterol [HDL-C].

WC was measured midway between the lowest rib and the iliac crest using an inelastic tape. Blood pressure was

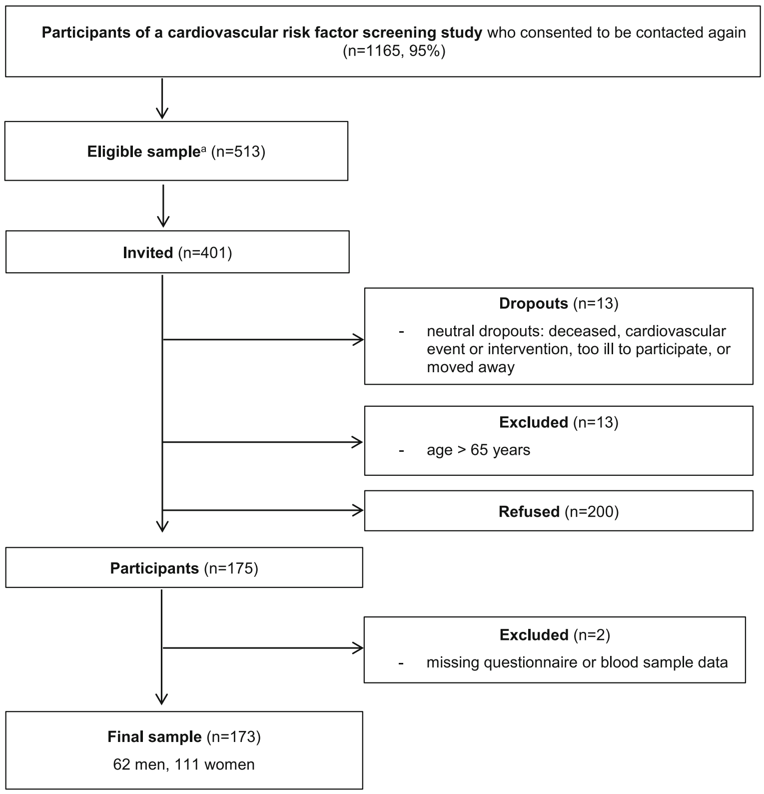

Fig. 1 Flow of participation. [a] Eligibility criteria: no history of cardiovascular event (myocardial infarction, stroke), or vascular intervention, body mass index ≤ 35 kg/m^2, residency in a pre-defined zip-code area, and age ≥ 40 and ≤ 65 years

measured after a five-minute resting period three times at the right arm in a seated position using a digital blood pressure monitor (705IT, Omron Corporation, Tokyo, Japan). The first and the second reading were followed by another resting period of 3 min each. For analyses, the means of the second and third measurements of SBP and DBP were used. If an antihypertensive medication within the last 12 months was reported, we added 10 mmHg to the original observed value of SBP and DBP [20]. Non-fasting blood samples were taken, and plasma triglycerides, HDL-C, and glucose were determined by standard methodology at the Institute for Clinical Chemistry and Laboratory Medicine of the University Medicine Greifswald. Values of plasma triglycerides were converted into corresponding fasting values by subtracting 3.7% of the triglyceride value per hour of non-fasting values. This calculation was made up to 8 h for men and up to 7 h for women [21].

The clustered cardiometabolic risk score [CMRS] was calculated according to Knaeps et al. [16] by the following method: glucose, triglycerides, and HDL-C were normalized ($\log_{10}$) due to their strongly skewed distributions. Each cardiometabolic variable was standardized by using sex-specific sample means and standard deviations [SD]. We standardized the scores of WC, SBP, DBP, glucose, triglycerides, and HDL-C. Because the standardized HDL-C is inversely related to metabolic risk, it was multiplied by − 1. CMRS was created by summing the standardized values of the six cardiometabolic risk factors and dividing the sum by 6 to account for the number of variables included. A higher CMRS indicates a higher cardiometabolic risk.

Sedentary behavior

We used a modified version of the "last 7-d sedentary behavior questionnaire" ([SIT-Q-7d], Section 5: Screen time and other activities) [22] to quantify the amount of time spent in different leisure-time SBs: watching TV, using a computer, playing computer games, reading, doing household tasks, caring for others, pursuing hobbies, and socializing. Because playing computer games was rarely present in our sample ($n = 25$), we summed time spent on using a computer and on playing computer games. Average time per day in hours (h/ day) was calculated.

Covariates

Sex, age, living in a partnership (yes/ no), and employment status (employed/ unemployed) were used as covariates. To account for other health-related confounders [2], leisure-time PA in Metabolic equivalent of task [MET]-hours per week and time spent traveling in a motor vehicle in minutes per day were assessed using the International Physical Activity Questionnaire [IPAQ] [23] and calculated according to the IPAQ protocol. The leisure-time domain includes walking, PA on a moderate-intensity level, and PA on a vigorous-intensity level. Especially prolonged time spent sitting in cars has shown to be associated with a more-adverse cardiometabolic risk profile [24]. Therefore, the single item of the IPAQ traveling in a motor vehicle was used as covariate.

Statistics

Descriptive participant characteristics (mean [M] with SD and median [Med] with interquartile range [IQR]) were calculated. Leisure-time SB and PA variables were square root transformed to account for their right-skewed distributions. The constant 1 was added to the original value in order to anchor the variables at a place where square root transformation will have the optimal effect [25].

We performed multiple imputation using chained equations (m = 20 imputed datasets) to account for missing values. The six cardiometabolic risk factors included in the outcome variable (CMRS), the predictor variables (watching TV, using a computer, reading, and socializing), socio-demographic covariates (sex, age, living in a partnership, and employment status), PA covariates (leisure-time PA and traveling in motor vehicles), and auxiliary variables (e.g., body mass index, total cholesterol, glycated hemoglobin, low-density lipoprotein cholesterol) were considered for imputation models. To handle skewed continuous variables, we used the predictive mean matching method in the imputation procedure [26].

For analyzing associations of leisure-time SB with CMRS, we applied ordinary least-squares [OLS] regression. In regard of heteroscedasticity, we used robust standard errors estimations. Furthermore, we applied quantile regression [QR]. This method is not influenced by outliers in the distribution of the outcome variable [27] and served to explore the association of different leisure-time SBs across the entire distribution of CMRS [28]. We examined associations of SB variables at the 25th, 50th, and 75th percentiles of CMRS.

For the OLS and QR analyses, adjustments were made for socio-demographics and for time spent in the other leisure-time SBs (model 1). Subsequently, we adjusted for time spent physically active in leisure time and for time spent traveling in motor vehicles (model 2). Additionally, OLS and QR analyses using complete cases of the leisure-time SB variables were calculated as a sensitivity analysis. All variables of OLS regression analyses were tested for normality and residuals were tested for homoscedasticity, linearity and independence. To diagnose multicollinearity, the variance inflation factor was calculated. Values over 5 were considered as an indication of multicollinearity [29]. *P*-values below 0.05 were considered statistically significant. Statistical analyses were performed using STATA v.14.1 software (Stata Corporation, College Station, TX) [30].

Results

Characteristics of participants

In our sample, the mean age was 54.4 years (SD = 6.2), 64% were women, 81% were employed, and 72% lived in a partnership (Table 1). The mean CMRS was – 0.0 (SD = 0.6) with a minimum value of – 1.3 and a maximum value of 1.6.

Leisure-time sedentary behaviors

Doing household tasks was reported by 53, caring for others by 36, and pursuing hobbies by 87 study participants. Thus, they were excluded from the analysis and we analyzed associations of time spent watching TV, using a computer, reading, and socializing in leisure time (n = 161, n = 112, n = 156, and n = 113, respectively, with values over zero) with CMRS.

In median, participants spent 2.5 h/ day (IQR: 1.8–3.5) watching TV, 0.4 h/ day (IQR: 0.1–1.0) using a computer, 0.5 h/ day (IQR: 0.4–1.0) reading, and 0.4 h/ day (IQR: 0.0–1.0) socializing during leisure time (Table 1).

