# Application of multiday 24h-accelerometry in epidemiology to study habitual overall physical activity, activity intensity levels, and their determinants

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**Walking is man’s best medicine**

Hippocrates

# Abstract

Physical activity (PA) is an established protective lifestyle factor for chronic disease risk. Reliably assessing PA, deriving unbiased PA estimates, and knowing determinants of PA are preconditions for drawing persuasive conclusions on exposure-disease associations in epidemiology and for successfully implementing PA promotion strategies. Most of the evidence regarding PA relies on subjective PA assessments, bearing the risk of measurement error. Objectively assessing PA using 24h-accelerometry that requires persons to continuously wear a device measuring accelerations of the body has been introduced in epidemiological studies only recently. The aim of the present thesis was to study the application of 24h-accelerometry in epidemiology to assess habitual overall PA, activity intensity levels, and activity determinants in the general adult population.

First, the reliable assessment of PA using 24h-accelerometry was investigated in an epidemiological study by analyzing variability, number of needed assessment days, and reliability of habitual 24h-accelerometry-based PA. Secondly, to enable determination of unbiased PA estimates, sensitivity and specificity of different algorithms for accelerometer non-wear time (NWT) detection in 24h-accelerometry data were examined in two independent epidemiological studies. Finally, potential determinants of habitual time in overall activity and active time spent in different activity intensities were investigated in a Germany-wide feasibility study. In all studies, PA was assessed using triaxial 24h-accelerometry over one week to two weeks.

Within-person day-to-day variability was found to be high, accounting for around 60% of the total variance observed in habitual 24h-accelerometry-based overall activity and time in different activity intensities. Neither the day of assessment nor the day of the week substantially explained variability of the PA parameters. Assessing 24h-accelerometry over approximately one week reliably estimated habitual PA. Regarding NWT detection, applying a common algorithm defining NWT as periods of >60 consecutive minutes of zero-acceleration readings substantially overestimated NWT in 24h-accelerometry due to a low sensitivity and specificity of the algorithm over the total assessment time and, especially, during sleeping encompassed in 24h-accelerometry. Generally, NWT detection in 24h-accelerometry was limited, but an algorithm requiring 120 minutes of zero-acceleration readings seemed to be the most suitable approach among those tested. Finally, higher body mass index, having a university entrance qualification, and not being employed were negatively associated with time in overall activity, whereas male sex, higher age, never consuming alcohol, current and former smoking status, and not reporting the net household income were associated with the proportion of time spent in different activity intensities in the general adult population.

Presented information on variability and reliability of 24h-accelerometry-based PA allows planning 24h-accelerometry assessment lengths in new epidemiological studies and enables calculation of deattenuated risk estimates from completed studies. Additionally, knowing the suitability of algorithms for NWT detection provides information for evaluating accelerometer wearing compliance to derive unbiased PA estimates from 24h-accelerometry. Finally, biological, behavioral, and economic potential determinants of PA identified in this thesis may help to integrate PA influencing factors in public health PA promotion strategies as well as in data collection and analyses, thus, allowing for meaningful conclusions in epidemiology on 24h-accelerometry-based PA as health-related lifestyle factor.

**Keywords:** 24h-accelerometry, physical activity, variability, reliability, non-wear time, determinants

# Kurzfassung

Körperliche Aktivität (physical activity, PA) ist ein etablierter protektiver Lebensstilfaktor chronischer Erkrankungen. Die reliable Erfassung und unverzerrte Schätzung von PA, sowie die Kenntnis von PA Determinanten sind Voraussetzungen, um überzeugende Schlussfolgerungen über Assoziationen von Exposition und Erkrankung in der Epidemiologie ziehen zu können und um Strategien zu Förderung der PA zu implementieren. Die Mehrheit der Evidenz zu PA beruht auf subjektiven Messungen, die das Risiko von Messfehlern bergen. Die objektive Erfassung der PA durch 24h-Akzelerometrie, für die Personen kontinuierlich ein Gerät zur Messung der Beschleunigung des Körpers tragen, wird erst seit Kurzem in epidemiologischen Studien eingesetzt. Ziel der vorliegenden Dissertation war die Untersuchung der Anwendung der 24h-Akzelerometrie in der Epidemiologie zur Erforschung der habituellen körperlichen Gesamtaktivität, Aktivitätsintensität und deren Determinanten in der erwachsenen Allgemeinbevölkerung.

Als Erstes wurde die zuverlässige Erfassung der PA durch 24h-Akzelerometrie in einer epidemiologischen Studie untersucht, indem die Variabilität, Anzahl benötigter Untersuchungstage, sowie Reliabilität der habituellen 24h-Akzelerometrie-basierten PA analysiert wurden. Zweitens wurden Sensitivität und Spezifität verschiedener Algorithmen zu Detektion von Akzelerometer Nicht-Tragezeiten (non-wear time, NWT) in 24h-Akzelerometriedaten in zwei unabhängigen epidemiologischen Studien berechnet, um eine unverzerrte Bestimmung von PA Schätzern zu ermöglichen. Schließlich wurden potentielle Determinanten der habituellen Gesamtaktivitätsdauer sowie der in unterschiedlichen Aktivitätsintensitäten verbrachten aktiven Zeit in einer deutschlandweiten Machbarkeitsstudie untersucht. In allen Studien wurde PA mittels 24h-Akzelerometrie über eine Woche oder zwei Wochen erhoben.

Es zeigte sich, dass die Tag-zu-Tag Variabilität innerhalb einer Person groß war und etwa 60% der Gesamtvarianz der habituellen 24h-Akzelerometrie-basierten Gesamtaktivität und Zeit in unterschiedlichen Aktivitätsintensitäten ausmachte. Weder der Untersuchungstag noch der Wochentag erklärten wesentlich die Variabilität in den PA Parametern. Anwendung der 24h-Akzelerometrie über etwa eine Woche erlaubte eine zuverlässige Schätzung der habituellen PA. Bei der NWT Detektion zeigte sich, dass die Anwendung eines üblicherweise genutzten Algorithmus‘, der NWT als Perioden von >60 konsekutiven Minuten ohne aufgezeichnete Beschleunigung definiert, in der 24h-Akzelerometrie aufgrund einer geringen Sensitivität und Spezifität des Algorithmus‘ über die Gesamtuntersuchungszeit und insbesondere in Schlafphasen, die in

24h-Akzelerometrie enthalten sind, zu einer deutlichen Überschätzung der NWT führt. Grundsätzlich war die NWT Detektion in der 24h-Akzelerometrie limitiert, aber ein Algorithmus, der 120 Minuten ohne aufgezeichnete Beschleunigung voraussetzt, erschien als am besten geeigneter Ansatz unter den getesteten. Schließlich waren in der erwachsenen Allgemeinbevölkerung höherer Body Mass Index, Besitzen der Hochschulreife und Nicht-Beschäftigung negativ mir der Gesamtaktivitätsdauer assoziiert, wohingegen männliches Geschlecht, höheres Alter, kein Alkoholkonsum, aktuelles und früheres Rauchen sowie Nicht-Berichten des Nettohaushaltseinkommens mit dem Anteil der in unterschiedlichen Aktivitätsintensitäten verbrachten Zeit assoziiert waren.

Die vorgelegten Informationen zu Variabilität und Reliabilität der 24h-Akzelerometrie-basierten PA erlauben die Planung der Messdauer der 24h-Akzelerometrie in neuen epidemiologischen Studien und ermöglichen die Berechnung deattenuierter Risikoschätzer in bereits durchgeführten Studien. Kenntnis über die Eignung von Algorithmen zur NWT Detektion liefert Information zur Beurteilung des Akzelerometer-Trageverhaltens, um unverzerrte PA Schätzer aus der 24h-Akzelerometrie ableiten zu können. Schließlich können die in dieser Dissertation identifizierten biologischen, verhaltensbedingten und ökonomischen potentiellen PA Determinanten helfen, PA beeinflussende Faktoren in PA Förderstrategien im Bereich Public Health sowie in der Datenerhebung und -auswertung einzubeziehen, um aussagekräftige Schlussfolgerungen in der Epidemiologie zu 24h-Akzelerometrie-basierter PA als gesundheitsrelevanten Lebensstilfaktor zu ermöglichen.

**Schlagwörter**: 24h-Akzelerometrie, körperliche Aktivität, Variabilität, Reliabilität, Nicht-Tragezeit, Determinanten

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| | |
|---|---|
| 95% CI | **95 % C**onfidence Interval |
| accelero. | **ACCELERO**metry (in **Figure 10**, **Figure 11**) |
| ActivE | study aiming to quantify **ACTIV**ity-related **E**nergy expenditure based on accelerometry |
| $AEE_{min}$ | minimal activity-induced energy expenditure |
| β | estimate for fixed effects based on linear regression |
| BMI | **B**ody **M**ass **I**ndex (kg/m²) |
| CI | **C**onfidence **I**nterval |
| cm | **C**enti**M**eter(s) |
| cpm | **C**ounts **P**er **M**inute |
| D, D | number of **D**ays necessary to estimate habitual physical activity with a given confidence |
| d | day |
| DALY | **D**isability-**A**djusted **L**ife **Y**ear |
| DEDIPAC | **DE**terminants of **DI**et and **P**hysical **Ac**tivity |
| g | **G**ram |
| G | **G**ravitational units |
| GM | **G**eometric **M**ean |
| Hz | **H**ert**Z** |
| ICC | **I**ntraclass **C**orrelation **C**oefficients |
| $ICC_s$ | **I**ntraclass **C**orrelation **C**oefficients, **S**ingle-day reliability |
| $ICC_t$ | **I**ntraclass **C**orrelation **C**oefficients, desired (**T**argeted) reliability |
| IQR | **I**nter**Q**uartile **R**ange |
| KH | **K**nowledge **H**ub |
| KORA | **KO**operative Gesundheitsforschung in der **R**egion **A**ugsburg; Cooperative Health Research in the Region of Augsburg |

| | |
|---|---|
| kg | **K**ilo**G**ram(s) |
| m | **M**eter(s) |
| MET | **M**etabolic **E**quivalents of **T**ask |
| min | **MIN**utes, for reporting time (min/d) or defining an epoch (‘-min’) |
| N | total **N**umber of the study population |
| n | **N**umber of a subpopulation |
| n. a. | **N**ot **A**vailable |
| NWT | **N**on-**W**ear **T**ime |
| OR | **O**dds **R**atio |
| p | ***P*-**value |
| PA | **P**hysical **A**ctivity |
| PAF | **P**opulation **A**ttributable **F**raction |
| r | assumed correlation between the observed and true mean of a physical activity parameter |
| RQ | **R**esearch **Q**uestion |
| $s_b^2$ | **B**etween-person variance |
| SD | **S**tandard **D**eviation |
| SOP | **S**tandard **O**perating **P**rocedure |
| $s_w^2$ | **W**ithin-person variance |
| U.S. | **U**nited **S**tates |
| vs. | **V**er**S**us |
| VV | **V**igorous-to-**V**ery-vigorous |
| WHO | **W**orld **H**ealth **O**rganization |

# 1 Introduction

In the last century, substantial changes in the working and physical environment exerted a considerable impact on the individual and population physical activity (PA) behavior: occupational PA demands decreased, technology and sitting time increased, and ongoing urbanization led to less attractive environments for active travel and time spent outdoors, while inactive transport facilities, like going by car became more convenient [1-5]. However, now there is abundance of epidemiological evidence indicating regular PA to be an independent protective factor for numerous non-communicable diseases and premature death, whereas a lack of PA increases the morbidity and premature mortality risk [6-20].

Habitual individual PA behavior can not only be characterized in terms of its total volume, but also in terms of time spent in different activity intensity levels, like low, moderate, and vigorous activity. The World Health Organization (WHO) recommends to accumulate at least 150 minutes of moderate activity, 75 minutes of vigorous activity, or an equivalent combination of these per week to achieve a sustained effect on health and to prevent chronic diseases [7]. The WHO further recognized the importance of PA for the global burden from non-communicable diseases and premature death and, with the *Global Strategy on Diet, Physical Activity and Health* in 2004 and a draft on the *WHO global action plan on physical activity 2018 – 2030* in 2017, called for national PA action plans to counteract the increasing prevalence of physical inactivity across Member States [7, 21]. In line with this and among other national and international PA action plans, the Council of the European Union as well as the German Ministry of Food and Agriculture and the Federal Ministry of Health recommend promotion of regular PA at the federal level [22, 23]. Nevertheless, still, in 2010, up to one third of adults globally, in Europe, and in Germany was not sufficiently active to meet the WHO PA recommendation, and the prevalence is expected to further increase globally [1, 13, 14, 24]. As a consequence, low PA accounts for a huge, but avoidable disease and economic burden, being among the five leading risk factors for mortality and among the seven leading risk factors for disability-adjusted life years (DALYs[1], 'person-years lived free of disability') in the world [8, 13, 25, 27].

[1]A summary indicator of a 'health gap' representing the current and avoidable total disease burden as the number of years of healthy life expectancy lost due to a specific medical condition [25], [26]. It is calculated based on the life expectancy at birth corrected by the weighted years lived with disability and quantifies the time period between onset and ending (i.e., recovery or death) of a disease, taking into account its incidence, average duration or survival rate, and a measure of quality of life [25], [26]. One DALY lost is equivalent to losing one year of healthy life expectancy (or living two years being impaired by 50% and so forth) [26].

A reliable assessment of PA is not only a premise for national PA surveillance systems [1], but rather is pivotal for researchers aiming to understand the relationship of PA and health risk. Drawing sound exposure-disease associations regarding PA relies on the determination of 'true' mean, i.e., habitual PA measures as a premise to derive approximate true, unattenuated relative risk estimates [28]. Nevertheless, the assessment and evaluation of PA data in epidemiology is challenging, given that PA is a complex, multidimensional, modifiable, highly individual, and context-dependent lifestyle behavior [11, 29, 30]. Thus far, evidence on PA levels and on PA in the etiology of chronic diseases is mainly based on studies that assessed PA subjectively [1, 6, 8-19, 31, 32]. However, self-reported PA potentially provides limited validity and information on activity intensities, while bearing the risk of bias and misreporting, especially of activity intensities [33-44]. In contrast, a comprehensive PA assessment is relevant for epidemiological research, since different patterns of overall activity and activity intensity levels may have distinct impacts on health [45-57].

Today, wearable devices that records accelerations of the human body in all three spatial axes allow to objectively and comprehensively assess habitual PA under free-living conditions, capturing also types of activity besides those being typically perceived and reported as 'activity' [31, 36, 40, 58, 59]. These accelerometers have shown good validity and technical reliability and enable the assessment of PA over several days [36, 60-69]. However, so far, most studies used accelerometry during waking hours only, while 24h-accelerometry assessed over multiple days has been introduced only recently into new large cohort studies, like the ongoing German National Cohort [31, 70-76].

Knowing individual and environmental factors associated with PA behavior is pivotal: On the one hand, it is a precondition to successfully implement PA promotion programs that aim to reduce the burden caused by inactivity [29, 77-79]. On the other hand, understanding facilitators and barriers to PA is important to rule out unmeasured confounding and to, thus, derive unbiased PA measures from epidemiological studies [26, 30, 80, 81]. Previous studies suggest that several biological, behavioral, psychological, physical, socio-cultural, economic, and political factors are associated with PA across all ages [82-93]. Although research into factors associated with PA has increased in the last decade, studies on determinants of PA using 24h-accelerometry are missing.