Associations between leisure-time sedentary behaviors and clustered cardiometabolic risk score

In both models, OLS regression revealed that there was a positive association between watching TV and CMRS (model 1: b = 0.27 [*CI*: 0.03; 0.52]; model 2: b = 0.30 [*CI*: 0.05; 0.56]). As shown in Table 2, QR analysis revealed that watching TV was positively associated with the 25th (model 1: b = 0.35 [*CI*: 0.07; 0.63]; model 2: b = 0.34 [*CI*: 0.09; 0.59]), the 50th (model 1: b = 0.32 [*CI*: 0.02; 0.62], model 2: b = 0.37 [*CI*: 0.07; 0.66]), and the 75th percentiles (model 2: b = 0.32 [*CI*: 0.01; 0.63]) of CMRS. Furthermore, the 50th (model 1: b = – 0.43 [*CI*: -0.79; – 0.07]) and the 75th percentiles (model 1: b = – 0.71 [*CI*: -1.27; – 0.14]) of CMRS revealed a negative association with using a computer. These significant associations disappeared after additionally adjusting for time spent physically active in leisure time and for time spent traveling in motor vehicles (model 2, 50th percentile: b = – 0.28 [*CI*: -0.81; 0.24]; model 2, 75th percentile: b = – 0.55 [*CI*: -1.10; 0.01]). There were no statistically significant associations between reading or socializing and CMRS. OLS and QR analyses using complete cases of the leisure-time SB variables yielded similar results (see Additional file 1: Table S1).

Table 1 Descriptive characteristics of the study sample (n = 173)

Variables	Number	Missing data %	Values
Socio-demographic variables			
Age, years (M, SD)	173	–	54.4 ± 6.2
Gender (n, %)			
Female	173	-	111 (64.2)
Employed (n, %)	170	2	138 (81.2)
Partnership (n, %)	173	–	124 (71.7)
Cardiometabolic variables			
WC, cm (M, SD)	172	1	91.6 ± 12.5
SBP, mmHg (M, SD)	164	5	131.2 ± 16.1
DBP, mmHg (M, SD)	164	5	80.7 ± 11.0
Non-fasting glucose, mmol/l (Med, IQR)	163	6	5.3 (4.9–5.8)
HDL-C, mmol/l (M, SD)	167	3	1.4 ± 0.4
Plasma triglyceride, mmol/l (Med, IQR)	151	13	1.1 (0.7–1.7)
CMRS (M, SD)	170	2	−0.0 ± 0.6
Leisure-time sedentary behavior variables			
Watching TV, h/day (Med, IQR)	165	5	2.5 (1.8–3.5)
Using a computer, h/day (Med, IQR)	142	18	0.4 (0.1–1.0)
Reading, h/day (Med, IQR)	160	8	0.5 (0.4–1.0)
Household tasks, h/day (Med, IQR)	154	11	0 (0–0.1)
Caring for others, h/day (Med, IQR)	140	19	0 (0–0.1)
Hobbies, h/day (Med, IQR)	153	12	0.1 (0–0.4)
Socializing, h/day (Med, IQR)	151	13	0.4 (0–1.0)
Physical activity variables			
Leisure-time physical activity, MET-h/week (Med, IQR)	145	16	15.6 (3.3–33.1)
Traveling in motor vehicles, min/day (Med, IQR)	165	5	30 (10–60)

M mean, *SD* standard deviation, *Med* median, *IQR* interquartile range, *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HDL-C* high-density lipoprotein cholesterol, *CMRS* clustered cardiometabolic risk score, *TV* television, *MET* metabolic equivalent of task
Presented are means and standard deviations for normally distributed variables, medians and interquartile ranges for non-normally distributed variables, and absolute values and percentages for categorical variables

Discussion

There were two main findings of our study. First, watching TV was positively associated with CMRS. In addition, depending on the quantiles of CMRS, QR analysis revealed a negative association between computer time and CMRS. However, this association disappeared after adjusting for PA in leisure time and time spent traveling in motor vehicles. Second, no associations were present between reading or socializing and CMRS.

Our results suggest that study participants who spend higher amounts of time watching TV are at higher cardiometabolic risk than individuals with low levels of TV time. This association remained significant after adjusting for leisure-time PA and time spent traveling in motor vehicles. Furthermore, QR analyses revealed an association between computer time and CMRS that otherwise is hidden if using the mean of CMRS in OLS regression analysis. Among study participants in the medium and in the highest cardiometabolic risk group, higher amounts of time using a computer were associated with a more favorable cardiometabolic profile. However, this association disappeared after adjusting for leisure-time PA and time spent traveling in motor vehicles.

Our findings on associations between TV time and CMRS are in line with current evidence on associations between TV time and individual cardiometabolic risk factors [12, 10, 2]. Additionally, watching TV has been shown to be associated with lower energy expenditure [31], an increased intake of food with high energy density and overall unhealthy dietary habits [32, 33] compared with other sedentary activities such as using a computer. A combination of these factors may explain our findings [12, 10]. According to the QR result, time spent sedentary while using a computer may be differentially associated with CMRS. Whereas a population-based study suggested no association between using a computer in leisure time and individual risk factors of

Table 2 Results of linear and quantile regression of multiply imputed data (n = 173)

	OLS		QR25		QR50		QR75	
CMRS[a]	*b* [95% CI]	p^b	*b* [95% CI]	p^b	*b* [95% CI]	p^b	*b* [95% CI]	p^b
Watching TV								
Model 1[c]	0.27* [0.03; 0.52]	0.029	0.35* [0.07; 0.63]	0.015	0.32* [0.02; 0.62]	0.039	0.26 [−0.09; 0.62]	0.143
Model 2[d]	0.30* [0.05; 0.56]	0.021	0.34** [0.09; 0.59]	0.008	0.37* [0.07; 0.66]	0.015	0.32* [0.01; 0.63]	0.041
Using a computer								
Model 1[c]	− 0.35 [−0.70; 0.00]	0.051	−0.15 [−0.67; 0.18]	0.251	−0.43* [−0.79; − 0.07]	0.019	−0.71* [− 1.27; − 0.14]	0.015
Model 2[d]	− 0.26 [−0.65; 0.13]	0.188	−0.26 [−0.66; 0.13]	0.191	−0.28 [−0.81; 0.24]	0.277	−0.55 [−1.10; 0.01]	0.052
Reading								
Model 1[c]	− 0.07 [−0.57; 0.42]	0.766	− 0.18 [−0.71; 0.35]	0.502	−0.21 [−0.95; 0.53]	0.573	0.06 [−0.72; 0.83]	0.888
Model 2[d]	− 0.17 [−0.68; 0.34]	0.515	−0.36 [−0.84; 0.13]	0.145	−0.33 [−1.17; 0.50]	0.429	−0.04 [−0.77; 0.70]	0.922
Socializing								
Model 1[c]	− 0.08 [−0.38; 0.21]	0.578	0.07 [−0.33; 0.48]	0.718	−0.09 [−0.44; 0.26]	0.616	−0.26 [−0.72; 0.19]	0.255
Model 2[d]	− 0.06 [−0.37; 0.24]	0.687	0.08 [−0.23; 0.38]	0.619	−0.07 [−0.46; 0.31]	0.708	−0.20 [−0.64; 0.24]	0.374

OLS ordinary least squares regression, *QR* quantile regression, *b* unstandardized regression coefficient, *CI* confidence interval, *TV* television
[a] Presented are multiply imputed data using chained equations (m = 20 imputed datasets) to account for missing values
[b] Based on robust standard errors, ** $p < 0.01$, * $p < 0.05$
[c] Model 1: Adjusted for socio-demographic (sex, age, partnership, and employment) and other leisure-time sedentary behavior variables
[d] Model 2: Adjusted for socio-demographic (sex, age, partnership, and employment), leisure-time physical activity, traveling in motor vehicles, and other leisure-time sedentary behavior variables

cardiometabolic health [11], Heinonen et al. [10] reported a positive association between computer time and WC as well as body mass index among women but not among men in a middle-aged sample. In contrast to these studies, our results of QR revealed a negative association between using a computer and CMRS among individuals in the medium and in the highest cardiometabolic risk group. After adjusting for two PA variables, the statistically significant association between using a computer and CMRS disappeared whereas the negative direction of the association remained. Thus, different behaviors in which individuals spend their time in a sitting or reclining posture may not influence the magnitude and direction of the association with clustered cardiometabolic risk in the same manner.

Our second finding adds to the literature that there seems to be no association between reading and socializing and clustered cardiometabolic risk. This finding is in line with previous studies that examined associations between time spent sedentary while reading or socializing and individual cardiometabolic health factors [7–12, 17]. The less time spent reading or socializing in leisure time might be an explanation for the findings in our sample. In addition, accuracy to recall across contexts may vary [2] in the sense that it may be easier for people to remember how long they have watched TV than how much time they have spent reading or in company with others [34].