However, for drawing conclusions on determinants of multiday 24h-accelerometry-based PA, reliable PA estimates are key requirements to use 24h-accelerometry as PA assessment tool in epidemiology. Nevertheless, little information is currently available about the variability of overall activity and of time spent in different activity intensities on a 24h day-to-day basis, and, thus, about the observational time necessary to estimate habitual PA using 24h-accelerometry. Such information is important, given that for drawing conclusions on PA, researchers are usually interested in the ‘average’ amount of PA that is typically performed by an individual, representing the ‘long-term’ exposure.

Further, to obtain unbiased PA estimates based on multiday 24h-accelerometry, sound information about periods of accelerometer non-wear time (NWT) is required, since unknown inclusion of NWT as periods of zero-acceleration readings may result in a misclassification of PA. While time-consuming NWT detection based on participants’ diaries is not feasible in large-scale studies, automated NWT detection from accelerometry may be an efficient alternative. However, existing algorithms that define NWT as periods of consecutive minutes of zero-acceleration readings were derived using accelerometry during waking only, and it is, therefore, unclear if they are suitable to detect NWT in 24h-accelerometry data that includes sleeping times with potentially long motionless periods [73, 94].

The aim of this thesis was to examine the application of multiday 24h-accelerometry in epidemiology to investigate habitual overall activity, activity intensities, and activity determinants under free-living conditions in the general adult population. To address this aim, three objectives were put forward:

1) To quantify variability of habitual overall activity and of habitual time spent in different activity intensities, to calculate the number of days needed to assess habitual PA, and to examine the reliability of habitual PA using multiday 24h-accelerometry in an epidemiological study under free-living conditions.

2) To assess the applicability of NWT algorithms requiring consecutive minutes of zero-acceleration readings to automatically detect NWT in multiday 24h-accelerometry data assessed in two epidemiological studies under free-living conditions.

3) To investigate potential determinants of habitual time in overall activity and in different activity intensities using multiday 24h-accelerometry in an epidemiological study under free-living conditions.

# 2 Background

## 2.1 Habitual physical activity

Generally, PA comprises 'any body movement provided by the skeletal muscles that results in a substantial increase over the resting energy expenditure' as defined by Bouchard and Shephard [95]. Thus, PA encompasses as subcomponents structured, planned, and mainly repetitive activities of moderate to vigorous intensity, performed intending to enhance or maintain health (i.e., 'exercise'), as well as incidental baseline activities of daily life for any purpose, involving all large muscles and being mainly of low intensity [6, 10, 11, 36, 40, 42]. The resulting 'activity-induced energy expenditure' is the most variable component of the 'total energy expenditure' accounting for 10% to 15% [11, 36, 40, 42, 96]. The 'resting metabolic rate' (i.e., energy expenditure at fasting basal and sleeping conditions to maintain vitality functions (see section 2.1.1)) accounting for 60% to 75% and the 'diet-induced energy expenditure' (i.e., thermogenesis due to ingestion and assimilation of food) are the other two components determining the total energy expenditure [36, 40, 42, 96]. Consequently, 'PA' and 'energy expenditure' describe two different constructs, with the former resulting in the latter [97]. A third independent construct is 'physical fitness' that describes the individual cardiorespiratory or aerobic capacity (i.e., the physiological ability to supply sufficient oxygen during sustained PA), and musculoskeletal capacity (i.e., muscular strength, endurance, balance, flexibility, agility, coordination, and bone health) to perform activities of daily life without fatigue or lack of energy [6, 11, 43, 98].

In epidemiology, one usually aims to assess 'habitual' PA, encompassing the whole spectrum from structured to unstructured activities that characterize the individual overall 'activity' behavior [6, 95]. This means, researchers typically aim to assess the 'average' PA that is usually performed by a person, representing the long-term 'exposure' and, thus, being relevant for investigating exposure-disease associations regarding PA. However, capturing habitual PA in the context of epidemiological studies is challenging and nontrivial, since PA is a complex and manifold behavior. Its temporal pattern can be characterized not only regarding its quantity, i.e., its total amount, but also regarding its quality, describing context pattern characteristics: The *domain* of PA represents the setting or purpose of PA being typically distinguished between occupational (work place, educational institution), domestic, active transportation, or leisure time PA, while the *dimension* of PA indicates its type or mode, frequency, duration, and intensity [6, 36, 40-42].

### 2.1.1 Physical activity intensity

Despite having a similar total energy expenditure, PA patterns in terms of the proportion of time spent in different activity intensities can substantially differ [99]. Thus, assessing the intensity in addition to the amount of PA is relevant for epidemiology.

The intensity of a PA behavior is directly associated with its energy cost, i.e., the higher the intensity, the higher is the activity-induced energy expenditure [40, 100-102]. However, determining energy expenditure for each activity and participant is not feasible in large-scale epidemiological studies. Thus, activity intensities are commonly defined based on a standard 'metabolic equivalent of task' (MET) that provides a quantitative unit to estimate the metabolic cost exerted to perform an activity [40, 100-103]. As reference, 1 MET represents the energy expenditure requiring an oxygen consumption of 3.5 ml per kilogram body weight in adults during one minute of resting in a thermoneutral environment [40, 100-102]. This resting metabolic rate, in turn, equals the energy metabolism of 4.184 kilojoules or 1 kilocalorie per kilogram body weight and hour [40, 100-102]. Any activity above this resting requires larger amounts of oxygen consumption due to an increase in the metabolic turnover, and the energy expenditure due to specific activities can, therefore, be expressed as multiple of the resting energy expenditure [40, 100-103]. Thus, the MET value represents the ratio of the working compared to the resting metabolic rate on an absolute scale [40, 100-102]. Derived by measuring the oxygen consumption during the specific activity, MET values for a large number of diverse behaviors are now available in the Ainsworth Compendium of PA for adults as 5-digit coded standard activities, with METs ranging from 0.9 during sleeping to 23.0 during running at 22.5 kilometers per hour [100-103]; more recently, a comparable Compendium was derived for youths [104]. Based on the specific MET value, PA behaviors can thereby be assigned to different absolute intensities, commonly distinguishing between light, moderate, and vigorous intense activity defined as ≥1.0 to <3.0 (e.g., eating, personal hygiene, slow walking), 3.0 to 5.99 (e.g., gardening, playing golf, mopping), and ≥6.0 METs (most sports, e.g., aerobics; carrying groceries or heavy items upstairs), respectively [7, 14, 100-103] (**Figure 1**). On a scale describing the relative activity intensity, moderate activity is typically described as activity, where one starts to sweat or get out of breath, requiring 50 to 69% of the maximal heart rate (light activity, <50%; vigorous activity, ≥70%), or as a 5 to 6 on a 0-to-10 scale relative to the individual capacity (vigorous intensity, 7 to 8) [7, 40]. However, since biological factors, like age or sex affect the resting metabolic rate, while METs were derived from group averages [36, 100-102], the absolute activity intensity based on METs is only an approximate estimate for the relative activity intensity, and both may deviate from each other [40]; the epidemiological relevance, however, may be stronger for the relative than for the absolute intensity [58]. From light activity intensity, sedentary behavior can further be separated, being defined as PA during waking above resting while sitting or reclining, requiring ≥1.0 to ≤1.5 METs [99, 102] (**Figure 1**).

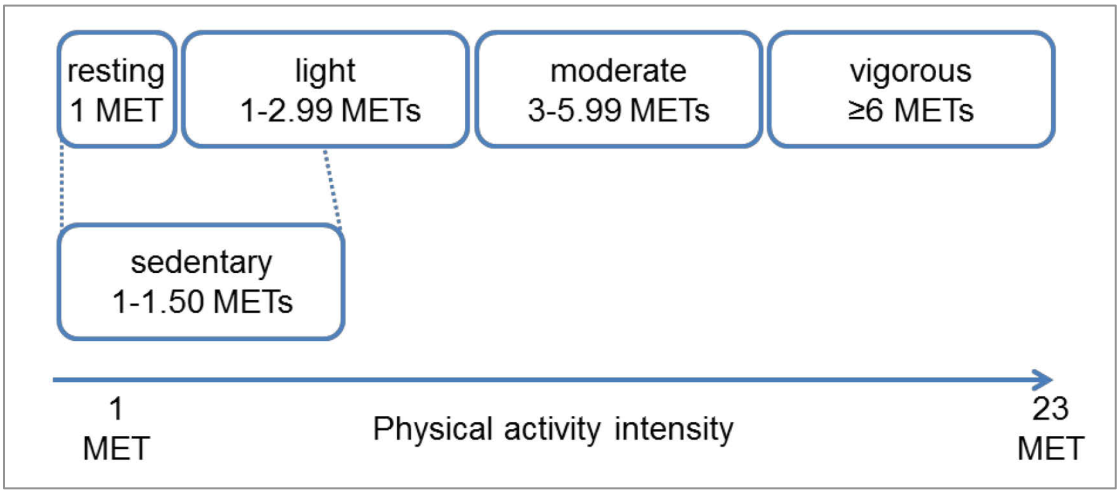


**Figure 1**: Physical activity intensity defined based on the metabolic equivalent of task
Physical activity intensity as defined based on the 'metabolic equivalent of task' (MET), with 1 MET reflecting the energy expenditure that requires the oxygen consumption of 3.5 ml per kilogram body weight in adults during one minute of resting in a thermoneutral environment (equaling the energy metabolism of 4.184 kilojoules or 1 kilocalorie per kilogram body weight and hour) [40, 100-102]. Referring to this resting metabolic rate, higher MET values represent higher activity intensities, with ≥1.0 to <3.0, 3 to 5.99, and ≥6.0 METs defined as light, moderate, and vigorous activity intensity, respectively [7, 14, 100-103]. From light activity, sedentary behavior can further be separated (≥1.0 to ≤1.5 METs) [99, 102].

Based on a sample of more than 440,000 adults from the United States (U.S.), it was estimated that more than two thirds of reported non-occupational aerobic activities are of moderate intensity (relating to all reported aerobic activities: walking, 47%; garden and lawn activities, 10%; conditioning exercises, 9%), while vigorous activities make up only a small proportion [105]. Sedentary behavior, in turn, is highly prevalent and has still been increasing in the last decades of decreasing occupational activity demands, especially in high-income countries and in persons with a high socio-economic status [1, 24, 106, 107]. With regard to sitting time that substantially contributes to sedentary behavior, more than one third of European and German adults report to sit at least 5.5 hours per day, and 47.3% of German adults reported to are 'mainly sitting or standing' during occupation [1, 24, 108]. However, overall activity and engagement in different activity intensities largely vary within and between populations [1, 13, 24, 32, 52, 109-112]. Therefore, assessing activity intensity in addition to overall activity allows for capturing a more holistic view on the habitual PA pattern as health-related lifestyle factor [40-42].

## 2.2 Habitual physical activity and health

Initiated by a landmark study by Morris et al. in 1953, showing that persons exercising a physically demanding profession (i.e., postal carriers and bus conductors of double-deck buses) had a decreased risk of mortality due to coronary heart disease compared to persons with occupations demanding little PA (i.e., postal office workers and bus drivers) [113], the worldwide interest in the impact of PA on health has increased. This has further been driven by the transition in risk factors over the last decades, with a decreased influence of 'traditional risks', like undernutrition and hygiene, while 'modern risks', like smoking or physical inactivity has gained in importance for global health [8].

Although physiological mechanisms caused by PA are still poorly understood [114], now there is a large body of epidemiological evidence showing an causal, independent, and inverse association of habitual PA and mortality, morbidity, and disability. Lack of PA is an established risk factor for a number of chronic diseases and as one part of a causal interplay, it may have direct and indirect effects on health [8]. Compared to lacking PA, regular PA is associated with a significant decrease in morbidity risk of 16-30% for coronary heart disease, 26% for ischemic stroke events, 20-28% for type 2 diabetes, 9-33% for breast cancer, and 16-32% for colon cancer [8, 9, 15, 20, 45]. Various other types of cancer are supposedly related to PA, too [20]. Further, lacking PA is a risk factor for psychological disorders (i.e., depressive symptoms, anxiety) and falling, as well as for risk factors of all the beforementioned medical conditions, i.e., for high blood pressure, hyperglycemia, dyslipidemia, overweight, abdominal/overall obesity, weight gain, or high levels of inflammation markers [8-14]. In contrast, regular PA is beneficial for the prevention of all these non-communicable conditions, is associated with higher self-rated health, preserves health and functioning into older ages (i.e., successful and healthy aging), and improves multiple physiological functions, including physical fitness, functional health (i.e., physical capacity; the extent of functional 'usability' or 'limitations'), and cognitive functioning (e.g., memory, attention) [6, 8-11, 15-19, 114]. Beneficial effects of regular PA are observed in healthy and in diseased populations [12, 17, 45, 115, 116]. Thus, it is key for primary as well as secondary prevention, as it may prevent the development and attenuate the severity of chronic diseases.

Bearing in mind that, in 2012, 68% of global deaths were attributable to chronic diseases, PA is also a relevant lifestyle factor related to longevity [13]. Depending on the definition of overall activity, there is strong evidence showing a significant reduction in all-cause mortality of 17-48%, when comparing the most and least physically active groups [9, 10, 12, 13, 45, 49, 51, 117-120]. A similar or even slightly higher risk reduction was found for cause-specific mortalities, like due to cancer, cardiovascular diseases, or type 2 diabetes [45, 51, 121]. A health and longevity benefit from PA is found across all strata of individual characteristics, like age, sex, race, anthropometry, lifestyle, education, or medical conditions, and is independent of the genetic background [12, 45, 51, 120]. For the association of overall PA and health risk, epidemiological studies support a continuous and graded dose-response association, with a significant risk reduction for all PA levels above 'inactivity'[2] [14, 15, 45, 49, 51, 117, 119-123]. A dose-response association is one of nine Bradford Hill criteria, indicating a causal relationship [26, 80]. However, while some studies suggest a linear inverse association [14, 49], others suggest an asymptotic (or U-shaped) association, with a change from 'inactivity' to an 'above-inactivity' level exerting the main beneficial impact, while increasing PA to higher doses provides a comparatively low additional health benefit [15, 45, 51, 117, 119, 120, 122, 123]. Thus, promoting even a slight increase in PA that is easy to achieve by inactive persons helps to reduce the health burden due to lacking PA.

Health benefits of regular PA were also consistently shown for children, adolescents, and older adults [7, 13, 124-127]. Furthermore, PA in adolescence tracks into adulthood and is positively associated with short- and long-term health [124, 128]. Thus, being physically active is crucial for health across all ages. However, capturing the life course was beyond the scope of this thesis, which will focus on adulthood.