Furthermore, we found that leisure-time SBs differed in their frequency of occurrence. Time spent sitting while doing household tasks, caring for others, or pursuing hobbies were less prevalent in our sample. Evidence suggests that different types of SB often co-occur compared to activities with higher energy expenditure (over 1.5 metabolic equivalents) [22], e.g. using the computer or doing household tasks while watching TV. Thus, it is important to consider not only the frequency of occurrence but also that of co-occurrence of leisure-time SB and how different types of leisure-time SB are linked to one another. Future studies should examine those patterns of leisure-time SB in detail and might include separate analyses for weekdays and weekends, because leisure-time SB patterns have been shown to vary between weekends and weekdays [35].

Some limitations of our study have to be discussed. First, subjects were assessed within a study aiming to test the feasibility of a tailored letter intervention regarding PA and leisure-time SB. The proportion of people who declined participation (53%) was high and a selection bias is likely. Thus, our findings may not be generalizable to the population as a whole. Second, there may be confounding variables such as diet, drinking habits, different activity patterns with certain energy expenditure during leisure-time SBs, sleep duration, or cardiorespiratory fitness that were not considered in our study. Third, we collected blood samples in the non-fasted state. Because levels of glucose or HDL-C are influenced by external factors like caloric intake or muscle activity [36], this may have implications for the clustered cardiometabolic risk. Although using fasting blood samples is recommended, there is evidence that using non-fasting blood samples is appropriate for decision making in the context of primary preventions regarding cardiovascular or cardiometabolic diseases [36, 37]. Fourth, we assessed leisure-time SB by self-report. Self-report assessments are sensitive to recall bias and social desirability [2]. In comparison to accelerometer measures of SB, self-report appears to capture different aspects of behaviors [38] because it provides information on the context. Keeping in mind that leisure-time SB is complex and includes multiple domains, dimensions, and correlates, there are still many methodological challenges of measuring leisure-time SB [39]. Finally, the design of our study does not allow for causal inference. To address this issue, more longitudinal studies are needed to understand the directionality of potential associations between leisure-time SBs and cardiometabolic health.

Conclusions

Watching TV was positively associated with a clustered cardiometabolic risk score, while results of time spent using a computer revealed inconsistent findings. No associations were present between reading or socializing and clustered cardiometabolic risk.

Our findings suggest that different leisure-time SBs and their differential associations with cardiometabolic risk should be considered. This approach would address the needs (i) for behavior specific assessments, (ii) to develop relevant public health recommendations and guidelines to maintain or enhance adults' health, and (iii) to encourage environmental and policy initiatives and interventions [2].

Additional file

Additional file 1: Table S1. Results of linear and quantile regression of complete cases. (DOCX 20 kb)

Abbreviations

CI: Confidence interval; CMRS: Clustered cardiometabolic risk score; DBP: Diastolic blood pressure; HDL-C: High-density lipoprotein cholesterol; IPAQ: International physical activity questionnaire; IQR: Interquartile range; M: Mean; Med: Median; MET: Metabolic equivalent of task; OLS: Ordinary least-squares regression; PA: Physical activity; QR: Quantile regression; SB: Sedentary behavior; SBP: Systolic blood pressure; SD: Standard deviation; SIT-Q-7d: Last 7-d sedentary behavior questionnaire; TV: Television; WC: Waist circumference

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Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

FW, UJ, MD, and SU contributed to the conception or design of the study. All authors contributed to the acquisition, analysis, or interpretation of data for the work. AU drafted the manuscript. LV, SB, FW, UJ, MD, and SU critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of work, thus ensuring integrity and accuracy.

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.
This study was approved by the clinical ethical committee of the University Medicine Greifswald, Germany (protocol number BB 002/15a) and retrospectively registered to the ClinicalTrials.gov Protocol Registration and Results System (Clinical trial registration number: NCT02990039). Informed written consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Paper 3

Ullrich A, Baumann S, Voigt L, John U, Ulbricht S: Reactivity and reproducibility of accelerometer-based physical activity and sedentary behavior in two measurement periods. *Scandinavian journal of medicine & science in sports* 2019; (*under review*).

Reactivity and reproducibility of sedentary behavior and physical activity in two measurement periods

Running title: Reactivity and reproducibility of SB and PA

Original article

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Abstract

Objectives: The aims of the study were to investigate measurement reactivity in sedentary behavior (SB), physical activity (PA), and accelerometer wear time in two measurement periods, to examine the reproducibility of these outcomes and to quantify measurement reactivity as a confounder for the reproducibility of SB and PA data.

Methods: A total of 136 participants (65% women, mean age = 54.6 years, study period 02/2015 to 08/2016) received 7-day accelerometry at baseline and after 12 months. Latent growth models were used to identify measurement reactivity in each period. Intraclass correlations (ICC) were calculated to examine the reproducibility using two-level mixed-effects linear regression analyses.

Results: At both measurements periods, participants increased time spent in SB (b=2.3 min/d; b=3.8 min/d), reduced time spent in light PA (b=2.0 min/day; b=3.3 min/d), but did not change moderate-to-vigorous PA. Participants reduced accelerometer wear time (b=4.6 min/d) only at baseline. The ICC coefficients ranged from 0.42 (95% CI=0.29-0.57) for accelerometer wear time to 0.70 (95% CI=0.61-0.78) for moderate-to-vigorous PA. In none of the regression models, a reactivity indicator was identified as a confounder for the reproducibility of SB and PA data.

Conclusions: The results show that measurement reactivity differentially influences SB and PA in two measurement periods depending on the intensity level of PA. Although 7-day accelerometry seems to be a reproducible measure of SB and PA, our findings highlight the importance of accelerometer wear time as a crucial confounder when using accelerometry in monitoring SB and PA or planning interventions.

Clinical trial registration number: NCT02990039 (retrospectively registered); December 12, 2016

Keywords: sitting position, physical health, exercise, accelerometry, measurement reactivity, adults

1. Introduction

In order to determine the level of sedentary behavior (SB) and physical activity (PA), to understand their relationship with health, and to evaluate the efficacy of behavioral interventions, an accurate measure of SB and PA is required.[1] This is challenging because both behaviors are characterized by considerable inter- and intraindividual variability.[2] Day-to-day variability around a mean level is a natural part of SB and PA and is described as the habitual level of SB and PA of an individual.[3, 4] This behavioral variability needs to be carefully studied because it has major implications for measurement and conclusions, drawn from data analysis.[4]

Accelerometry is frequently used to assess SB and PA. The reproducibility of accelerometer-based measures is subject to human-related sources of bias.[5] Participants can influence accurate data measurement by changing their behavior when wearing an accelerometer, even if they do not intend to do so.[6] The motivation to be physically more active than usual due to wearing such a device or social desirability may be reasons for the presence of accelerometer measurement reactivity (AMR).[7] So far, the evidence on AMR among adults is inconsistent.[8-14] Few studies investigated the influence of AMR on the entire intensity spectrum from SB to moderate-to-vigorous PA (MVPA).[14] To our best knowledge, none of these studies has examined whether and to what extent AMR occurs in more than one measurement period.

The vast majority of studies applied a 7-day accelerometry protocol to determine habitual levels of SB and PA.[15] However, this approach raises the question whether this length of monitoring protocol is sufficient to reflects the mean level on the entire intensity spectrum from SB to MVPA, as reliable data depend on the variability within a person's daily activity pattern,[3] especially for more than one measurement period.[16] Moreover, the potential impact of AMR on the reproducibility of SB and PA data was not investigated so far.

Therefore, the present study has two aims. First, to examine AMR over two measurement periods indicated by systematic changes in SB, light PA (LPA), MVPA, and accelerometer wear time. Second, to investigate the reproducibility of these outcomes and to quantify whether AMR should be considered as a relevant confounder to estimate the reproducibility of SB and PA data.

2. Methods

Study participants: From a sample of 1165 individuals aged between 40 and 70 years who had been recruited in general medical practices, job agencies, or via a health insurance company between June 2012 and December 2013, 95% gave written consent to be contacted again. Of those, a total of 401 persons were offered participation in a randomized-controlled study that aimed to assess the feasibility of a brief tailored letter intervention to increase PA and to reduce SB in leisure time. The design and participant flow were described in detail elsewhere.[17]

SB, LPA, and MVPA were measured with accelerometry at baseline (n = 175) and after 12 months (n = 165, 94%). Two participants at each measurement period were excluded due to missing accelerometer data (excluded, n = 4). In addition, we analyzed data only among those who have worn the accelerometer ≥ 10 hours per day on ≥ 5 days including at least one weekend day (excluded, n = 24). The final sample size comprised 136 participants.

Procedure: At baseline and after 12 months, all participants underwent the following procedure: (1) Cardiovascular health program including blood sample taking and standardized measurement of blood pressure, waist circumference, body weight, and height at the cardiovascular examination center of the University Medicine Greifswald. (2) Self-administered assessments of socio-demographics, SB, and PA. (3) Wearing an accelerometer for seven consecutive days. Study participants were instructed to wear the accelerometer on their right hip with an elastic band, to start the day after the cardiovascular health program in the morning after getting dressed, and to take it off during night's sleep and water activities. All participants were informed that PA would be recorded for seven days. (4) Protocolling daily working hours over the monitoring period.

After baseline assessments, participants were randomized into an assessment-only group (n = 85) or an intervention group (n = 90). Additionally, for all participants, self-administered assessments of SB and PA were conducted at month 1, 3, 4, and 6 after baseline. Only individuals of the intervention group received up to 3 letters tailored to their self-reported SB and PA at month 1, 3, and 4. The study was conducted between February 2015 and August 2016 and was approved by the clinical ethical committee of the University Medicine Greifswald (protocol number BB 002/15a).

Measures: Accelerometer-based data were assessed using a tri-axial ActiGraph Model GT3X+ accelerometer (Pensacola, FL). The accelerometers were initialized at a sampling rate of 100 Hertz and raw data were integrated into 10-second epochs. Data from the vertical axis were used. For statistical analysis, data from the accelerometers were downloaded and processed using ActiLife software (Version 6.13.3; ActiGraph).

Time spent in SB, LPA, MVPA, and wearing the accelerometer was determined by minutes per day (min/day). Non-wear time was calculated by the Troiano algorithm, defined as at least 60 consecutive minutes of zero activity intensity counts, with allowance for ≤ 2 minutes of counts (counts/min) between 0 and 100. To identify the time spent in different intensities of PA, we used cut points according to different intensity threshold criteria.[18] Values < 100 counts/min were determined as SB, values between 100 and 2019 counts/min as LPA, and values ≥ 2020 counts/min as MVPA.

Sex, age, and years of school education (< 10 years/ 10 to 11 years/ ≥ 12 years) were obtained by a self-administrative questionnaire. In addition, study group (assessment-only group/ intervention group), time (baseline/ after 12 months), recruitment site (general practice/ job center/ health insurance), first day of measurement (weekday/ weekend day)[19], season of data collection (winter/ spring/ summer)[20], and the average number of working hours[4] on each day the accelerometer was worn were included as covariates.

Statistical analyses: We decided to include data from both study groups as all participants received almost the same assessment procedure, the feasibility study was not powered to detect differences between assessment-only group and intervention group, and previously published data revealed that there were no differences in self-reported PA and SB between groups after 12 months.[17]

SB, LPA, and accelerometer wear time were approximately normally distributed, thus untransformed values were used for analyses. To account for their right-skewed distributions, MVPA data were square root transformed. For all analyses, p-values below 0.05 were considered statistically significant.

Latent growth models were used to investigate AMR for both measurement periods.[21] In line with Baumann et al [14], time spent in SB, LPA, MVPA, and wearing the accelerometer on each of the seven days of measurement was represented by seven observed indicators of these continuous latent variables (growth factors). The indicators were regressed on latent growth factors representing trajectories of outcomes over a week.[21] A maximum likelihood estimator with robust standard errors was used. The shape of the growth curves was determined by time scores defined in the measurement model of the growth factors and matched with the observed day number of the measurement week. To specify nonlinear growth curves, an overall change function (e.g., linear, quadratic, cubic) was fitted to the sample by adding quadratic and cubic slopes of time scores to the models. Rescaled Likelihood Ratio Tests[22] were used to test whether higher order functions of time scores and free growth factor variances were required. Accelerometer wear time and working hours may have been taken into account as time-varying covariates that were specified to predict outcomes at the corresponding day of measurement. Non-zero time trends in the outcomes over the days of measurement would imply reactivity. In the models, the slope factor was freely estimated if appropriate and treated as a reactivity indicator reflecting the individual average change in outcome over time. Therefore, the factor scores of outcomes were saved and included as a reactivity indicator in further analysis. Statistical analyses were performed using Mplus version 7.316.[22]

For each outcome, the average of the 7 days of measurement was calculated. Two-level (individual and time) mixed-effects linear regression analyses were performed to assess changes in accelerometer-based outcomes from baseline to 12 months apart, including a random intercept for subjects. All regression models were adjusted for sex, age, education, study group, time, recruitment site, first day of measurement, and season of data collection. In addition, we added the individual average value of accelerometer wear time, the reactivity indicator of accelerometer wear time, the reactivity indicator of the respective SB and PA outcome, and a combination of these factors as potential covariates step-by-step.

We used intraclass correlation (ICC) coefficients to decide which model for each outcome was most appropriate. The ICC is a measure of reproducibility of replicate measures from the same subject.[23] The ICC coefficient is classified as follows: less than 0.4 indicates poor, between 0.4 and 0.75 fair to good, and 0.75 or more excellent reproducibility.[23] To illustrate the agreement between both measurement periods and to estimate the limits of agreement interval (95% Confidence Interval, CI), Bland Altman plots were applied. Statistical analyses were performed using Stata/ SE version 14.2.[24]

3. Results

Sample characteristics: In our sample, the mean age was 54.6 years and 65.4% were women. The majority of the participants attended school 10 to 11 years (70.4%). Table 1 provide data on time spent in SB, LPA, and MVPA and wearing the accelerometer from baseline to 12 months.

- *Table 1* -

Accelerometer measurement reactivity: As shown in Figure 1, at baseline and after 12 months, participants increased time spent in SB by 2.3 min/day and by 3.8 min/day and reduced time spent in LPA by 2.0 min/day and by 3.3 min/day, respectively. Neither at baseline nor after 12 months participants significantly changed time they spent in MVPA. Participants significantly reduced the accelerometer wear time by 4.6 min/day at baseline. After 12 months, participants did not significantly change accelerometer wear time. The reactivity indicators of accelerometer wear time ($p < 0.001$), SB ($p = 0.008$), and LPA ($p = 0.006$) significantly differed from baseline to 12 months apart. Results of baseline and after 12 months parameter estimates for latent growth models of SB, LPA, MVPA, and accelerometer wear time are shown in additional file 1 (Tables S1/ S2).

- *Figure 1* -

Reproducibility of accelerometer-based outcomes: The ICC (95% CI) ranged from fair to good reproducibility of the outcomes; coefficient values lied between 0.41 (0.28, 0.56) for accelerometer wear time and 0.70 (0.61, 0.78) for LPA (Table 2). The regression model additionally adjusted for the average value of accelerometer wear time was most appropriate for SB (ICC = 0.68), for LPA (ICC = 0.68), and for MVPA (ICC = 0.70). For accelerometer wear time, none of the additional adjustments were appropriate (ICC = 0.42).

- *Table 2* -

The Bland Altman plots visualize the agreement between the two measurement periods, as a function of the mean of these two measurement periods (Figure 2). For accelerometer wear time values of ten participants (7.4 %), for SB values of nine participants (6.6 %), for LPA values of eleven participants (8.1 %), and for MVPA values of four participants (2.9 %) lied outside the limits of agreement.

- *Figure 2* -

Using the most appropriate regression model for each outcome, neither the time spent in SB, LPA, MVPA, nor accelerometer wear time significantly declined or increased over time (Table 3). In all SB and PA regression models, the average value of accelerometer wear time was a significant confounder.

- *Table 3* -

4. Discussion

The present study has two main findings. First, there was a significant linear trend in SB and LPA time series as an indicator of AMR for baseline and 12 months apart, whereas MVPA does not seem to be affected by AMR. Further, the systematic changes within accelerometer wear time differed between the two measurement periods. Second, our results showed that the time spent in SB, LPA, and MVPA and wearing the accelerometer are fairly stable between the two measurement periods. AMR operationalized by a reactivity indicator could not be identified as a relevant confounder for the estimation of the reproducibility of SB and PA data.