### 2.2.1 Physical activity intensity and health

Independent of total activity, total energy expenditure, or the contribution of activity intensities to the energy expenditure, evidence indicates that the impact of distinct activity intensities on morbidity risk, incidence of morbidity risk factors, as well as premature mortality risk is more pronounced in or even limited to a specific compared to other activity intensities [12, 45, 50-52, 129]. For example, compared to inactive people, all-cause mortality risk is decreased by 18% for individuals doing moderate activity, but by 33% for those being vigorously active at a same total PA level [45]. Further, studies in the last decade have shown that sedentary behavior is an independent, causally health-related risk factor [53-57, 107, 130, 131]. For example, being in the most compared to the least sedentary group is a strong predictor of health, increasing the morbidity risk of type 2 diabetes by 91-112% and the all-cause mortality risk by 24% [53, 54]. Regular PA, meeting PA guidelines, and breaks in sedentary behavior may ameliorate, but not fully compensate the negative health consequences of prolonged seden-

[2] In the following, the terms 'inactivity' and 'insufficient' PA are used as stated in the original study referenced, unless the definition in the original study require re-definition to ' 'insufficient' PA (i.e., not meeting a PA recommendation) or inactivity' (i.e., not being active beyond baseline activity), respectively, for the context of this thesis (please also refer to 2.2.2).

tary time [53-57, 130, 132]. Generally, a distinct effect of different activity intensities on health seems reasonable due to a differentiated activation of the skeletal muscle and of the muscular metabolism depending on a respective activity intensity [53].

The evidence that the individual amount and intensity of PA are independent from each other [45, 53, 99] and that both are independently relevant for health [45-57] underpins the importance of assessing overall activity as well as activity intensity in epidemiology.

### 2.2.2 Prevalence of insufficient physical activity levels

Several recommendations have been published since the middle of the 20th century to advise a sufficient PA volume that is supposed to provide health-enhancing effects [14, 133, 134][3]. Nowadays, the recommendation most commonly applied is stated by the WHO and is based on activity intensities: For adults (18 to 64 years), the WHO recommends to accumulate at least 150 minutes of moderate or 75 minutes of vigorous activity per week, or to achieve a metabolic 'equivalent' of both to prevent non-communicable diseases [7]. Minutes in moderate or vigorous activity should be performed in consecutive periods, so called 'bouts', of at least ten minutes spread throughout the week [7]. Preferably, this is complemented by conditioning and muscle-strengthening exercises on at least two days a week [7]. For further health benefit, achieving 300 and 150 minutes of moderate and vigorous activity per week, respectively, are recommended [7]. These WHO criteria are globally recognized and build the basis, among others, for European and national PA guidelines, as well as for action plans by the Council of the European Union, the German Federal Ministry of Health, or the U.S. Department of Health and Human Services [10, 22, 135]. Additionally, in light of its high prevalence and detrimental effects, recommendations on reducing and breaking up sedentary behavior are now implemented in public health guidelines, for example, in Germany, Australia, or by the World Cancer Research Fund [14, 135, 136].

Meeting the WHO PA recommendation was consistently shown to be associated with the most significant health benefit, while increasing PA to a multiple of the recommendation provided a proportionally low additional benefit [15, 45, 49, 51, 57]. For example, meeting versus not meeting the recommendation was associated with a 14 to 31% risk reduction in premature all-cause mortality, while reaching at least twice the recommendation was related to a risk reduction of 26 to 37% [49, 51]. Although adverse cardiovascular effects of excessive endurance exercise are under debate [137-139], reaching up to ten times the WHO PA recommendation seems to not be harmful [51].

[3]'Insufficient PA' is different from 'inactivity', with the latter being defined as absence of any activity that requires energy expenditure and of activity beyond baseline activity of daily life, like standing or slow walking [7], [10], [95]

Nevertheless, although being a modifiable and, thus, avoidable risk factor, based on the WHO PA recommendation, 23% of adults worldwide (men, 20%; women 27%), 34.8% of European adults (men, 27.9%; women, 33.9%), and 21.1% of German adults (men, 18.7%; women 23.5%) are currently not sufficiently active [1, 13, 32][4]. Recent reports of the Robert Koch-Institute and on German survey data reported the prevalence of insufficient PA to be considerably higher in Germany and in Europe [32, 108, 140, 141]. However, in these surveys, 'insufficient PA' was only approximately determined based on moderate activity, thereby neglecting persons reaching the recommendation through vigorous activity or a metabolic equivalent, and, thus, reports presumably overestimate prevalence of insufficient PA [32, 108, 140, 141]. A majority of European and German adults reports to never exercise or play sports (42% and 29%, respectively) or, when asked over the last week, to not have been vigorously (54% and 41%) or moderately (44% and 26%) active [24]. Further, one fifth of adults globally and in Europe are considered as habitually inactive, i.e., to do 'no or very little PA' [11].

Insufficient PA is, thus, up to twice as prevalent as obesity worldwide [1, 13, 32, 142-144]. These data indicates that the public health burden attributable to lacking PA is supposed to be substantial [8, 13, 25, 27].

### 2.2.3 Public health relevance of insufficient physical activity levels and physical inactivity

In addition to being a relevant health risk for the individual, the public health burden that is attributable to insufficient or lacking PA substantially increased since 1990 [145]. Now, the WHO states physical inactivity as fourth leading risk factor for global mortality, being responsible for 3.2 Million (WHO European Region, 992,000) or 5.5% of deaths globally (Germany, 5.9%), which is only slightly lower as the mortality burden related to overweight and obesity [8, 25, 144, 146]. Recent estimates based on comprehensive national and global data suggest the population attributable fraction (PAF[5] [26, 147]) of physical inactivity to be 7.4 to 9.4% for deaths worldwide, in the European Region, and in Germany, which is about twice the proportion observed for obesity [9, 120]. Disease-specific morbidity PAFs for the major chronic diseases are similar and considerably higher for the total burden due to morbidity and mortality [9, 11, 25]. This public health burden could be avoided, when eliminating the risk factor 'physical inactivity' [9, 120,

[4]Hallal et al. applied a WHO-adapted PA recommendation to determine whether persons were sufficiently active: 150 minutes of moderate or 60 minutes of vigorous aerobic PA per week

[5]deaths in a population being theoretically avoidable, when reducing a risk factor to the minimum feasible; calculated based on the proportion of people under exposure and the relative risk of the disease of interest, when comparing people under and not under exposure [26], [147]

147]. Avoiding all inactivity would further result in an increase in life expectancy at birth at the population level of 0.68 and 0.70 years globally and in Europe, respectively (Germany, 0.47 years) [9, 120].

Taking into account deaths and non-fatal outcomes, physical inactivity and insufficient PA are responsible for 69.3 million or 2.8% of total DALYs globally and for 8.3 million or 3.5% of DALYs in the European Region (Germany, 3.2%) [8, 13, 25, 146, 148]. Lacking PA is, thus, among the ten leading health risk factors worldwide (10$^{th}$ place), in Western Europe (4$^{th}$), and in Germany (8$^{th}$) [145, 146]. Regarding morbidity and mortality, it is as important for chronic disease risk as current smoking, above moderate alcohol consumption, unhealthy diet, or obesity, and exerts detrimental effects comparable to or even twice as high as traditional risk factors, for example, as hypertension for cardiovascular disease risk [9, 12, 120, 131, 149, 150]. Furthermore, lacking PA is supposedly a driver for the increase in overweight and obesity prevalence in the last decades, thus, further contributing to a substantial public health burden [14, 143, 144, 151].

These numbers reveal lacking PA as major public health issue [25], implying a substantial macrosocial economic impact. In 2014, when summed across the five major non-communicable diseases, i.e., coronary heart disease, stroke, type 2 diabetes, breast cancer, and colon cancer, not meeting the WHO PA recommendation was responsible for 53.8 billion international $ (equivalently to US$) of direct costs for health care systems (Germany, 2.1 billion $) and, further, indirectly contributed to 13.7 billion $ in productivity losses globally (Germany, 565,523 $) [148]. Economic burden estimates are considerable higher based on less conservative assumptions [148]. Thus, in 2005, the European Council launched the 'European Network for the Promotion of Health-Enhancing Physical Activity' aiming to develop and support PA promotion strategies across European countries [152-155]; similar action plans were stated in the U.S. [13]. Further, in 2014, as one of nine global targets, the WHO has called for national multisectoral PA action plans to reduce the prevalence of insufficient PA by 10% by 2025 to globally attenuate the public health and economic burden due to non-communicable diseases [13, 21].

Public health relevance of lacking PA is further reflected by the still growing epidemiological research on PA. However, assessment of PA in humans is challenging, especially in the context of large cohort studies that aim to estimate habitual PA under free-living conditions. According to the World Cancer Research Fund, PA is not properly assessed in most studies, at least with regard to cancer epidemiology [14].

## 2.3 Assessment of physical activity in epidemiology

Assessing habitual PA in humans is complex, given that PA is deeply interwoven with other individual factors, comprises sporadic as well as planned activities, and displays a multidimensional and individual pattern of PA dimensions and domains [11, 29, 30]. Thus, raising the issue *how* to assess PA and to choose the 'right' PA measurement method in advance is a premise to capture an individually representative and valid PA measure for sound analyses in epidemiology. Generally, PA can be assessed either in a laboratory (e.g., 24h-stay in a metabolic chamber), or under free-living and unrestrained conditions [36, 96, 156]. The latter is intuitively more representative for habitual PA, since participants can pursue their daily routine.

Ideally, PA assessment methods allow detection of all dimensions, domains, and settings of PA. Nevertheless, although several reviews on PA measurements are available, there is currently no clear recommendation on the 'best' method [40, 43, 59]. Weighing and, if necessary, making a compromise between practical considerations (like financial, technical, and methodological feasibility), the method's validity and reliability, data quantity and quality, as well as the burden for participants, study personnel, and researches can significantly influence the choice of the most suitable PA measurement [36, 40, 42, 43]. Authors suggested decision matrices, providing assistance for choosing the 'best' PA measurement technique depending on the specific study aim, the study population, and the primary outcome of interest, with the latter being the most decisive aspect [40, 43]. However, no measurement is supposed to validly and reliably capture all PA dimensions, domains, and context information at the same time, and thus, no method is supposed to be most appropriate for all settings [40, 42, 43].

To test criterion validity of a PA measurement, i.e., the agreement with a reference method [157], there may be no general 'gold standard reference' for PA due to the complex nature of PA, with all methods probably missing any PA characteristic. However, since researchers typically aim to estimate the total energy expenditure in epidemiology (see section 2.1), mainly, standard references in validation studies on PA assessment tools are indirect calorimetry under laboratory and the doubly labeled water technique under free-living conditions, with the latter being most appropriate to assess habitual PA of daily life, but not being affordable at large scale [29, 36, 37, 40, 96, 158].

Besides measurements of the total energy expenditure or the physical fitness that can be applied to indirectly assess the activity-induced energy expenditure (see section 2.1), nowadays there are different direct PA assessment methods available [36, 40, 41, 96].[6] These, broadly, can be characterized as subjective methods that rely on self-reports on PA, or as objective measures from wearable devices that directly detect physiological markers, like heart rate or acceleration of the human body [36, 40, 43, 96]. Both methods are supposed to have strengths and limitations.

### 2.3.1 Subjective physical activity assessment

Subjective PA assessment tools require the individual to report its past PA, either recorded or recalled [36, 40]. Typically, they allow assessing the individual PA *behavior* and its structural and temporal pattern [42, 59]. The most common subjective PA measurements are PA records or diaries, and questionnaires.

#### 2.3.1.1 Physical activity records and diaries

Using PA records or diaries requires persons to self-report their activities, either at or close to the time of occurrence (activity-by-activity) or in detail at predefined intervals, for example, every 15 minutes or hour-by-hour over a given period [36, 40, 59]. Typically, persons are asked to record starting and ending of PA, its (perceived) intensity, and its type, with the latter two being given as categorized items, on Likert scales, or in the form of free texts [37, 40, 59]. Later on, this information is coded by the researcher, mainly according to standard activities available in the Ainsworth Compendium, being thereby assigned to behavior-specific METs [36, 40, 101-103]. Thus, deriving absolute activity intensities and prediction of energy expenditure is possible [36, 37, 40].

#### 2.3.1.2 Physical activity questionnaires

In contrast, PA questionnaires ask for behaviors that are self-reported by the person in retrospect, either self-administered or administered in an interview context, and either performed as paper-pencil or computer-assisted tool [36, 40, 41]; sometimes, only PA of a minimal length is queried [29]. Like for records and diaries, PA assessed in questionnaires can be assigned to METs to determine intensities or overall PA, e.g., as MET-hours per week [40, 101-103]. Questionnaires vary in their extent and detail, and assess PA over the last 24h to longer periods [29, 36, 40, 41, 59]. Global questionnaires are short, encompassing few, mainly two to four items, allowing to capture a rough picture of individual PA levels, like for classifying people, for example, based on the WHO criteria [29, 36, 40, 41]. Recall questionnaires typically encompass four to around 30 items (up to 75 items) and are applied to categorize PA levels and, far more

[6]Since the focus of this thesis is on PA, methods to assess energy expenditure (e.g., indirect or direct calorimetry by doubly labeled water) or physical fitness (e.g., maximal oxygen uptake) are not addressed.

than global instruments, allow determination of overall PA, for example, as minutes or MET-based scores, as well as of different PA dimensions and domains [29, 36, 40]. Finally, quantitative history questionnaires aim to assess long-term exposure of PA over the past months to years or even up to lifetime [29, 40]. Thus, they are most commonly applied in epidemiological studies on exposure-disease associations, and, due to their lengths and detailedness, are often applied in personal or computer-assisted interviews [40]. Although PA questionnaires are probably more valid when interview-administered [36], face-to-face interviews may not always be feasible in large-scale studies.

#### 2.3.1.3 Strengths and limitations of a subjective physical activity assessment

Depending on the extent of the subjective assessment, a differentiated picture on PA behavior can be derived in terms of its context, domain, and type, particularly, of structured and regularly performed PA that is easy to remember [36, 40, 43, 59]. Besides such predominantly qualitative information on PA, advantages of subjective PA measurements are their typically low cost and, thus, good affordability in large studies; their good acceptability and convenient handling and, thus, feasibility; and the comprehensibility of data obtained [36, 40, 41, 43, 59]. When using identical standardized methods, comparison between studies should be possible [36]. In contrast, inter-method agreement was found to be poor to modest due to a lack of standardization in items asked between measurements [29]. Assigning METs to subjectively assessed PA allows extrapolating of energy expenditure [36, 40]. However, when assigning an absolute (group average) intensity to a relative (individually perceived) activity intensity, both, the usage of standard energy costs that may not reflect the individual effort (see 2.1.1) as well as the uncertainty in reporting intensities may result in biased PA measures [37, 159]. Especially, if assessed in detail, subjective PA measurements may further be associated with a considerable time burden for the individual reporting and for the researcher evaluating the data [36, 40, 41, 59]. For specific populations, the ability to recall PA may be limited, e.g., for children, elderly, or persons with cognitive dysfunctions [36, 43, 59]. Then, subjective measurements may only assess PA by proxy, for example, parents reporting their offspring's PA [36]. Even in the general healthy population, the cognitive demands on recall may limit precise reporting of PA duration and intensity [42, 43, 159]. This may particularly be relevant for sporadic, incidental, or light activities that are mainly daily routine activities, and, thus, hardly remembered or not considered as 'PA' by the individual [37, 41, 58, 100-102]. Detection of light activities is further limited by subjective measures due to a 'floor effect', i.e., the measured value is below the measurement's limit or sensitivity range [37, 41, 58, 100-102, 160]. Additionally, although they can be applied in almost every population, subjective measurements may need adaptions for usage in specific or culturally diverse populations [36, 37, 40, 41, 43]. Otherwise, cultural bias or missing relevant PA sources and key activities that are relevant for the individual may result in an underestimation of habitual PA. Similarly, within and between populations, ambiguity of wording may bias the assessment of supposedly the same dimensions and domains of PA [36]. A main shortcoming of PA questionnaires and records is their susceptibility to respondent and social desirability bias, since persons may unintentionally or intentionally overestimate active, and underestimate sedentary or inactive time, especially in a face-to-face context [36, 37, 40-42]; computerized questionnaires may provide a more anonymous atmosphere [43]. For PA records, there is the risk of an observational bias due to a change in behavior, i.e., reactivity, since participants may be aware of being studied and increase their activity to a non-habitual level [31, 41, 58, 59]. Especially regarding PA frequency and intensity, subjective tools show shortcomings, since people may tend to report the highest, rather than the mean frequency, and to report the relative, rather than the absolute intensity of habitually performed PA [37]. Following the variety of beforementioned drawbacks, subjective PA measurements have consistently shown limited criterion validity and at best moderate test-retest reliability (reproducibility, see section 2.5.1.3), with few having both, good validity and reliability for assessing overall activity, PA dimensions, and energy expenditure [33-39]. Reliability is particularly low for long recall periods and light activities [37]. Low reliability of a measurement, however, limits the ability to detect true changes in the outcome over time (see section 2.5.1.3) [28, 36, 37] and the impact of PA on health risk may, thus, be underestimated using self-reported PA [37, 159].