In line with previous literature, the results of the present study indicate that persons change SB and PA in the presence of an accelerometer.[9, 10, 12-14] This study adds to the literature by showing that AMR differentially influences SB and PA in two measurement periods depending on the intensity level of PA. In line with Baumann and colleagues, participants appeared to replace SB with LPA.[14] In addition, this study showed that the trend of both time series seems to be the same over the two measurement periods. Evidence in recent studies showed that LPA includes standing and walking at a light pace, and therefore logically tends to be more related to SB activities than MVPA.[25] Moreover, adults may know the current PA recommendations and they may not move enough.[6] Therefore, attempts are made to reduce this potential discrepancy when wearing a device,[7] and mostly replace SB with LPA. For behavioral interventions, it can be assumed that AMR has a similar impact on SB and LPA over time. The best advice for reducing bias due to AMR is to consider this in the planning of the study.[26] In case of brief interventions, measurement periods in terms of duration and frequency as well as number of methods used to assess SB and PA should be balanced to identify potential intervention effects.

Furthermore, our results showed that MVPA seemed to be less altered by AMR than SB and LPA. This could be because of MVPA typically requires more planning and is likely to be more structured than lighter physical activities. Furthermore, the ICC coefficient value showed that MVPA was the most reproducible of all outcomes using a 7-day accelerometry monitoring. This seems to be in contrast to recent findings. It has been argued that MVPA is less predictable on a day-to-day basis and requires more monitoring days to determine reproducible habitual behavior.[3, 4] Further, a recently published study that examined the reproducibility in accelerometer-assessed SB and PA reported the highest ICC values for SB.[16] It should be mentioned that in both studies the samples differed from our sample. While Kozey-Keadle and colleagues investigate reproducibility in older adult women with a mean age of 71 years, Bergman used a convenience sample consisting of younger university students and staff.[3, 16] It should be noted that ICC coefficients are constrained by the sample in which it was collected, because the magnitudes of intra- and inter-individual variability in SB and PA depends on the characteristics of the study sample.[27] Although the results reported in this study indicate that a 7-day accelerometry monitoring seems to be a reproducible measure of SB and PA, Bland Altman plots showed that there is a high variability in SB and PA. Therefore, the findings should be interpreted with caution and future studies are required to verify the findings of the present study using a larger sample of adults.

Our findings on accelerometer wear time highlight the importance of this factor. In terms of AMR, the systematic changes in time of wearing the accelerometer differed in the magnitude between the repeated measurements. Further, the lowest ICC coefficient value was found for accelerometer wear time compared to the SB and PA ICC coefficient values. In this regard, providing clear instructions to constantly wear the device to provide valid data at each measurement time could be helpful to enhance the compliance of participants over time.[28] Accelerometer wear time was the only relevant predictor in all SB and PA regression models, whereas AMR operationalized by a reactivity indicator could not be identified as a relevant confounder for the reproducibility of PA and SB data. In line with other studies, this indicates that accelerometer wear time should be considered as a crucial confounder in data analysis of accelerometer data.[27, 29]

Some limitations have to be discussed. First, the study was not designed to address AMR and therefore, our findings may suffer from a lack of power to examine AMR. Second, generalizability of our results may be compromised due to selection bias. Our sample was highly motivated and compliant, with an average wear time of 13 hours per day. As reactivity may be most pronounced in people with a high motivation to change behavior, AMR may have been overestimated in our study. Third, we used hip-worn accelerometers that cannot differentiate between sitting and standing still because movement is determined by acceleration rather than body posture.[30] Thus, our findings regarding SB and LPA can give a distorted picture on AMR. Finally, using the slope factor as a reactivity indicator to operationalize AMR is just one of several other ways to account for AMR for estimating the reproducibility of SB and PA data.

In conclusion, individuals seems to change their behavior in the presence of an accelerometer, with AMR differentially influence SB and PA in two measurements periods, 12 months apart. Although a 7-day accelerometry monitoring seems to be a reproducible measure of SB and PA, our findings highlight the importance of accelerometer wear time as a crucial confounder when using accelerometer in monitoring SB and PA or planning interventions.

5. Perspectives

The findings of the present study may have important implications for researchers planning and analyzing studies using accelerometer-based SB and PA data. For studies that aimed to reduce SB and increase PA, it can be assumed that over time AMR seems to have a similar impact on SB and light PA in two measurement periods, whereas moderate-to-vigorous PA does not appear to be affected by AMR. Further, accelerometer wear time should be considered as a crucial confounder in data analysis because it may influence potential interventional effects in different ways over time. To reduce AMR and, on the other hand, increase the precision of the measurement, a longer measurement period may be reasonable. Although a longer measurement period might improve reproducibility, the burden for study participants and study feasibility should be considered because it influences the response rate and compliance.[27]

The results of the reproducibility of SB and PA data showed that there are activity-specific differences. Moreover, SB and PA occur in multiple separate contexts such as work or leisure time and this seems to have different impact of the reproducibility of SB and PA data. Thus, variability in daily movement behavior depends on the characteristics of the observed population.[4] Using only one accelerometer to capture SB and PA cannot measure the context in which movement behavior is occur. It is therefore important to combine objectively measured (e.g., combinations of different placements of accelerometer) and self-reported SB and PA data in future studies.[31, 32]

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Table 1. Descriptive characteristics of the study sample (n = 136)

	Baseline	After 12 months*
Socio-demographic variables		
Age (years) (M ± SD)	54.6 ± 6.3	
Sex, n (%)		
Women	89 (65.4)	
School education, n (%)		
< 10 years	7 (5.2)	
10-11 years	95 (70.4)	
≥ 12 years	33 (24.4)	
Variables related to data collection		
Recruitment site, n (%)		
General practice	54 (39.7)	
Job center	24 (17.6)	
Health insurance company	58 (42.7)	
First day of measurement, n (%)		
Weekday	113 (83.1)	107 (78.7)
Season, n (%)		
Winter	9 (6.6)	7 (5.2)
Spring	118 (86.8)	120 (88.2)
Summer	9 (6.6)	9 (6.6)
Working hours, h/day (M ± SD)	4.1 ± 3.0	3.5 ± 3.0
Accelerometer-based variables, min/day (M ± SD)		
Accelerometer wear time	880.8 ± 85.9	864.8 ± 93.6
Sedentary behavior	602.6 ± 96.6	593.8 ± 99.2
Light physical activity	230.9 ± 60.1	227.5 ± 57.9
Moderate-to-vigorous physical activity	47.3 ± 24.4	43.5 ± 23.0

M, mean; SD, standard deviation; min, Minutes; h, hours. * One participant with missing values on accelerometer-based variables.

Table 2 Results of intraclass correlation values for different multilevel mixed-effects linear regression models for minutes of sedentary behavior, light physical activity, moderate-to-vigorous physical activity, and accelerometer wear time (n = 136).

	SB (95% CI)	**LPA** (95% CI)	**MVPA** (95% CI)	**Accelerometer wear time** (95% CI)
Basic model [a]	0.58 (0.46, 0.69)	0.65 (0.55, 0.75)	0.70 (0.60, 0.78)	**0.42 (0.29, 0.57)**
Add [b]: Average wear time	**0.68 (0.58, 0.76)**	**0.68 (0.58, 0.77)**	**0.70 (0.61, 0.78)**	-
Add [b]: Reactivity indicator of wear time	0.58 (0.47, 0.69)	0.66 (0.56, 0.75)	0.69 (0.60, 0.78)	0.41 (0.28, 0.56)
Add [b]: Reactivity indicator of physical activity	0.57 (0.45, 0.68)	0.64 (0.54, 0.74)	- [c]	-
Add [b]: Average wear time and reactivity indicator of physical activity	0.66 (0.55, 0.75)	0.68 (0.58, 0.76)	- [c]	-
Add [b]: Average wear time and reactivity indicator of wear time	0.68 (0.58, 0.76)	0.68 (0.58, 0.78)	0.70 (0.61, 0.78)	-
Add [b]: Average wear time, reactivity indicator of wear time, and reactivity indicator of physical activity	0.66 (0.55, 0.75)	0.68 (0.58, 0.76)	- [c]	-

SB = Sedentary behavior, LPA = Light physical activity, MVPA = moderate-to-vigorous physical activity, CI = Confidence Interval. Notes: Results of models with the highest intraclass correlation (ICC) values were highlighted in bold letters. ICCs were estimated using multilevel mixed-effects linear regression analysis with data of baseline and 12 months after entered in the models. [a] Adjusted for sex, age, school education, first day of measurement, season of data collection, and recruitment site. [b] Additionally adjusted for average of accelerometer wear time and the reactivity indicators for accelerometer wear time and physical activity if appropriate, [c] Growth mixture modeling revealed no results for minutes per day of MVPA when linear slope variances were freely estimated. Therefore, no results of intraclass correlation values for a reactivity indicator of MVPA can be presented in linear regression modeling with multilevel mixed-effects.