Nevertheless, although subjective PA assessment tools may be prone to measurement error, these methods are justified in several settings, for example, when aiming to assess PA behavior regarding its context, mode, and domain [42, 43, 59]. Investigating these is epidemiologically relevant, since different types or domains of PA may have a distinct effect on health risk [12, 49, 50, 52, 122, 161, 162]. Since subjective PA measurements are more reliable on the population than on the individual level, they further allow classification of PA, for example, regarding the WHO PA recommendation, and, thus, are suitable PA ranking and monitoring tools [31, 36, 37, 40, 59].

When assessing PA in epidemiology, so far, researchers mainly aimed to estimate the energy cost of PA, i.e., the activity-induced energy expenditure [36, 40, 96]; the concept of assigning MET values to specific PA behaviors is in accordance with this. In contrast, in the last decades, the epidemiological interest has shifted from activity-induced energy expenditure due to structured, mainly moderate-to-vigorous intense activity (i.e., exercise) to the interest in habitual PA in daily life regardless of PA domain, type, and setting, that is, towards total energy expenditure or total movement [42, 95] (see section 2.1). Given that subjective assessments particularly allow assessing *PA behavior*, rather than *overall movement* that may have favored the current or future health status, and given that they show shortcomings to assess structured as well as unstructured activity with good validity, reliability, and sensitivity to changes, objective PA measurements has been increasingly developed and applied in epidemiology [42].

### 2.3.2 Objective physical activity assessment

Typically, objective PA measurements allow a quantitative assessment of the individual overall *habitual movement* under free-living conditions, encompassing structured and incidental activities [42]. The most commonly applied objective PA measures in epidemiological studies are direct observation, heart rate monitors, and motion sensors.

#### 2.3.2.1 Direct behavioral observation

For direct behavioral observation, a study assistant constantly observes a person of interest over a given time and records its behavior in predefined intervals in detail [40, 59]. Later on, observations are coded as standard activities that can be assigned to METs, allowing, in total, to capture a quite complete picture of the person's behavior in terms of PA type, setting, intensity, duration, frequency, as well as factors promoting or hindering activity within a defined context [40, 43, 59, 101-103]. However, this technique requires trained personnel and is labor-intensive for observers recording and researchers evaluating the data, and is, thus, mainly applied in small and pediatric studies in special contexts, e.g., in school environments [29, 40, 41, 43, 59, 163]. It also bears the risk of reactivity, when participants are aware of being observed [31, 40, 43, 58]. Further, although standard criteria are applied by the observer, direct observation is partly a subjective assessment, since PA is 'reported' by a third person. Thus, limitations inherent to subjective PA assessment methods (see section 2.3.1) may to some extent also be true for direct behavioral observation, and some authors actually evaluate this method as subjective PA measurement [36].

#### 2.3.2.2 Heart rate monitors

In contrast, heart rate monitors are suitable for large-scale studies, since costs for purchase and operation as well as their application are feasible [36, 40, 43]. Nowadays, heart rate monitors typically consist of a receiver (e.g., worn at the wrist) that collects heart rate signals wirelessly emitted from electrodes attached to the chest [40, 59]. As the heart rate is linearly associated with energy expenditure for moderate to vigorous intense activities, after calibration, heart rate monitors allow estimation of the free-living energy expenditure and activity of moderate to vigorous intensity [36, 40, 41, 43, 59]. However, estimation of energy expenditure is more valid on a group than on an individual level [164]. Further, the heart rate can substantially be influenced by others than PA-related factors, like arousal, temperature, or caffeine intake, and further may be less valid for capturing sporadic PA of short duration (due to a delayed increase in the heart rate), for estimating activity during rest, light and very vigorous activity (due to a non-linear association of heart rate and energy expenditure), and for mainly lower body part-related activities (due to an unproportionally high energy expenditure compared to the heart rate due to the effort of large muscles, e.g., of legs) [36, 40, 41, 43, 59]. Additionally, biological characteristics, such as age, sex, or body composition may affect the linear relationship of heart rate and energy expenditure, reducing the validity of heart rate monitors to estimate PA [59].

#### 2.3.2.3 Pedometers

Pedometers are motion sensors that are attached to the body, for example, at the hip, wrist, or upper thigh, and detect taken steps by capturing vertical movements [36, 40, 43, 59]. Determination of walking behavior enables characterizing the person's PA level, for example, as sedentary to highly active or with regard to PA recommendations, like '10,000 steps per day' [36, 165]. A large number of pedometers using different techniques is now available, with devices being (mostly) affordable, valid for step detection, easy to handle by participants and study personnel, applicable on a large scale and across all ages, and data obtained being intuitively interpretable [36, 40, 43, 59]. However, step detection may be less valid in older adults exerting low paces and for distance or energy expenditure estimation and, further, depends on the pedometer attachment site, the foot part first contacting the ground (i.e., the foot strike), the body height, the leg and step length, the pace, and may further be manipulated through shaking [36, 40, 59]. Finally, detecting dimensions, domains, and types of PA is limited using pedometers [40, 59].

#### 2.3.2.4 Accelerometry to assess habitual physical activity

Today, accelerometers as second type of motion sensors are increasingly used in epidemiology [31, 59]. In 2014, they were applied in 76 at least medium-sized studies across all continents [166]. Large cohorts already using accelerometry during waking to assess PA are the UK National Diet and Nutrition Survey, the Health Survey for England, and the U.S. National Health and Nutrition Examination Survey, while, in Germany, the German National Cohort and the Cooperative Health Research in the Region of Augsburg use 24h-accelerometry [167-171]. For children, an international database on studies using accelerometry has already been established [172]. Compared to pedometers or subjective measurements, accelerometers potentially provide a vastly more detailed picture of the individual PA, allowing to assess overall PA and time spent in different activity intensities [31, 43, 59, 65, 173]. By measuring accelerations of the human body, accelerometers primarily enable detection of body movements and their intensity and volume over time [31, 41, 43, 59, 173]. Enclosed in a sealed polycarbonate case and equipped with an internal memory and a rechargeable lithium battery, accelerometers are mainly attached with an elastic belt to the hip aligned with the right anterior axillary line (**Figure 2**) [36, 40, 173]. Attaching the accelerometer to the hip is due to the assumption that energy expenditure is directly associated with body mass [96]. Since this is mainly accumulated at the trunk, a spatial change of the center mass presumably best predicts energy expenditure. Devices can be worn continuously over a predefined period for 24h per day.

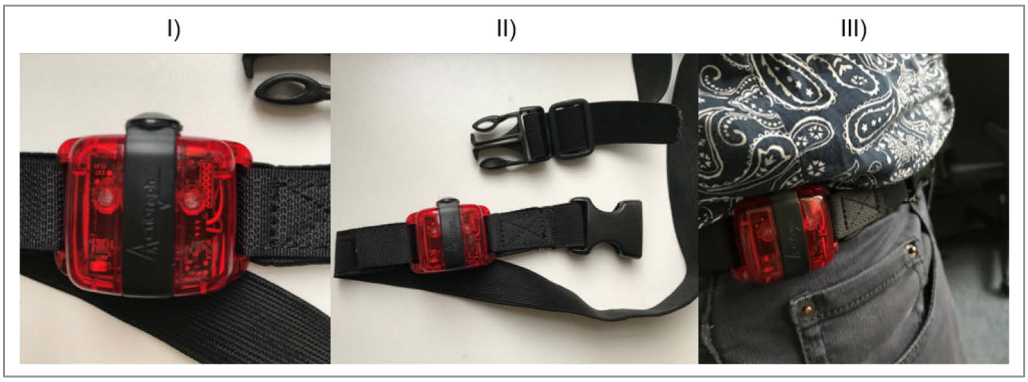


**Figure 2**: Photographs of an ActiGraph accelerometer in detail and worn on the hip
Photographs of an ActiGraph GT3X+ (ActiGraph LLC, Pensacola, FL, USA) in detail (panel **I**), with a non-absorbent strap (panel **II**), and worn at the hip aligned with the right anterior axillary line (panel **III**). Copyright of the photograph belongs to the author.

Accelerometers are capacitive elements that are able to detect static as well as dynamic acceleration, i.e., steady force of gravity and force due to movement, in terms of gravitational units, G, with 1 G equaling acceleration of 9.8 meters per squared second (m/s²) [36, 40, 43, 173]. Acceleration is recorded with a predefined sampling frequency, with this rate ideally being chosen in a way that enables to capture all human movements, i.e., around at least 16 to 50 Hertz (Hz, equaling 16 to 50 measures per second) [173]; new devices allow to individually select the sampling rate within a specific range. Accelerometers are piezoelectric acceleration sensors: Within a micro-electro-mechanical system, occurring accelerations trigger swinging of a moveable seismic mass relative to fixed piezoelectric elements, which generates a change in capacitance and finally results in a change in voltage [31, 65, 173]. This change in analog, electronic voltage signal is proportional to the amplitude and frequency of the occurred acceleration [31, 65, 173]. Dynamic acceleration reflects the change in velocity with respect to time, while velocity or speed, in turn, results from changing the spatial position over time [36, 173, 174]. Thus, acceleration can be used as measure of the body's movement [36, 173, 174]. Since accelerometers assess static as well as dynamic acceleration, the acceleration outcome is directly associated with the external force that counteracts the activity, and, thus, reflects the energy cost of movements [36, 43, 173]. After filtering out too high or too low frequencies and a subsequent amplification, digitalization of the voltage signal by a built-in analog to digital converter, and rectification, the accelerometry data is downloaded from the internal memory, when data collection has been completed. Then, data can be processed by proprietary software to device-specific activity-related units, with the most common unit being a 'count', but for some devices, raw data can be stored as well [43, 64, 65, 173]. The arbitrary count is, however, an artificial and counterintuitive measure of movement, and for most accelerometers, the underlying algorithms for its derivation remain company secret [31, 173]. Broadly, a count can be interpreted as the weighed acceleration units accumulated over a predefined epoch length, with weights being proportional to the magnitude of the acceleration per epoch [173]. Data obtained should pass a quality check (e.g., check for spurious data, like abnormal high accelerations or counts) and quantity check (i.e., completeness of data), either by using implemented algorithms or own criteria [31]. To analyze and interpret counts data, appropriate device-specific software can be used to determine PA measures, like intensities, or to make inferences about the metabolic cost of the persons' movement, i.e., to predict energy expenditure [31, 40]. First generations of accelerometers were uniaxial and later biaxial, i.e., they collected accelerations only by the vertical axis, or by the vertical plus horizontal (anteroposterior) or perpendicular (mediolateral) axis, respectively [36, 40, 59, 173]. Today, accelerometers are able to capture accelerations by all three orthogonally orientated spatial axes, i.e., by the vertical, horizontal, and perpendicular axis [36, 40, 59, 173]. As predominance of spatial forces differs between PA behaviors (e.g., for walking versus climbing), triaxial accelerometers may more entirely capture the PA spectrum [31, 36, 173]. Indeed, associations with energy expenditure measured by indirect calorimetry were stronger, and sedentary behavior and light activity more precisely captured based on triaxial than on biaxial and uniaxial accelerometry, respectively [36, 173, 175].

#### 2.3.2.4.1 Accelerometry-based physical activity and health

Confirming the evidence from subjectively assessed PA (see section 2.2), epidemiological studies show a dose-response association for accelerometry-based PA and health outcomes, with low PA and high (uninterrupted) sedentary time being a predictor of premature mortality risk, poor quality of life, metabolic risk factors, as well as of the economic burden due to chronic conditions and the utilization of health care [31, 53, 58, 162, 176-190]. However, accelerometry-based PA was shown to be more strongly associated with health outcomes, like cardiometabolic risk factors than self-reported PA [31, 33, 191, 192]. The true impact of PA on health may, thus, be underestimated using subjective measurements. Although accelerometer counts are to some extent an arbitrary unit, studies also show counts-based measures to have a negative association with premature mortality risk and metabolic risk factors [162, 180]. Further, regarding activity intensities, accelerometry-derived light activity was shown to be independently associated with metabolic risk factors, self-reported health and psychosocial variables, depressive symptoms, multimorbidity, and premature all-cause mortality [193-197]. This further supports the conclusion to promote even light activities to reduce the burden related to inactivity (see section 2.2) [31]. Given that the assessment of light activity is limited by subjective measurements (see section 2.3.1), while it may be more precise by accelerometry [175], accelerometry-based PA provides the opportunity to investigate the impact of light intense activity on health in more detail. However, most previous studies on PA as health-related lifestyle factor used subjective PA measures, while accelerometry was rarely used [9, 11-19, 31].

#### 2.3.2.4.2 Strengths and limitations of accelerometry to assess physical activity

Compared to standard references, accelerometers have been shown to enable a precise and technically reliable assessment of locomotor activities that is less biased and more comprehensive than based on subjective methods [31, 33, 40, 41, 43]. Besides determining a huge number of PA measures, accelerometry-assessed PA data is time-stamped and, thus, enables to depict individual temporal PA patterns (e.g., regarding regularity) [40, 59]. There are no contraindications for an application of accelerometry, and devices are small in size, lightweight, easy to handle for participants and study personnel, affordable for an application on large scale, and exerting maximal little burden or risk, while large memory capacities allow capturing data over several days to weeks [31, 36, 40, 59]. Additionally, in contrast to some pedometers, they typically have no direct visual feedback, like a display showing the current activity that would bear the risk of a behavioral bias [31, 43]. Accelerometers enable a more precise assessment of time and breaks in sedentary behavior than subjective measures, since these behaviors are probably hardly remembered and estimated by the individual [36, 187, 198, 199]. Nevertheless, accelerometry-derived counts are counterintuitive and the amount of data is extensive and complex, requiring knowledge on data reduction and processing [31, 40, 59]. Thus, taking full advantage of triaxial accelerometry data is labor-intensive. Further, standards and consensus on key decisions on data collection and data reduction are lacking, although decisions may influence findings on PA outcomes [59, 158, 200, 201]. There is a plethora of algorithms available to derive activity intensities and energy expenditure, but not all are validated, especially with respect to specific populations and study aims [40, 43, 59, 173, 202-204]. Determination of activity intensities in a population largely depends on the algorithm used, which may influence findings regarding exposure-disease associations and, thus, may limit the method's objectivity [59, 202]. The abundance of accelerometer brands and models applied across studies as well as of algorithms and procedures for data handling further limits comparability between studies, even when the same device is used [59, 158, 166]. Thus, PA researchers call for standardization of accelerometry data collection, processing, and analytic approaches [158, 166]. Further, accelerometers do not allow capturing isometric muscle constructions, the effort of muscular work, e.g., when bearing or lifting weights, or other static movements that does not involve moving the center mass (e.g., leg or arm exercises) [31, 36, 40, 41, 43]. However, assuming that most persons doing regular muscle strengthening (that may not be captured by accelerometry) also do regular aerobic activities (that are captured by accelerometry), accelerometry-based PA may still be a proxy for isometric activities [31]. Furthermore, predicting energy expenditure using accelerometry is limited and add little value to common prediction equations based on individual characteristics, such as age or sex [96, 205, 206]. Finally, accelerometers are most commonly applied only once, although seasonal, day-to-day, and month-to-month intra-individual variability (e.g., due to changes in occupation, health status, or residential area) of habitual PA may be relevant for estimating the 'true' mean, i.e., habitual PA [31, 207-214].

Compared to subjectively assessed PA, agreement with accelerometry-based PA is limited and moderate at best for overall activity and time in activity intensities [34, 42, 44, 215-217]. Besides limited ability to remember, estimate, and self-report PA, differences between both methods in overall activity estimates may partly be explained by the fact that some subjective measures only assess PA of minimal lengths [29], and, that, even if asked for any activity, short activities may be hardly remembered or not considered (see section 2.3.1). In contrast, accelerometry captures all movements. Regarding activity intensities, differences between objective and subjective PA estimates may partly be due to the comparison of absolute (accelerometry) and relative (reported) intensities [37, 42]. Deviation between both methods may also reflect the disability of accelerometers to detect static-movements, or may indicate that subjective measures are prone to respondent and social desirability bias. The latter assumption is supported by the findings that body mass index (BMI), sex, age, and education are associated with the deviation between both methods, and that the proportion of people fulfilling the WHO PA recommendation tend to be lower and sedentary time tend to be longer based on objective than on self-reported PA [42, 44, 215-217]. However, little agreement between both measurements may not inevitably imply a limitation of any of the two methods, since both may simply have measured different aspects of PA [29].

#### 2.3.2.4.3 ActiGraph accelerometer

Several accelerometer brands are available [40, 59, 206], with, in 2014, the models of ActiGraph (ActiGraph LLC, Pensacola, FL, USA; formerly 'Computer Science and Applications' or 'Manufacture Technology Incorporated' [173]) being used in more than half of all published at least medium-scale studies [166]. In newer studies, the triaxial GT3X(+) models are the most common ActiGraph models (**Figure 2**) [36]. The GT3X+ that was released in September 2010 is as lightweight (19 gram, g) and compact (4.6 × 3.3 × 1.5 centimeter, cm) device that enables sampling of raw acceleration data within a dynamic range of ± 6 G at a sampling rate of 30 to 100 Hz, using a 12 bit analog to digital converter [69, 218, 219]. Waterproofing (submersible) makes removing for water activities unnecessary, when using non-absorbent straps [218]. The GT3X+ has a built-in inclinometer and lux detector that are supposed to allow detection of the person's anatomical position (distinguishing between lying, sitting, standing or 'off') and ambient light, respectively [218, 220]. However, as the validity of the inclinometer was reported to be acceptable at best, with cycling, walking, and sitting being often misclassified [221-224], and since the device is mostly covered by clothes, the meaningfulness of the inclinometer and lux data is questionable. For initialization of devices and for downloading and processing the recorded data, the company owned ActiLife software (ActiGraph LLC, Pensacola, FL, USA) is available [218]. During initialization, participants' characteristics (i.e., sex, date of birth, height, weight, ethnicity, placement of wearing, and handedness), the sample rate, and start and end time of recording are preset [220]. While recording data, built-in algorithms filter out baseline noise and abnormal high accelerations (e.g., due to driving a car) [218] and after completion of data collection, either raw data can be downloaded and stored, or raw data can be compressed by choosing conversion into 1-second to 240-seconds epochs (ActiLife, version 6.13.3) for one to all three spatial axes that are then stored as processed data [218, 220]. Further, there is the option to download steps, lux, and inclinometer data [220]. In addition to displaying basic variables, i.e., the time-stamp, counts per axis, and, if enabled, steps, lux, and inclinometer data, for further data processing based on the counts data, there are different algorithms for detection of accelerometer NWT, data scoring (i.e., determination of activity intensities, energy expenditure, MET values, and detection of time in bouts), and data graphing implemented in ActiLife [220]. Further tools allow specific analyses that are not relevant for this thesis, e.g., sleep analyses [220].

In case the triaxial data is downloaded, the 'vector magnitude counts per minute (cpm)' comprising accelerations detected via the vertical, horizontal, and perpendicular axis is generated as squared root of the sum of the squared accelerometry data per axis (**Equation 1**), which then can be used for further data scoring [220]:

$$vector\ magnitude, counts\ per\ minute\ (cpm) = \sqrt{(acceleration_{axis\ 1})^2 + (acceleration_{axis\ 2})^2 + (acceleration_{axis\ 3})^{2a}}$$

**Equation 1**: Vector magnitude counts per minute based on triaxial accelerometer data

[a]the vector magnitude counts per minute is calculated based on the accelerations detected via the vertical (axis 1), horizontal (axis 2), and perpendicular axis (axis 3)

ActiGraph accelerometers, including the models used in this thesis, show good inter- and intra-instrument reproducibility (see section 2.5.1.3) and good criterion validity compared to indirect calorimetry, oxygen uptake, doubly labeled water, or direct observation, when used during waking hours for the estimation of overall activity, activity intensities, and energy expenditure [36, 60-69].

Nevertheless, using PA data captured by accelerometry involves several decision-making steps from planning and conducting the data collection to having a valid and for the study aim appropriate data set available [31, 58, 158].

## 2.4 Application of accelerometry and operationalization of accelerometry-based physical activity in epidemiology

### 2.4.1 Application of accelerometry in epidemiological studies

First, using accelerometry to assess PA in epidemiology requires decisions on the application, i.e., on *how* to collect data, and on the operationalization of PA, i.e., on *what* to determine from the plethora of accelerometry data and variables provided (**Table 1**).

For the application of accelerometry in epidemiology, first, the *length of assessment* has to be defined prior to starting the measurement [58], varying between one day and several years [70-75, 225, 226]. Researchers usually aim to assess mean habitual PA, thus, using accelerometry over longer periods is favorable, since a higher number of repeated measurements reduces variability of PA and improves the estimation of the true mean PA [81, 227]. However, the length of assessment is restricted by resources, feasibility, and burden of participants. In previous studies, the length of assessment mainly encompassed one week to assess each day of the week [70-74]. Nevertheless, knowing the variability of habitual accelerometry-based PA is important to define the number of days needed to reliably assess PA using accelerometry in epidemiology. This issue will be addressed as one objective in this thesis (see section 2.5.1).

**Table 1**: Key characteristics on application and operationalization for using accelerometry to assess physical activity in epidemiological studies

| | **examples [reference]** |
|---|---|
| **characteristics of application** | |
| **length of assessment** | one day [225]<br>one week [70-74]<br>three weeks [75]<br>one year [226] |
| **frequency of assessment** | once [70-74]<br>repeated [193, 201, 228] |
| **selection of assessment days** | randomly<br>continuously [70-74] |
| **daytime** | waking [58, 70-75]<br>24h per day [167, 191, 229] |
| **characteristics of operationalization** | |
| **processing of accelerometry data** | unbouted (raw) [230]<br>bouted (processed) [70, 72-74] |
| **scale of activity parameters** | continuous [162, 189, 231]<br>categorical [57, 71, 162] |
| **definition of activity parameters** | overall activity (counts, cpm) [74, 162, 180]<br>time in overall activity (min/d) [231]<br>time in activity intensities (min/d) [162, 188, 189]<br>% time in activity intensities [177, 190, 231] |

cpm, counts per minute; min/d, minutes per day

Further, determining the *frequency of assessment* of accelerometry is important, i.e., whether the assessment is performed only once per person [70-74] or repeated over time [193, 201, 228]. The latter has the advantage to enable longitudinal analyses of temporal relationships of PA, like drawing exposure-disease association and causal inferences [80, 227], and to assess different months and seasons per person, which may be relevant regarding variability of PA [31, 207-214]. Applying accelerometry only for a single measurement allows cross-sectional analyses, like estimation of PA levels or investigating associations of PA, for example, with prevalent conditions or individual characteristics [80, 227]. Since it is more feasible than repeated measures, most large-scale epidemiological studies assess accelerometry-based PA only once [70-74].

*Selection of accelerometry assessment days* can be randomly or consecutively. Random selection of days has the advantage to theoretically better represent habitual mean PA. However, it is probably not practicable on large scale due to the organizational effort, and wearing the device several times for short periods may further bear a higher risk of reactivity compared to one long assessment, where awareness of being studied is supposed to diminish over time [31, 58, 59]. At the best of one's knowledge, currently, there is no epidemiological study using accelerometry on randomly selected single days. However, a recent study indicates that randomly selecting one out of seven continuous days allows estimation of the group mean PA [74]. Thus far, in most studies using accelerometry, assessment is performed over consecutive days [70-74].

Finally, the *daytime* of accelerometry assessment has to be specified [58], i.e., whether to assess PA during waking only [70-75] or continuously over 24h per day [167, 191, 229]. Although 24h-accelerometry has several advantages, as discussed in section 2.5, still, most previous studies used accelerometry during waking only [58, 70-75]. This is most probably due to the assumption of complaints during the night due to wearing the device or to the assumption that PA during (reported) sleeping phases is not relevant for overall activity; however, this will be addressed in detail in sections 2.5 and 5.1.

### 2.4.2 Operationalization of accelerometry-based physical activity in epidemiological studies

As first step for operationalization of accelerometry-based PA, *processing of accelerometry data* has to be defined, i.e., whether to use raw, unbouted data as sampled by the accelerometer with the preset sampling rate [230], or to use processed, bouted data averaged over a predefined epoch length, like 60 seconds (**Table 1**) (see section 2.3.2.4.3) [70, 72-74]. This is important, since most, although not all studies comparing both approaches show a distinct impact of bouted versus unbouted data on health outcomes [180, 232-236]. Using bouted data diminishes the detailed information being initially captured by accelerometry with high frequency (with up to 100 Hz) on short-term temporal variations of PA, especially in terms of activity intensities [40, 173]: Averaging activity intensities over a predefined epoch may result in an underestimation of high intense activities that typically are of short duration and more likely intermittent than PA of lower intensities [173]. Using bouted data further misses sporadic PA per se, like fidgeting, although it (cumulatively) may be relevant for overall activity and health [31, 158, 237]. Misclassifying and missing PA intensities become more pronounced the longer the epoch length of accelerometry data is chosen, which may result in equal PA estimates for substantially different PA patterns [173]. However, analyzing raw accelerometry data requires knowledge on handling of complex data [31, 40, 59]. While several sophisticated approaches that may presumably allow to exploit the detailed accelerometry information have already been examined based on uniaxial accelerometry data captured during waking, including the application of artificial neural networks or machine learning techniques, latent class analyses, hidden Markov models, or quadratic discriminant analyses [173, 232, 238-240], still, the majority of previous studies used processed data to examine accelerometry-based PA [70, 72-74]. Indeed, bouted data can be justified, for example, to study prevalence of 'insufficient PA' according to the WHO, where activity in 10-minutes bouts is used (see section 2.2.2) [7].

Further, choosing the *scale of the activity parameters* derived from accelerometry. On the one hand, continuous PA measures can be determined, like minutes in total or dimension-specific PA (e.g., minutes per day in moderate activity) [162, 189, 231]. They allow a continuous analyses, like linear regression or dose-response analyses, making use of the distinct informative value provided [26]. On the other hand, categorized PA measures can be assessed. In this context, often, classification regarding the fulfillment of a PA recommendation or the PA amount (e.g., 'inactive' versus 'highly active') is investigated [57, 71, 162]. Categorical measures allow contrasting distinct exposure levels, for example, by performing logistic regression analyses [26]. However, they diminish the details in the available comprehensive accelerometry-based information.

Finally, the *definition of activity parameters* is important for using accelerometry in epidemiology, i.e., the measure derived from accelerometry data that is used for calculating the PA outcome of interest. For example, overall activity may be defined based on count values [74, 162, 180, 203] or based on the total length of active behavior, e.g., based on the time in activity intensities [203, 231]. Time-based measures have the advantage that they are directly interpretable. However, since it relies on time in intensities that, in turn, relies on bouted counts data, information on 'extreme' intensities within an intensity level may have gone lost (see above). In contrast, counts measures are counterintuitive, but more directly reflect the person's acceleration, i.e., habitual overall movement. Furthermore, PA parameters can be defined as absolute measures, like minutes in overall activity or activity intensities per day that have the advantage of being directly interpretable [162, 188, 189, 203, 231], and since they are intuitively understood by lay public, they are typically used for PA recommendations (e.g., '150 minutes of moderate PA per week', '10,000 steps per day') [7, 165]. However, time under investigation may vary between participants and days, making assessment of proportions of active time favorable (e.g., % of light activity regarding total activity) [177, 190, 203, 231]. This allows comparability between individuals and populations, and, further, investigation of relative shifts of subcomponents of an overall measure, for example, when light activity increases at the expense of moderate activity.

However, although they allow capturing PA with high resolution over days to weeks, and although an extended observational time over 24h is recommended, when aiming to investigate exposure-disease associations [14, 31], multiday 24h-accelerometry is still rarely used [31].

## 2.5 Using 24h-accelerometry in epidemiology

There are recommendations that PA in epidemiological studies on exposure-disease associations should be assessed objectively, over several days, including waking and sleeping periods, and with regard to activity intensities [14, 31]. However, most pervious large epidemiological studies assessed PA using subjective methods, thus, bearing the risk of measurement error [33-44]. Large studies and cohorts that have already used accelerometry mainly assessed PA during waking only [70-75, 200, 241].