Table 3 Results of multilevel mixed-effects linear regression models for minutes of sedentary behavior, light physical activity, moderate-to-vigorous physical activity, and accelerometer wear time (n = 136).

	SB		**LPA**		**MVPA**		**Accelerometer wear time**	
	β [95% CI]	*p*	*β* [95% CI]	*p*	*β* [95% CI]	*p*	*β* [95% CI]	*p*
Study group (Ref. assessment-only group)	22.92 [-0.33, 46.18]	0.053	-22.94 [-41.75, -4.13]	0.017	0.15 [-0.51, 0.54]	0.955	7.93 [-22.21, 38.07]	0.606
Time (Ref. baseline)	9.50 [-4.52, 23.52]	0.184	2.84 [-8.41, 14.10]	0.620	-0.29 [-0.59, 0.01]	0.061	-20.13 [43.81, 3.54]	0.096
Study group x time	-8.78 [27.55, 10.00]	0.360	3.91 [-11.16, 18.98]	0.611	0.42 [0.01, 0.82]	0.043	8.9 [-23.41, 41.33]	0.588
Accelerometer wear time	0.72 [0.64, 0.80]	<0.001	0.20 [0.14, 0.27]	<0.001	0.00 [0.00, 0.01]	<0.001	-	

Notes: SB = Sedentary behavior; LPA = Light physical activity; MVPA = moderate-to-vigorous physical activity; *β*, Standardized regression coefficient; CI, Confidence interval; Interaction term (study group x time). All models were adjusted for sex, age, education, study group, time, first day of measurement, season of data collection, and recruitment site.

Figure 1. Estimated average linear growth curves for minutes spent in sedentary behavior (A), light physical activity (B), moderate-to-vigorous physical activity (MVPA) (C), and wearing the accelerometer (D) to baseline and after 12 months. Adjusted for accelerometer wear time and working hours if appropriate.

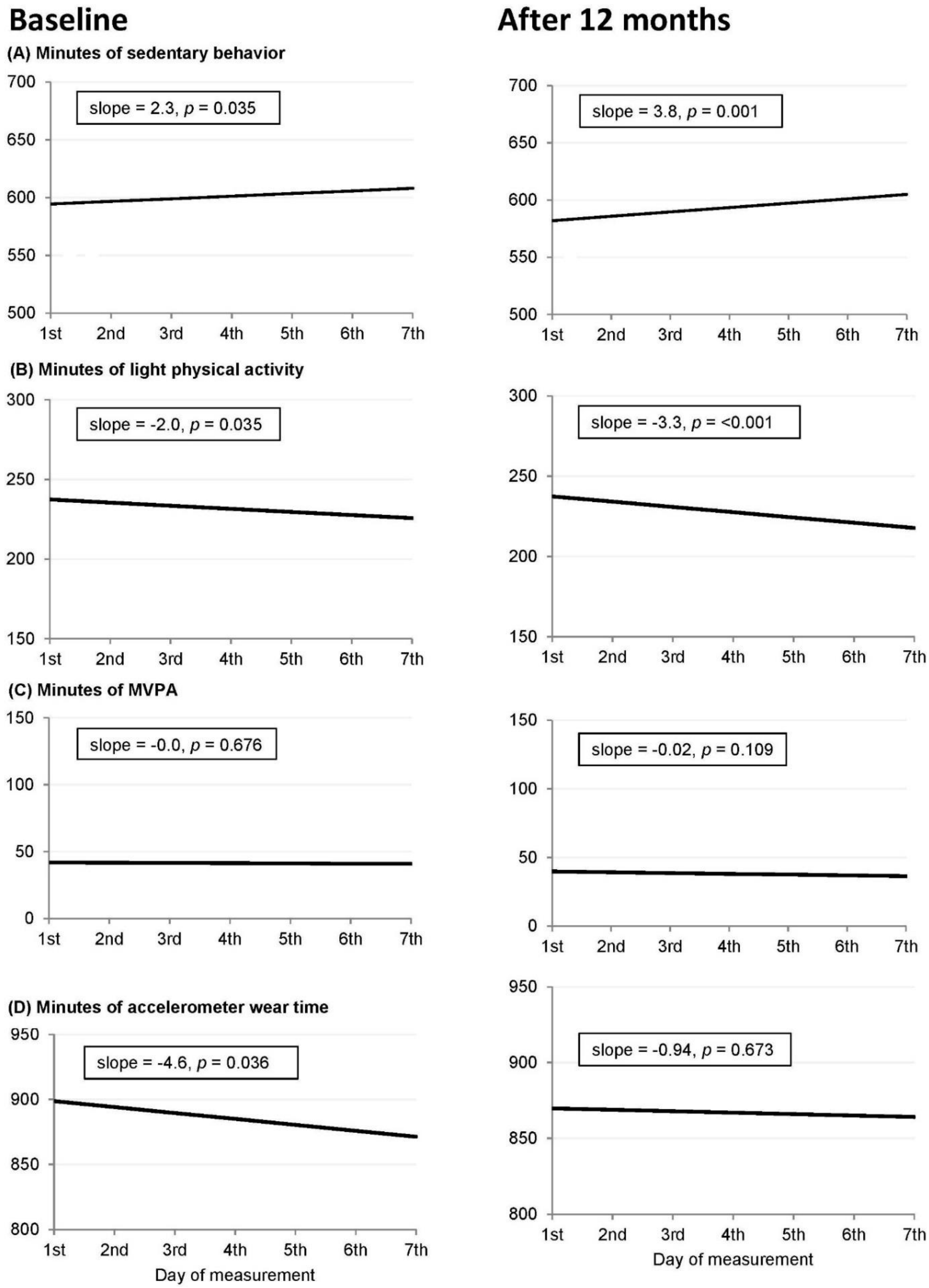
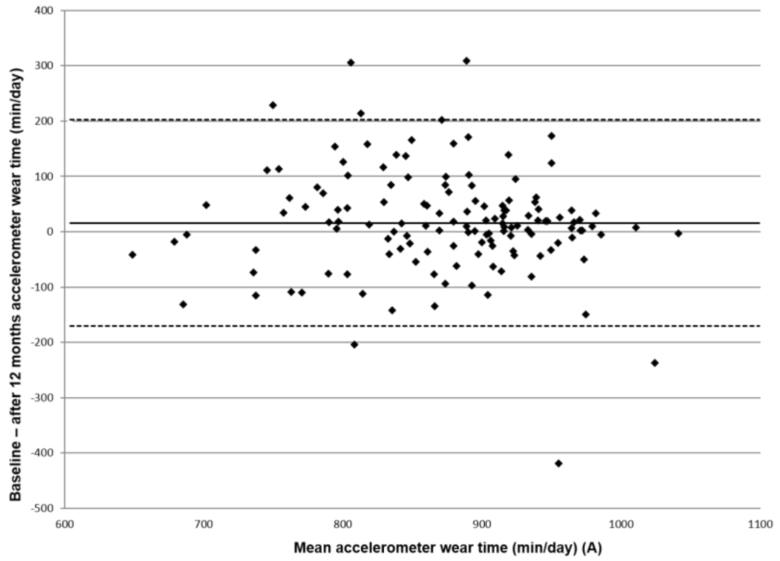
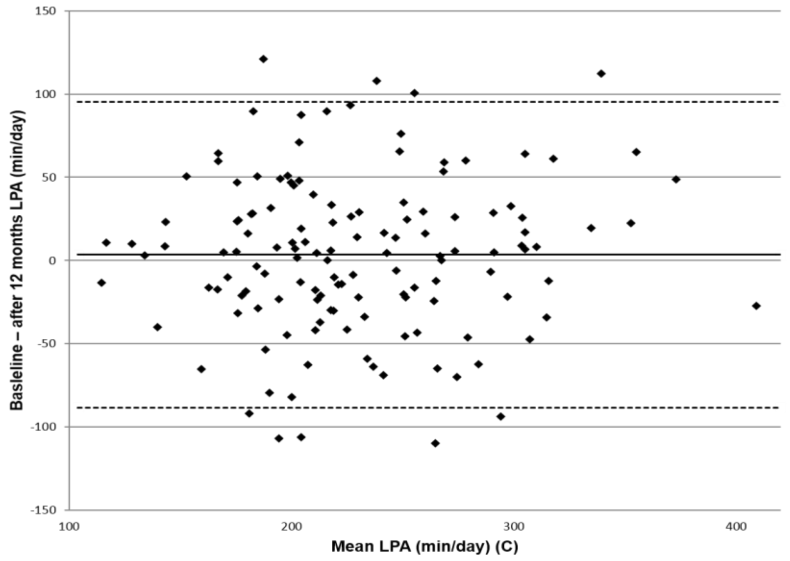
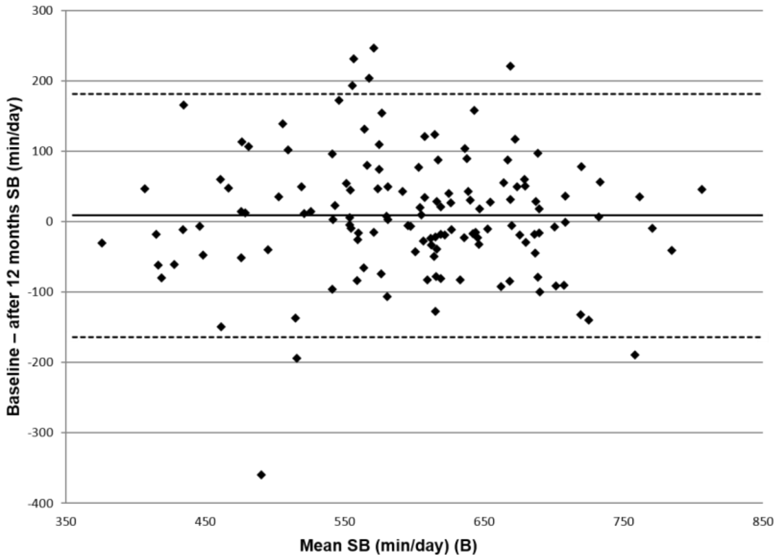
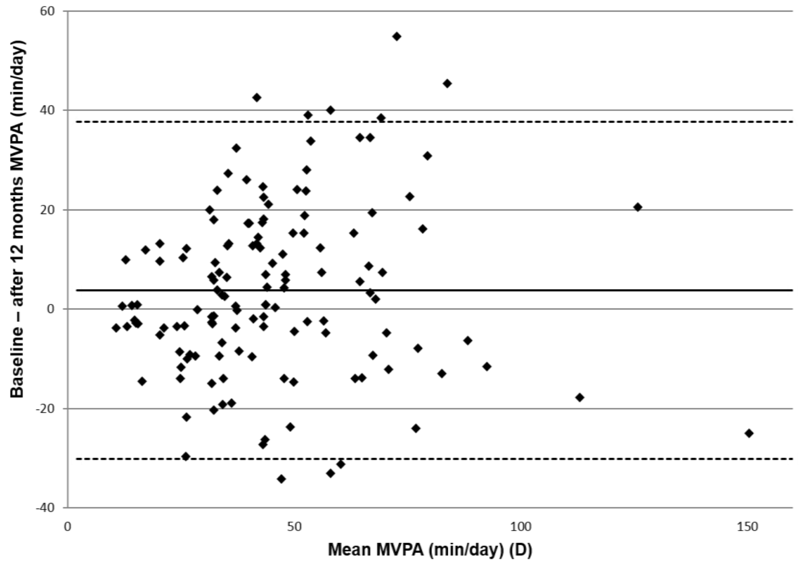

Baseline
After 12 months
(A) Minutes of sedentary behavior
slope = 2.3, p = 0.035
slope = 3.8, p = 0.001
(B) Minutes of light physical activity
slope = -2.0, p = 0.035
slope = -3.3, p = <0.001
(C) Minutes of MVPA
slope = -0.0, p = 0.676
slope = -0.02, p = 0.109
(D) Minutes of accelerometer wear time
slope = -4.6, p = 0.036
slope = -0.94, p = 0.673
1st
2nd
3rd
4th
5th
6th
7th
Day of measurement

Figure 2. Bland Altman plots of agreement for different outcome variables at baseline and after 12 months. Bland Altman plots for minutes spent wearing the accelerometer (A), in sedentary behavior (SB) (B), in light physical activity (LPA) (C), and in moderate-to-vigorous physical activity (MVPA) (D). The full line is the mean between baseline and after 12 months, whereas the dotted lines are in the 95% Confidence Interval.


Baseline – after 12 months accelerometer wear time (min/day)
Mean accelerometer wear time (min/day) (A)


Baseline – after 12 months LPA (min/day)
Mean LPA (min/day) (C)


Baseline – after 12 months SB (min/day)
Mean SB (min/day) (B)


Baseline – after 12 months MVPA (min/day)
Mean MVPA (min/day) (D)

Supplement files

S1 Table Baseline parameter estimates for latent growth models of accelerometer wear time, sedentary behavior, light physical activity, and moderate-to-vigorous physical activity (n = 136).

	Accelerometer wear time (min/day)[a]			**Sedentary behavior (min/day)**			**Light physical activity (min/day)**			**Moderate-to-vigorous physical activity (sqrt min/day)[b]**		
	Est.	(SE)	p	Est.	(SE)	p	Est.	(SE)	p	Est.	(SE)	p
Fixed effects												
Intercept	898.2	(9.0)	<0.001	594.5	(7.2)	<0.001	237.5	(6.1)	<0.001	3.7	(0.1)	<0.001
Linear slope	-4.6	(2.2)	0.036	2.3	(1.1)	0.038	-1.9	(0.9)	0.033	-0.0	(0.0)	0.676
Random effects ([co-] variances)												
Intercept	5199.7	(2446.4)		5849.4	(1429.9)		4166.9	(858.7)		0.2	(0.0)	
Linear slope	196.0	(150.5)		62.8	(27.5)		46.5	(19.7)		-		
Intercept & linear slope	-503.7	(536.9)		-334.8	(190.5)		-221.6	(116.3)		-		

Notes: Est. = estimate: mean (fixed effects), standard deviation (random effects: intercept, linear slope), correlation (random effects: intercept & linear slope), SE = standard error, – fixed at zero as indicated by rescaled likelihood ratio test. Models adjusted for working hours and accelerometer wear time if appropriate. a additionally calculated with a random effect of working hours b Growth mixture modeling revealed no results for minutes per day of moderate-to-vigorous physical activity (MVPA) when linear slope variances were freely estimated. Therefore, no results of random effects of linear slope of MVPA can be presented.

S2 Table Parameter estimates for latent growth models of accelerometer wear time, sedentary behavior, light physical activity, and moderate-to-vigorous physical activity after 12 months (n = 135).

	Accelerometer wear time (min/day)[a]			**Sedentary behavior (min/day)**			**Light physical activity (min/day)**			**Moderate-to-vigorous physical activity (sqrt min/day)[b]**		
	Est.	(SE)	p	Est.	(SE)	p	Est.	(SE)	p	Est.	(SE)	p
Fixed effects												
Intercept	869.8	(9.8)	<0.001	582.0	(7.1)	<0.001	237.4	(6.0)	<0.001	3.7	(0.1)	<0.001
Linear slope	-0.9	(2.2)	0.673	3.8	(1.2)	0.001	-3.3	(0.9)	<0.001	-0.0	(0.0)	0.109
Random effects ([co-] variances)												
Intercept	1938.5	(2013.2.6)		5111.6	(1001.2)		3704.3	(651.3)		0.2	(0.0)	
Linear slope	-106.4	(185.8)		63.1	(30.2)		37.3	(19.5)		-		
Intercept & linear slope	781.0	(519.2)		-282.2	(132.6)		-193.9	(89.7)				

Notes: Est. = estimate: mean (fixed effects), standard deviation (random effects: intercept, linear slope), correlation (random effects: intercept & linear slope), SE = standard error, – fixed at zero as indicated by rescaled likelihood ratio test. Models adjusted for working hours and accelerometer wear time if appropriate. a additionally calculated with a random effect of working hours b Growth mixture modeling revealed no results for minutes per day of moderate-to-vigorous physical activity (MVPA) when linear slope variances were freely estimated. Therefore, no results of random effects of linear slope of MVPA can be presented.

The author's contribution to the scientific papers

Table 3. The first author's contribution to the scientific papers

	Paper 1	**Paper 2**	**Paper 3**
Data acquisition	no	no	no
Data management/ cleaning	no	yes	yes
Data analysis	yes	yes	yes
Data interpretation	yes	yes	yes
Manuscript conception	yes	yes	yes
Writing draft/ revision	yes	yes	yes
Corresponding author	yes	yes	yes

Greifswald, 30.08.2019

Antje Ullrich

Eidesstattliche Erklärung

Hiermit erkläre ich, dass ich die vorliegende Dissertation selbstständig verfasst und keine anderen als die angegebenen Hilfsmittel benutzt habe.