In contrast, 24h-accelerometry over multiple days allows capturing a more complete picture of the PA spectrum, possessing essential advantages compared to accelerometry applied during waking only [229]. First, asking participants to continuously wear the accelerometer is supposed to considerably decrease the likelihood of forgetting to put the device on again after waking up [242]. Secondly, since 24h-accelerometry does not require participants to put the device on and take it off every morning and evening, respectively, there is presumably a lower risk of reactivity of wearing, since awareness of being studied is decreased [31, 41, 58, 59]. One may suggest that the continuous wearing protocol also increases the compliance of wearing, which is important regarding the aim of assessing habitual PA. This assumption is supported by findings in children, where an increased wear time was found, when applying a 24h-wearing protocol compared to accelerometry assessed during waking only [229]. Thirdly, since the prescribed wearing time is the same across all participants, comparability of data obtained between persons is higher and the risk of bias in estimating PA due to differences in wearing or waking time is reduced for 24h-accelerometry. Fourthly, 24h-accelerometry allows to capture active behaviors during actual sleeping phases, like interruptions of sleeping or periods in between being awake and asleep, such as lying awake, reading a book, using the bath, or picking a glass of water that all may contribute to overall movement [229, 242]. Even if one does not perform any of the beforementioned activities, moving during reported sleeping may be of moderate intensity (**Figure 3**). Although the contribution of these activities to the health-enhancing effect of habitual PA is unclear, the cumulative impact of short active periods on the overall amount of movement, however, is assumed to be relevant. This assumption is supported by the finding by Panter et al. using a uniaxial ActiGraph model during waking, showing that the time in moderate-to-vigorous activity is positively associated with wearing time [243]. Thus, capturing behaviors contributing to the total amount of movement as comprehensive as possible throughout the day is favorable, in order to capture a valid picture of the individual habitual PA [229]. Finally, using 24h-accelerometry allows to study health-related sleeping behavior [58, 244, 245], providing, thus, an objective assessment of activity and sleep characteristics by one device. As a whole, features and advantages of multiday 24h-accelerometry possess the crucial value for epidemiology.

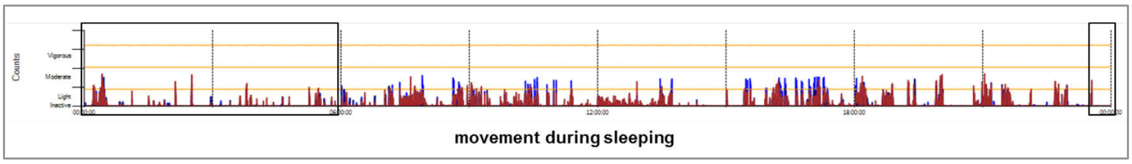


**Figure 3**: Exemplary illustration of physical activity occurring during sleeping phases assessed using 24h-accelerometry under free-living conditions
Physical activity of one person assessed over 24h using the triaxial accelerometer ActiGraph GT3X+ (ActiGraph LLC, Pensacola, FL, USA). Acceleration data shows body movements of up to moderate intensity during sleeping (black framed boxes). These observations support usage of 24h-accelerometry to capture the entire spectrum of habitual activity-related behavior, i.e., movement, under free-living conditions. Picture extracted from the ActiLife software (version 6.13.3; ActiGraph LLC, Fort Walton Beach, FL, USA). Each row represents 24h-accelerometry data as processed 'counts', collected using all three spatial axes per participant and day from 0 a.m. to 12 p.m. From bottom to top, horizontal orange lines indicate intensity limits for moderate (2,691-6,166 counts per minute, cpm), vigorous (6,167-9,642 cpm), and very vigorous (≥9,643 cpm) activity (below moderate: inactivity, 0-78 cpm; low activity, here called 'light', 79-2,690 cpm), see section 3.4.3 [246]. Vertical light blue, dark blue, and red lines indicate accelerometry data captured via the vertical, horizontal, and perpendicular axis, respectively. Informed consent was provided by the respective person to present the data shown in this figure.

However, although now being an available approach, 24h-accelerometry is still rarely used in epidemiology to assess PA, especially in the general adult population [167, 168]; most studies using 24h-accelerometry focus on children or elderly [226, 229, 247]. Additionally, time spent in different activity intensities that is important for health and can substantially differ even for a similar overall activity level [1, 24, 45-57, 99, 109] features one underused possibility to investigate PA as lifestyle factor in more detail. As reflected by the wide range in time in overall and differentially intense activity levels achieved (see sections 2.2.2 and 2.1.1), PA is a modifiable behavior, implying the presence of factors promoting and hindering the individual to be active. However, factors particularly influencing accelerometry-based PA are largely unknown, although they may provide relevant information to understand PA behavior and to identify targets for PA promotion plans (see section 2.2). Lacking evidence on determinants of PA is even more true for 24h-accelerometry and activity intensities.

Thus, the aim of the present thesis was to investigate the application of multiday 24h-accelerometry in epidemiology to study habitual overall activity, activity intensities, and activity determinants under free-living conditions. However, few studies are available on underlying assumptions and principles of 24h- accelerometry-based PA, like its variability and reliability, or criteria, like completeness of accelerometer wearing time to enable a reasonable and valid application of 24h-accelerometry over multiple days in an epidemiological setting. Thus, to examine the application of 24h-accelerometry in epidemiology, the following three issues were addressed.

### 2.5.1 Variability of habitual physical activity using multiday 24h-accelerometry under free-living conditions

In epidemiology, researchers are mainly interested in assessing the 'average' exposure of PA by a single measurement. This information is then used for drawing exposure-disease associations to estimate, to what extent individuals with higher PA levels differ in risk of chronic diseases compared to those with lower PA. However, although aiming to assess habitual PA, in most studies thus far, accelerometry is assessed over one week only [70-74]. Assuming that such a single assessment is representative for the true mean long-term exposure, however, requires a high reliability of the measurement [26, 43, 157, 248]. To evaluate this, in turn, variability of PA must be known, to define the number of days needed to validly estimate habitual PA, while keeping the participants' burden to a minimum and the feasibility of the assessment to a maximum [200].

#### 2.5.1.1 Day-to-day variability of habitual physical activity using accelerometry

Regarding accelerometry, there are different possible sources contributing to the within-person variability of habitual PA between days. First, across *the days of assessment*, one might expect a decline in PA due to reactivity of wearing the device [31, 58, 59]. While initially, participants may be aware of being studied, over time, this effect is supposed to diminish. Further, one may speculate that across the *days of the week*, individuals may tend to have some kind of activity plan [31, 249]; for example, one person will go to the gym every Monday and Friday, while another one will jog every Tuesday and Saturday. Finally, in previous studies using uniaxial accelerometry-based PA during waking, variations in PA across the days of the week were reported, with *weekend* *days versus weekdays* showing lower activity levels, and, thus, it was recommend to require at least one weekend day for a valid PA data set [36, 43, 200, 241, 250-252]. Few authors have already investigated the intra-individual variability of habitual PA using objective measurements. However, most of these used other assessment techniques, such a pedometers, other than the ActiGraph accelerometers, or where restricted to specific populations (e.g., obese participants of a weight loss intervention trial) [213, 253, 254]. In one study, using the GT3X+ over 24h per day, the within-person variance was shown to make up the largest proportion of variability of occupational and leisure steps, sitting, standing, and moderate-to-vigorous activity [214]. Thus, one may suggest that several assessment days of triaxial 24h-accelerometry are needed to validly estimate PA (see section 2.5.1.3).

#### 2.5.1.2 Number of days needed to estimate habitual physical activity using accelerometry

Lacking evidence is similarly true for the number of days needed to reliably estimate habitual PA, when taking the within-person day-to-day variability into account. Using ActiGraph models, so far, in most studies investigating the suitable length of PA assessment using accelerometry, accelerometry was used during waking only over a 1-week period, while applying an older, uniaxial accelerometer generation, and studies were partly focused on specific age groups, like toddlers, adolescents, or older ages [62, 74, 201, 241, 255]; few were conducted over longer periods [75, 200, 241]. These studies suggest that one day to seven days of accelerometry during waking over a single period are required to validly estimate PA [74, 75, 241, 255]. This is in line with the study protocol of most studies using accelerometry during waking [70-74]. However, there are also reports suggesting longer assessment periods to be necessary [31, 62].

#### 2.5.1.3 Reliability of habitual physical activity using accelerometry

On the one hand, reliability of an assessment like accelerometry depends on the short-term test-retest reliability or technical reproducibility, i.e., the stability of a measure, when the assessment is repeated under the same circumstances [26, 80, 157, 256]. Good intra-instrument reproducibility has already been shown for the accelerometers used in this thesis [36, 60-69]. However, additionally, the reliability of an assessment depends on the within-person (intra-individual) variability of the measure, i.e., on true changes or fluctuations in accelerometry-based PA over time, as compared to the between-person (inter-individual) variability because of differences in PA due to the subject [26, 157, 211]. A low within-person or high-between person variability both result in a high reliability (and validity) that, in turn, is a precondition for sensitivity of a measurement, i.e., for the ability to detect small true changes over time and to rule out the possibility that observed changes in the measure are due to random variability [26, 28, 43, 157, 248, 256]. In contrast, a high within- or low between-person variability attributable to the overall variability of PA both end up in a low reliability and in requiring a high number of repeated measurements to validly assess PA [26, 157, 211, 248, 257]. A low reliability of a measurement further limits the determination of the ‘true average’ PA amount, and may attenuate and, thus, mask existing exposure-disease associations in epidemiology [28]. Knowing the reliability of the measurement then allows to account for the within-person variability and to calculate approximate true, deattenuated relative risk estimates [28]. Additionally, knowing the within-person variability and reliability of a measure provides valuable information for planning the assessment length in future studies. Considering the within-person variability (see section 2.5.1.1) and calculating the number of days needed to estimate PA from 24h-accelerometry data (see section 2.5.1.2), one may examine the reliability of PA as assessed over the number of days required. Previous studies on accelerometry-based PA indicated a good to excellent reliability of the measurement over time, but these studies used uniaxial accelerometry during waking only [75, 201]. One may suggest that the restriction to both, accelerometer data of one axis and assessment of waking only reduces ‘sources’ of variability compared to triaxial 24h-accelerometry data.

#### 2.5.1.4 Reliable assessment of physical activity using multiday 24h-accelerometry under free-living conditions (research question 1)

However, day-to-day variability of triaxial 24h-accelerometry-based PA, and, thus, the number of days needed as well as the reliability of 24h-accelerometry-based overall activity and time spent in different activity intensities are largely unknown for the general adult population. In line with studies using accelerometry during waking [70-74], cohorts already assessing 24h-PA use accelerometry over a 1-week period [76, 229, 247], but the basis of the decision-making on the length of the assessment is unclear.

The first objective of this thesis was to investigate the reliable assessment of habitual overall activity and time spent in different activity intensities using multiday 24h-accelerometry in the general adult population. Thus, first, the proportion of the within-person (day-to-day) variability accounting for the total variability of these PA measures was quantified over a 2-weeks period. Secondly, it was assessed, if and to what extent overall activity and time spent in different activity intensities systematically differ between consecutive days of assessment, the days of the week, and between weekdays and weekend days. Thirdly, the number of consecutive days needed to validly estimate habitual 24h-accelerometry-based PA was calculated. Finally, the reliability of overall activity and of time spent in different activity intensities was determined using 24h-accelerometry over multiple days under free-living conditions.

### 2.5.2 Accelerometer non-wear time in multiday 24h-accelerometry-based physical activity

In addition to the number of assessment days needed to estimate PA, defining the minimal required daily length of captured PA data is pivotal [200]. After initialization, accelerometers continuously record data, no matter, whether the device was appropriately worn by the participant, or not. If a period of consecutive zero-acceleration readings is detected, this can either be due to an actual wearing time of inactivity (e.g., sleeping or quiescent wakefulness) or since the participant took off the device and put it aside (**Figure 4**). Although, theoretically, a 24h wearing protocol does not require to take the device off (at least, when using a waterproofed device and non-absorbent straps), still, accelerometer NWT periods of varying lengths are possible, for example, due to unwillingness of wearing, high-contact sports, or changing clothes.

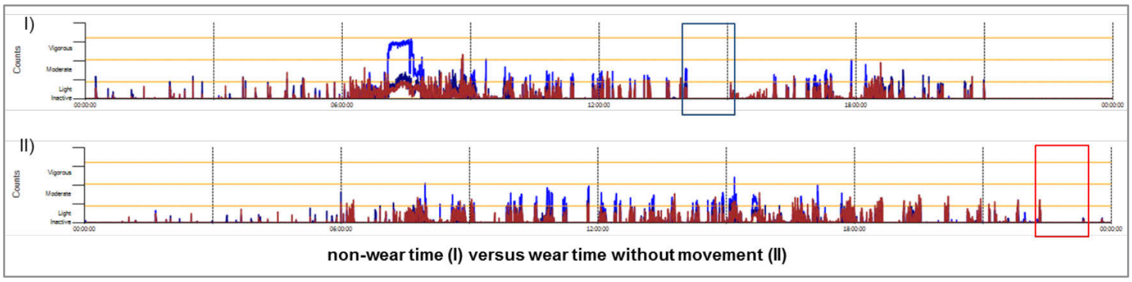


**Figure 4**: Exemplary illustration of accelerometer non-wear time in physical activity assessed using 24h-accelerometry over multiple days under free-living conditions (research question 2) Physical activity (PA) of one person assessed over two days for 24h per day using the triaxial accelerometer ActiGraph GT3X+ (ActiGraph LLC, Pensacola, FL, USA), showing two times of continuous zero-acceleration readings longer than 60 minutes that can either reflect an actual accelerometer non-wear time (panel I, blue framed box) or true wear time without movement (panel II, red framed box). Picture extracted from the ActiLife software (version 6.13.3; ActiGraph LLC, Fort Walton Beach, FL, USA). Each row represents 24h-accelerometry data as processed 'counts', collected from one person using all three spatial axes per day from 0 a.m. to 12 p.m. From bottom to top, horizontal orange lines indicate intensity limits for moderate (2,691-6,166 counts per minute, cpm), vigorous (6,167-9,642 cpm), and very vigorous (≥9,643 cpm) activity (below moderate: inactivity, 0-78 cpm; low activity, here called 'light', 79-2,690 cpm), see section 3.4.3 [246]. Vertical light blue, dark blue, and red lines indicate accelerometry data captured via the vertical, horizontal, and perpendicular axis, respectively. Informed consent was provided by the respective person to present the data shown in this figure.

Thus, a second premise for a valid interpretation of habitual PA from 24h-accelerometry is knowledge about participants' compliance with the wearing protocol and the occurrence, time, and length of accelerometer NWT, i.e., about times, when the accelerometer was not worn [31].

#### 2.5.2.1 Detection of accelerometer non-wear time for estimation of habitual physical activity

Regarding data quality, a specific and sensitive NWT detection of period lengths as short as possible is favorable. This is important, since identified NWT are most commonly excluded from accelerometry data for analyses [36, 73, 74, 239, 258, 259]. Thus, misclassification of accelerometer NWT may substantially affect conclusions on accelerometry-based PA estimates: Not knowing the presence and time points of true NWT periods, NWT cannot be excluded for analyses. However, inclusion of zero-acceleration readings from NWT may result in an overestimation of time spent in the least intense activity level and an underestimation of the proportion of time spent in true activity if the person was active while not wearing the device. False positive NWT identification and exclusion of a true wear time without movements may, in contrast, lead to an underestimation of inactivity, sedentary time, or mean daily cpm, or, conversely, to an overestimation of the proportion of time in activity above the lowest intensity. Such effects were shown in children and adults [203, 247, 260-262]. Therefore, detecting NWT is essential to derive unbiased estimates of habitual PA using 24h-accelerometry.

Theoretically, NWT is the difference between the prescribed and the actual wearing time. However, in most cases, there will be no information on the latter. Even if recommended [36], asking participants to keep a diary on occurrence and time points of NWT is time-consuming and burdensome for participants and researchers, and, thus, less feasible in large studies. Similarly, although indicating high sensitivity and specificity to detect NWT [263], visually inspecting all data sets individually is not suitable on large scale. As an alternative and purportedly more efficient approach, automated detection of zero-acceleration readings in accelerometry data is currently applied, with different algorithms being available that mainly vary with regard to the minimal duration of zero-acceleration readings required [262]. Most previous studies defined NWT as periods of at least 60 consecutive minutes of zero-acceleration readings, while allowing for a 2-minute spike of less than 100 cpm, hereafter referred to as '60-min algorithm' [70, 177, 203, 258, 259, 264]. This definition was developed based on an algorithm proposed by Troiano et al. [73, 94, 203] and is implemented in the ActiLife software (**Figure 5**).

However, this 60-min algorithm was developed based on an older generation of uniaxial ActiGraph accelerometers that was worn during waking only [73, 94]. Additionally, previous studies have already indicated limitations of this algorithm to detect NWT during waking hours and supposed algorithms defining longer periods of zero-acceleration readings to enable a more precise NWT detection [203, 261, 265-268].

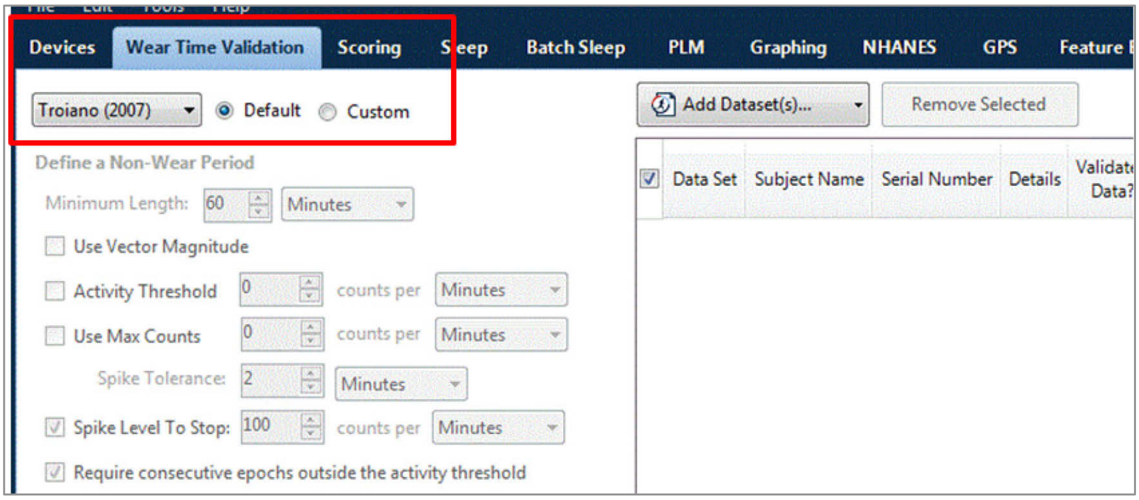


**Figure 5**: Implementation of the 60-min algorithm proposed by Troiano et al. into the ActiLife software to automatically detect non-wear times in accelerometry data
For detection of accelerometer non-wear times (NWT), the algorithm most commonly applied defines NWT as periods of 60 or more consecutive minutes of zero-acceleration readings, allowing for a 2-minute spike of less than 100 counts per minute [70, 258, 259, 264]. This definition was developed based on an algorithm proposed by Troiano et al. [73, 94] and is implemented in the ActiLife software (red framed box) that is proprietary to handle accelerometer data captured by ActiGraph accelerometers (both ActiGraph LLC, Pensacola, FL, USA). Picture extracted from the ActiLife software (version 6.13.3).

#### 2.5.2.2 Sensitivity and specificity of NWT detection compared to a standard reference

For evaluating the suitability of a diagnostic tool or measurement to assess an outcome of interest, like the detection of NWT in accelerometry data, the agreement with a ‘gold standard reference’ must be known [26, 269]. As standard reference, NWT events, for example, can be determined via a diary kept by participants or via direct observation by study personnel [261, 266-268]. To measure the agreement or validity of a measurement compared to a standard reference, calculation of sensitivity and specificity is a suitable approach [26, 80, 269]. The sensitivity of the assessment describes the probability of a positive test result on the condition that the trait is truly present, i.e., the proportion of true positive NWT detection or correct classification as ‘cases’, while the specificity of a measure reflects the likelihood of a negative test results on the condition that the trait is truly absent, i.e., the proportion of true negative NWT detection or correct classification as ‘noncases’ [26, 80, 269]. Consequently, the sensitivity gives information on NWT periods that occurred and were correctly detected (accuracy in classification of ‘cases’), while the specificity gives information on wear times that occurred and were correctly detected (accuracy in classification of ‘noncases’) [80]. Therefore, knowing the sensitivity and specificity of algorithms for NWT detection is pivotal, since it allows evaluating if NWT periods are precisely detected, which is a precondition to enable a valid estimation of PA. However, investigation of NWT detection in 24h-accelerometry has only been conducted during a single 24h-stay in a metabolic chamber so far [268], while its feasibility is largely unknown under free-living conditions.

#### 2.5.2.3 Overlap of lengths of NWT minutes compared to a standard reference

Besides knowing, whether a *NWT period* occurred, or not, considering the temporal dimension of occurring NWT is important, i.e., to identify the length of consecutive *NWT minutes*. Thus, in addition to knowing the measurement's sensitivity and specificity that are based on the binary comparison of the occurrence of consecutive NWT periods between 24h-accelerometry and the standard reference (yes versus no), examining the minute-by-minute overlap between NWT minutes derived from accelerometry and a reference method is relevant: Knowing the overlap in length of NWT enables to assess, to what extent an algorithm that requires consecutive zero-acceleration readings allows identification of NWT minutes at all. Thus, while sensitivity and specificity provide information on the accuracy of NWT period detection [80], the overlap in length of NWT quantifies the ability of NWT minutes detection in 24h-accelerometry.

#### 2.5.2.4 Detection of accelerometer non-wear time using multiday 24h-accelerometry under free-living conditions (research question 2)

Complexity is added to NWT detection using 24h-accelerometry that encompasses waking as well as sleeping times, with the latter potentially including motionless periods that are longer than during waking and longer than 60 minutes. This assumption is supported by a recent study, reporting that the majority of time in bed shows zero-accelerations and that periods without acceleration in bed are significantly longer than during waking [270]. However, this study was conducted using a wrist-worn accelerometer [270]. Since moving the hand or arm while sleeping is probably more likely than moving the center mass, motionless times in that previous study were shorter than it is expected for a waist-worn accelerometer, like in this thesis. Challenges in NWT detection in 24h-accelerometry are even more pronounced, when no information on sleep/wake phases is available. Thus, it is currently unclear if a 60-min algorithm allows a precise NWT detection to obtain unbiased PA estimates from 24h-accelerometry.

The second objective of this thesis was to examine, to what extent algorithms defining periods longer than 60 consecutive minutes of zero-acceleration readings as NWT are suitable for NWT detection in 24-accelerometry in the general adult population. Analyses were performed in two independent epidemiological studies on adults across Germany and separately for the total time of assessment, waking, and sleeping. First, the proportion of reported NWT periods longer than 60 minutes was quantified. Then, sensitivity and specificity of NWT detection as well as the overlap with reported NWT minutes were calculated, when using algorithms defining NWT as more than 60, 90, 120, 150, and 180 consecutive minutes of zero-acceleration readings in multiday 24h-accelerometry under free-living conditions.

### 2.5.3 Determinants of multiday 24h-accelerometry-based physical activity

As reflected by the heterogeneity within and across populations in reported PA levels and times in different activity intensities achieved by individuals (see sections 2.1.1 and 2.2.2), PA amount and its intensity are modifiable and, thus, preventable lifestyle risk factors. This implies that there are preceding factors related to PA that in turn is related to health.

#### 2.5.3.1 Models explaining physical activity and influencing factors

Factors influencing PA either act as determinant (causally related factor) or correlate (associated factor) [30]. Ecological models are well-established approaches to explain health-related behaviors, including PA [77, 79, 271]. These suggest a multilevel impact on the individual of intrapersonal (i.e., demography, biology, psychology, and behavior), interpersonal (i.e., socio-culture), physical, community, organizational, and policy factors (**Table 2**) [77, 79, 271]. Following the ecological approach, according to the '*Analysis Grid for Environments Linked to Obesity*' framework, factors influencing PA either belong to the proximate micro-environment of the individual, including, inter alia, the 'homes' level, or to the less individually modifiable and more distal macro-environment, encompassing, for example, the 'urban/rural development' level [78].

However, assessing factors related to a specific behavior that is relevant for health, like PA is complex, since they interact in an interwoven framework of forth and back directed as well as direct and indirect influences on the individual [26]. Further, since both, PA and factors influencing PA are highly variable within and between populations, and since both are heterogenic with regard to their definition, assessment, and operationalization (see sections 2.1, 2.3, 2.4), the majority of evidence on factors affecting PA is inconclusive, while causal inferences are challenging [82-93]. Knowing facilitators and barriers to PA and understanding their complex interplay is, on the one hand, a premise for planning and successfully implementing appropriate and effective PA promotion strategies [29, 58, 77-79]. Inherent to ecological concepts is the assumption that targeting the levels and factors influencing a specific behavior builds supportive and motivational environments, which, in turn, may help the individual, when being educated, to make the healthiest decision [77, 271]. Similarly, expert panels agree that, when being culturally and for the setting (e.g., workplace) appropriate, interventions that target known PA determinants are promising approaches to enhance engagement in PA in the long-term [27, 272-274]. On the other hand, knowing factors related to PA is pivotal for planning future and evaluating existing epidemiological studies: They may guide the choice of what to assess in a future study, while for analyses of existing data, including known PA influencing factors in statistical models allows a more persuasive estimation of effect sizes in analyses on PA as outcome of interest [26, 30, 80, 81].

**Table 2**: Classification of potential determinants of physical activity

| **Level of influence on physical activity** | **examples of potential determinants** |
|---|---|
| ***I. ecological model*** | |
| **intrapersonal** | age, self-efficacy, smoking |
| **interpersonal** | social support, companion for PA, familiar commitments |
| **physical** | access to PA facilities, street connectivity<br>population density |
| **community** | social inclusion, social cohesion |
| **organizational** | member of organized sports<br>PA program availability, social disorganization |
| **policy** | inflexible working conditions, work hours<br>mass media campaigns |
| ***II. 'Analysis Grid for Environments Linked to Obesity[a]*** | |
| **MICRO-ENVIRONMENT** | |
| **homes** | age, self-efficacy, smoking<br>social support, companion for PA, familiar commitments<br>member of organized sports |
| **workplace** | inflexible working conditions, work hours |
| **neighborhood** | access to PA facilities<br>social inclusion, social cohesion<br>PA program availability, social disorganization |
| **MACRO-ENVIRONMENT** | |
| **media** | mass media campaigns |
| **urban/rural development** | population density |
| **transport system** | street connectivity |

[a]listed micro- and macro-environmental factors are selected from a wider range of factors [78]

### 2.5.3.2 Evidence on physical activity influencing factors

Not least because of the burden associated with lacking PA (see section 2.2), research in factors influencing PA has increased in the last decade. Several determinants and correlates are supposed to be related to PA across all ages including biological (e.g., age, sex), psychological (e.g., self-efficacy, goal orientation), behavioral (e.g., past PA, smoking), physical (e.g., local crime, proximity to green areas,), socio-cultural (e.g., social support, having a PA partner), economic (e.g., employment status, income), and political (e.g., urban design, land use policies) factors [82-84, 86-93, 275, 276]. Recently, the European Commission has initiated the ‘Joint Programming Initiative – A Healthy Diet for a Healthy Life’ to promote scientific collaboration, pool knowledge, and participate in joint research agenda, with the overall aim to foster healthy lifestyles across Europe [277]. Thus, as first joint action, in 2013, the ‘*DEterminants of DIet and Physical ACtivity Knowledge Hub*‘ (DEDIPAC KH) was launched as an inter-disciplinary consortium of experts and organizations encompassing, finally, more than 300 researches from more than 10 scientific disciplines and 68 research centers across 13 European countries [278, 279]. To investigate the ‘causes of the causes’ of unhealthy behavior, i.e., reasons for acting in a non-healthy way in terms of PA that, in turn, may cause adverse health outcomes, the DEDIPAC KH managed seven umbrella systematic literature reviews (i.e., reviews that compile and jointly evaluate a group of related systematic literature reviews [280]) on the current evidence on biological, psychological, behavioral, physical, socio-cultural, economic, and policy determinants of PA in children, adolescents, and adults [86-92, 278, 279, 281].

#### 2.5.3.3 Potential determinants of physical activity using multiday 24h-accelerometry under free-living conditions (research question 3)

However, besides being mainly inconclusive [82-92], evidence on determinants regarding their relation to PA for adults is scarce, since most systematic analyses on potential PA determinants focus on children and adolescents [82, 83, 86-92]. This is all the more true for accelerometry-based PA, although strength and presence of determinants may differ between objectively and subjectively assessed PA [243, 282, 283]. Existing studies on determinants of accelerometry-based PA is mainly limited to youths [70, 284-286]. Lack of evidence is still even more pronounced with regard to 24h-accelerometry and time spent in different activity intensities, although findings on PA influencing factors may depend on the activity intensity [287]. Given that 24h-accelerometry presumably provides a detailed picture of habitual overall activity and activity intensities that may have a distinct effect on health (see section 2.2.1 and 2.3.2.4.3), investigating, to what extent persons with different levels of 24h-accelerometry-based PA differ in terms of their characteristics (**Table 2**) is of epidemiological interest.

The third objective of this thesis aimed to identify potential determinants of habitual time spent in overall activity and in different activity intensities as assessed using multiday 24h-accelerometry in the general adult population. First, time in overall activity and the proportion of active time spent in different activity intensities were investigated as continuous outcome measures, and, secondly, the individual PA level was dichotomized regarding the fulfillment of the WHO PA recommendation to study potential determinants of multiday 24h-accelerometry-based PA under free-living conditions.

## 2.6 Research Questions

In consequence of the three objectives of the present thesis (see sections 2.5.1, 2.5.2, and 2.5.3) aiming to examine the application of multiday 24h-accelerometry under free-living conditions to study habitual overall activity, activity intensities, and activity determinants, the following three research questions (RQ) were addressed.

### 2.6.1 Reliable assessment of physical activity using multiday 24h-accelerometry under free-living conditions (research question 1)

RQ.1 What is the variability of habitual overall activity and of time spent in different activity intensities, how many days are needed to assess habitual PA, and how reliable is habitual PA using multiday 24h-accelerometry under free-living conditions?

### 2.6.2 Detection of accelerometer non-wear time using multiday 24h-accelerometry under free-living conditions (research question 2)

RQ.2 Is an objective algorithm defining NWT as 60 or more consecutive minutes of zero-acceleration readings suitable for an automated detection of accelerometer NWT in multiday 24h-accelerometry data assessed under free-living conditions, and to what extent?

### 2.6.3 Potential determinants of physical activity using multiday 24h-accelerometry under free-living conditions (research question 3)

RQ.3 What are potential determinants, i.e., facilitators and barriers, of habitual time in overall activity and proportion of time spent in different activity intensities as assessed using multiday 24h-accelerometry under free-living conditions?