Die Dissertation ist bisher keiner anderen Fakultät und keiner anderen wissenschaftlichen Einrichtung vorgelegt worden.

Ich erkläre, dass ich bisher kein Promotionsverfahren erfolglos beendet habe und dass eine Aberkennung eines bereits erworbenen Doktorgrades nicht vorliegt.

Greifswald, 30.08.2019

Antje Ullrich

List of publications

Peer-reviewed papers

Voigt L, **Ullrich A**, Siewert-Markus U, Dörr M, John U, Ulbricht S: Visualization of intensity levels to reduce the gap between self-reported and directly measured physical activity. *Journal of Visualized Experiments* 2019; 145: e58997.

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Ullrich A, Mittag O, Garbrecht M, Dibbelt S, Glattacker M: Partizipative Zielvereinbarung in der Rehabilitation (ParZivar II): Evaluation einer Intervention bei Patienten mit chronischen Rückenschmerzen [Collaborative Goal Setting in Rehabilitation (ParZivar II): Evaluation of an Intervention in Patients with Chronic Back Pain]. *Die Rehabilitation* 2015; 54: 317-324.

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Nagl M, **Ullrich A**, Farin E: Verständlichkeit von Patientenschulungen in der orthopädischen Rehabilitation: Qualitative Erhebung bei Rehabilitanden und Schulungsleitern [Comprehensibility of patient education in orthopaedic rehabilitation: a qualitative study on patients and providers]. *Die Rehabilitation* 2013; 52: 34-39.

Farin E, **Ullrich A**, Nagl M: Health education literacy in patients with chronic musculoskeletal diseases: development of a new questionnaire and sociodemographic predictors. *Health education research* 2013; 28: 1080-1091.

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Voigt L, **Ullrich A**, Baumann S, Dörr M, John U, Ulbricht S: What affects physical activity and sedentary time improvements after a cardiovascular examination? Poster presentation at the *11th European Public Health Conference (EPH)*, Ljubljana, Slovenia, Nov 28 – Dec 1, 2018. Abstract published in: *European Journal of Public Health* 2018; 28.

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Voigt L, **Ullrich A**, Dörr M, John U, Meyer C, Ulbricht S: Design einer randomisierten Kontrollgruppenstudie zur Wirksamkeitsmessung einer computergestützten Kurzintervention zur Blutdrucksenkung. Poster presentation at the *Gemeinsame Jahrestagung der Deutschen Gesellschaft für Epidemiologie (DGEpi), der Deutschen Gesellschaft für Medizinische Soziologie (DGMS) und der Deutschen Gesellschaft für Sozialmedizin und Prävention (DGSMP)*, Lübeck, Germany, Sep 5-8, 2017. Abstract published in: *Das Gesundheitswesen* 2017; 79: 776-77.

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Voigt L, Baumann S, **Ullrich A**, Weymar F, John U, Ulbricht S: Measurement effects from a cardiovascular examination programme on self-reported physical activity and sedentary time. Poster presentation at the *European Congress on Preventive Cardiology (EuroPrevent)*, Málaga, Spain, Apr 6-8, 2017. Abstract published in: *European Journal of Preventive Cardiology* 2017; 24: 156.

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Ullrich A, Glattacker M, Egle UT, Ehlebracht-König I, Geigges W, Köllner V, Kruse M, Jäckel WH: Psychologische Konstrukte als Prädiktoren der Krankheitsbelastung bei FMS-Patientinnen. Oral presentation at the *11. Deutschen Kongress für Versorgungsforschung und 4. Nationalen Präventionskongress, Deutschen Gesellschaft für Zahn-, Mund und Kieferheilkunde (DGZMK) gemeinsam mit dem Deutschen Verband für Gesundheitswissenschaften und Public Health (DVGPH) und dem Deutschen Netzwerk Versorgungsforschung (DNVF)*, Dresden, Germany, Sep 27-29, 2012. Abstract published in: *Deutsche Medizinische Wochenschrift* 2012; 137: 189

Ullrich A, Glattacker M, Egle UT, Ehlebracht-König I, Geigges W, Köllner V, Kruse M, Jäckel WH: Zugangswege zur psychosomatischen bzw. somatischen Rehabilitation bei Patientinnen mit Fibromyalgiesyndrom. Oral presentation at the *21. Rehabilitationswissenschaftliche Kolloquium*, Hamburg, Germany, Mar 5-7, 2012. Abstract published in: *DRV-Schriften* 2012; 98: 365-366.

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Ulbricht S, Voigt L, Weymar F, **Ullrich A**, Meyer C, John U: In Bewegung kommen - in Bewegung bleiben. Oral presentation at the *Fachtagung „Bewegungsförderung von Studierenden in der Lebenswelt Hochschule“*, Hannover, Germany, Dec 14, 2016.

Ullrich A, Schöpf AC, Farin-Glattacker E: Patientenschulung zur Förderung der Gesundheitskompetenz von chronisch Kranken. Oral presentation at the *Fachtagung Gesundheitspädagogik in Forschung und Praxis und 2. Treffen des Deutschen Netzwerkes Gesundheitskompetenz*, Freiburg, Germany, Oct 17-18, 2014.

Ullrich A: Preisverleihung des Hans Hench-Preises 2014. Oral presentation at the 42. Kongress der Deutschen Gesellschaft für Rheumatologie, *28. Jahrestagung der Deutschen Gesellschaft für Orthopädische Rheumatologie und 24. Wissenschaftliche Jahrestagung der Gesellschaft für Kinder- und Jugendrheumatologie*, Düsseldorf, Germany, Sep 17-20, 2014.

Ullrich A, Nagl M, Schöpf A, Farin-Glattacker E: „Aktiv in der Reha“: Eine patientenorientierte Schulung zur Förderung der Gesundheitskompetenz bei chronisch Kranken. Oral presentation at the *8. Reha-Symposium des NRFB*, Augsburg, Germany, Nov 14-15, 2013.

Ullrich A, Glattacker M, Egle UT, Ehlebracht-König I, Geigges W, Köllner V, Kruse M, Jäckel WH: Zugangswege zur psychosomatischen bzw. somatischen Rehabilitation bei Patientinnen mit Fibromyalgiesyndrom (FMS). Oral presentation at the *Deutscher Kongress für Orthopädie und Unfallchirurgie (DKOU)*, Berlin, Germany, Oct 23-26, 2012.

Oral and poster presentations

Ullrich A, Baumann S, Voigt L, John U, van den Berg N, Dörr M, Ulbricht S: Sedentary behaviour patterns using accelerometry and their association with cardiorespiratory fitness. Poster presentation at the *18th International Society of Behavioral Nutrition and Physical Activity (ISBNPA)*, Prague, Czech Republic, Jun 4-7, 2019.

Voigt L, **Ullrich A**, John U, Ulbricht S: Ergebnisse der Umsetzung einer computergestützten kardiopräventiven Kurzintervention durch nicht-ärztliches Personal in der Hausarztpraxis. Poster presentation at the *42. Wissenschaftlicher Kongress der Deutschen Hochdruckliga e.V. DHL - Deutsche Gesellschaft für Hypertonie und Prävention*, Berlin, Germany, Nov 22-24, 2018.

Siewert-Markus U, Ulbricht S, Voigt L, **Ullrich A**, Baumann S, Dörr M, John U, Freyer-Adam J: Effects of an intensity level video demonstration on self-reported physical activity. Oral presentation at the *9th European Society for Prevention Research (EUSPR) Conference*, Lisbon, Portugal, Oct 24-26, 2018.

Ullrich A, Voigt L, Baumann S, John U, Ulbricht S: Prospective changes in screen-based sedentary behaviour during leisure-time over 12 months among adults: Results of a brief intervention feasibility study. Poster presentation at the *8th European Society for Prevention Research (EUSPR) Conference*, Vienna, Austria, Sep 20-22, 2017.

Baumann S, Groß S, Voigt L, **Ullrich A**, Weymar F, Schwaneberg T, Dörr M, Meyer C, John U, Ulbricht S: Does accelerometer wearing bias physical activity data? Trending in time series of physical activity measured by accelerometry as an indicator of measurement reactivity. Oral presentation at the *7th European Society for Prevention Research (EUSPR) Conference*, Berlin, Germany, Oct 31 – Nov 2, 2016.

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