## 2.7 Hypotheses

### 2.7.1 Reliable assessment of physical activity using multiday 24h-accelerometry under free-living conditions (research question 1)

RQ.1 Based on the evidence, decreasing PA levels across the days of assessment due to an observation bias, and differences in PA across the days of the week are expected, with lower levels on weekend days than on weekdays. Further, around seven days of 24h-accelerometry with at least one weekend day are expected to be necessary to allow a reliable assessment of habitual PA. Finally, a moderate mid-term reliability of habitual PA based on 24h-accelerometry under free-living conditions is expected.

### 2.7.2 Detection of accelerometer non-wear time using multiday 24h-accelerometry under free-living conditions (research question 2)

RQ.2 The common NWT definition of 60 consecutive minutes of zero-acceleration readings is expected to overestimate NWT in 24h-accelerometry data due to motionless periods longer than 60 minutes during sleeping phases included in 24h-accelerometry data.

### 2.7.3 Potential determinants of physical activity using multiday 24h-accelerometry under free-living conditions (research question 3)

RQ.3 Among the individual characteristics available, based on the evidence, biological (e.g., age), behavioral (e.g., smoking), and socio-economic factors (e.g., employment status), as well as pre-existing medical conditions (e.g., diagnosed diabetes mellitus) are expected to be associated with habitual time in overall activity and habitual proportion of time spent in different activity intensities.

# 3 Study design and methods

## 3.1 Study designs and study populations[7]

For RQ 1 on the investigation of a reliable assessment of PA using multiday 24h-accelerometry, a secondary, cross-sectional analysis of data of the ActivE study was conducted (**Table 3**).

For RQ 2, to examine NWT detection in multiday 24h-accelerometry, data of two independent epidemiological studies on adults, the ActivE study (Berlin, Germany) and a follow-up study of the 4th KORA ('Kooperative Gesundheitsforschung in der Region Augsburg'; Cooperative Health Research in the Region of Augsburg, Neuherberg, Germany) S4 cohort, was used for secondary, cross-sectional analyses (**Table 3**).

For RQ 3, the investigation of potential determinants of multiday 24h-accelerometry-based PA was conducted as cross-sectional, secondary analysis of data collected during a nationwide multicenter feasibility study of the German National Cohort ('NAKO Gesundheitsstudie') (**Table 3**).

**Table 3**: Research questions and study populations addressed in this thesis

| research question | study population |
|---|---|
| 1. Reliable assessment of physical activity using multiday 24h-accelerometry under free-living conditions | ActivE study |
| 2. Detection of accelerometer non-wear time using multiday 24h-accelerometry under free-living conditions | ActivE study and KORA FF4 study |
| 3. Potential determinants of physical activity using multiday 24h-accelerometry under free-living conditions | pretest 2 of the German National Cohort |

[7]In the framework of this thesis, parts of the study designs and study populations for analyses on a reliable assessment of PA using multiday 24h-accelerometry have already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018); parts of the study designs and study populations for the analyses on NWT detection in 24h-accelerometry have already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

### 3.1.1 ActivE study (research questions 1 and 2)

Data of the ActivE study was collected between September 2012 and April 2014 in the Molecular Epidemiology Group, Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC), Berlin, Germany. Originally, ActivE aimed to quantify the activity-related energy expenditure using 24-accelerometry-based PA assessed over a 2-weeks period in 50 participants. Following a standardized recruitment protocol and stratified by sex (men, 50%), age (20% in each 10-years age group from 20 to 69 years), and BMI (33.3% in the BMI categories 'normal', 18.5 to 24.9 kg/m²; 'overweight/preobesity', 25.0 to 29.9 kg/m²; 'obesity', >30 kg/m² according to the WHO [289, 290]), participants were recruited as a convenience sample using internal and university mailing lists, newspaper advertisement, and public postings in the area of Berlin and Brandenburg. Predefined inclusion criteria were age between 20 and 69 years and BMI between 18.5 and 35.0 kg/m² at baseline, German language skills, and ability to give informed consent. Persons were excluded if they were limited in mobility, unable to perform a metabolic measurement at the study center, or if they had any physiological condition interfering with energy metabolism or weight stability (e.g., current pregnancy, breastfeeding, dieting).

### 3.1.2 KORA FF4 study (research question 2)

The initial KORA S4 study (4$^{th}$ KORA survey) was conducted between 1999 and 2001 at the Helmholtz Zentrum München – German Research Center for Environmental Health, Neuherberg, Germany, including 4,261 participants aged between 25 and 74 years at baseline [291]. This population-based sample on the general adult population was drawn from local municipal registries from 16 communities in the area of Augsburg, Germany [291]. For the present analyses on NWT detection (RQ 2), data from the second follow-up of the initial S4 study, KORA FF4 (in the following referred to as 'KORA'), was used that was collected between 2013 and 2014 including 2,279 participants. Of those, 1,043 were asked to participate in the 'Lung health & physical activity' section that included a 7-day 24h-accelerometry assessment. Finally, 562 agreed to take part in 24h-accelerometry and were considered for the following analyses.

### 3.1.3 Pretest 2 of the German National Cohort (research question 3)

The German National Cohort, funded by the Federal Ministry of Education and Research, the states of Germany, and the Helmholtz Association is a since 2014 ongoing large-scale population-based prospective cohort conducted in 18 Germany-wide study centers, aiming to totally include 200,000 adults from the general adult population in the age of 20 to 69 years [76, 167]. The study centers are grouped into eight regional clusters and the study center Berlin-North, belonging to the Berlin-Brandenburg cluster, is located at the MDC in the Molecular Epidemiology Group [76, 167]. The baseline investigation is planned to end in 2018/2019, with a secondary examination and follow-up starting five years after the first investigation [76, 167, 292]. The primary aim of the German National Cohort is to investigate potential causes of the major chronic diseases, i.e., cardiovascular diseases (including myocardial infarction, heart failure, stroke, and atrial fibrillation), diabetes mellitus, cancer, neurologic and psychiatric diseases (including stroke and depression), respiratory diseases (including chronic obstructive pulmonary disease and asthma), infectious diseases, diseases of the musculoskeletal system, as well as intermediary phenotypes of these conditions that show pre-clinical and functional impairments [76, 167]. For this purpose, participants are recruited as population-based sample, drawn randomly from municipal registries in the area of the respective study center [76, 167]. Standardized data collection is performed in two differently intense study protocols: All participants are intensely characterized and perform a computer-assisted personal as well as self-administered interview on, inter alia, socioeconomic, demographic, and lifestyle factors, medications, and medical and family history (level 1) [76, 167]. All participants perform an extensive anthropometric, blood pressure, physical, and medical measurement, and provide samples of biomaterials (i.e., blood, urine, saliva, nasal swab, and stool) [76, 167]. Further, 7-day 24h-accelerometry is performed as level 1 module [76, 167]. A representative sub-sample of 20% of all participants undergoes an intensified protocol, including more in-depth examinations as well as magnetic resonance imaging (level 2) [76, 167].

In the context of the German National Cohort, in advance, two nationwide feasibility studies ('pretests') were conducted in all study centers [76, 292, 293]. These pretests aimed to establish and test organizational, personnel, technical, and methodological local and general infrastructures, as well as procedures of examinations [292]. Depending on the finalization of standard operating procedures and the establishment of infrastructures, study protocols of the two pretests differed, with pretest 1 mainly including modules of level 1, and pretest 2 including refined level 1 as well as level 2 examinations [292-294]. Pretest 1 was conducted from May 2011 to April 2012, totally encompassing 2,610 participants across all study centers [294]. Data for the present analyses on potential determinants of 24h-accelerometry-based PA (RQ 3) was collected in the course of pretest 2 that was conducted from May 2012 to April 2013 at all 18 study centers, aiming to include at least 200 participants per study center, with 2,896 participants being finally included [293]. In accordance with the main phase of the German National Cohort, based on a recruitment protocol that was standardized across all study centers, a random sample from local municipal registries was drawn stratified by sex (men, 50%) and age (10% in each 10-years age group from 20 to 39 years; 26.7% in each 10-years age group from 40 to 69 years) [76, 292]; some study centers also included convenience samples [293]. Inclusion criteria were defined by a standard operating procedure and were age between 20 and 69 years, residence in the respective area of the local municipal registries, German language skills, and ability to give informed consent [295]. In pretest 2, the response rate was 18.7%, when considering registry-drawn participants [293]. In addition to a basic program that has already been established in pretest 1 and should have been applied to all participants, further advanced analyses should have been applied in all study centers, but not all participants (Category C1), or in selected study centers and selected participants (category C2) [293]. Seven-day 24h-accelerometry was a category C1 module [293].

## 3.2 Data protection and ethics[8]

In accordance with the guidelines on ‘Good Epidemiological Practice’ and ‘Good Practice Secondary Data Analysis’ [296, 297], the study protocol of ActivE was approved by the ethics committee of the Charité - Universitätsmedizin Berlin and the local data protection officer [242, 288].

The study protocol of KORA was approved by the ethics committee of the Bavarian Medical Association as well as by the Bavarian commissioner for data protection and privacy [291].

The study protocol of pretest 2 of the German National Cohort was approved by the local ethics committee of the respective study center as well as by the local data protection officer [76, 298].

All studies were carried out in accordance with the Declaration of Helsinki and all participants gave written informed consent before inclusion in the respective study [299].

[8] In the framework of this thesis, parts of the data protection and ethics for analyses on a reliable assessment of PA using multiday 24h-accelerometry have already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018); parts of the data protection and ethics for the analyses on NWT detection in 24h-accelerometry data have already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

## 3.3 Data collection[9]

### 3.3.1 ActivE study (research questions 1 and 2)

In ActivE, all participants visited the study center twice over a period of two weeks (**Figure 6**), with visits being performed on weekdays (Monday to Friday). At the first study center visit, manual anthropometric measurements following the WHO guidelines were taken [290]. Body height in cm was assessed using a stadiometer (SECA 240, Hamburg, Germany), body weight in kilograms (kg) using a bioelectrical impedance analysis device (SECA mBCA 515, Hamburg, Germany), and waist circumference in cm using a measuring tape (SECA 201, Hamburg, Germany). Measures were taken by trained personnel with an accuracy of one decimal place. BMI was subsequently calculated as body weight in kg divided by the square of the body height in m [289] (**Equation 2**):

$$BMI = \frac{body\ weight}{body\ height^2} \left[\frac{kg}{m^2}\right]$$

**Equation 2**: Calculation of the body mass index

Additionally, participants performed a personal interview (paper-pencil questionnaire) and were asked to report their age (years), their employment status (full time employed; part time employed, including marginally and occasionally employed; or not employed, including maternity leave and retirement), as well as if they have ever been diagnosed by a physician with diabetes mellitus, hypertension, coronary artery diseases, or cancer. Further, participants were provided with accelerometers. The second study center visit occurred two weeks after the first visit (**Figure 6**). During the second visit, owing to the primary aim of ActivE, participants performed a metabolic measurement to assess the diet-induced thermogenesis using a respiratory chamber. In avoidance of affecting this measurement, participants were instructed not to do sports (or to eat food rich in protein) the day before.

[9] In the framework of this thesis, parts of the data collection for the analyses on a reliable assessment of PA using multiday 24h-accelerometry have already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018); parts of the data collection for the on NWT detection in 24h-accelerometry data have already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

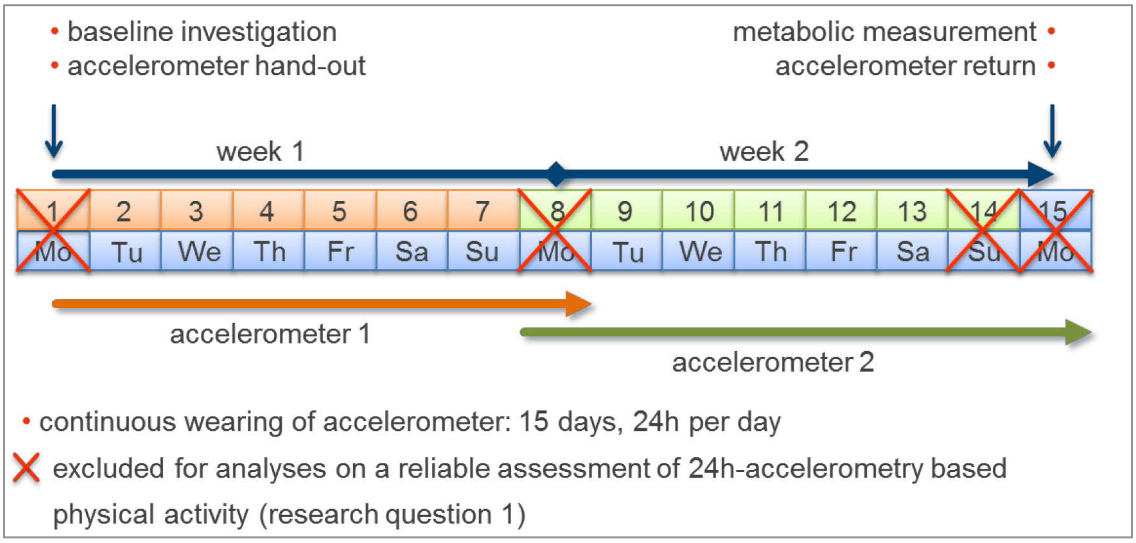


**Figure 6**: Schematic description of data collection in the ActivE study and of data selection for secondary analyses of a reliable assessment of physical activity using multiday 24h-accelerometry under free-living conditions (research question 1)
Participants of the ActivE study visited the study center twice within a period of two weeks (day 1 and day 15). Study center visits were performed on weekdays (Monday to Friday). During the first study center visit (day 1), participants underwent a basic investigation (personal interview and anthropometric measurement) and started wearing an accelerometer 24h per day for a total of two full weeks. Due to a limited storage capacity, all participants were provided with a second pre-initialized accelerometer for self-reliant exchange after one full week (day 8). During the second study center visit after two weeks (day 15), participants performed a metabolic measurement and returned the accelerometers. For the analyses on a reliable assessment of physical activity using multiday 24h-accelerometry (research question 1), the following days were excluded: days 1 and 15 (non-habitual activity behavior due to study center visit), day 8 (accelerometer exchange), and day 14 (non-habitual activity behavior due to instructions not to do sports on this day due to a metabolic measurement on day 15) resulting in 11 days per participant, with six days in week 1 and five days in week 2. Days 1 to 5 of both weeks were the same days of the week per participant. Depending on the first day of assessment, participants were assessed on different days of the week

For PA assessment, the triaxial accelerometer GT3X+ was used. The ActiLife software (versions 6.7.3 and 6.9.1 for initialization, versions 6.13.3 and 6.11.0 for data processing in RQ 1 and RQ 2, respectively) was used to initialize the accelerometers and to download raw acceleration data, as well as for processing accelerometer data by determining activity parameters. The raw acceleration data was sampled with a 100 Hz rate based on all three spatial axes, with the filter set to ‘normal’ (default, as proposed by manufacturer). The ‘Idle Sleep Mode’ that causes a lower sampling rate during sleeping was disabled. While downloading, raw accelerometer data was converted into 1-second (RQ 1) or 60-seconds epochs (RQ 2). The accelerometer to be worn during the first week (day 1 to 8, **Figure 6**) was initialized by the study personnel and put on during the first study center visit, starting to immediately record data. The study personnel instructed participants to continuously wear the accelerometer 24h per day on the right hip for a total time of assessment of two full weeks except for water activities, sauna visits, or high contact sports. Depending on the first day of assessment, participants were examined on different days of the week. Using a 100 Hz sampling rate did not allow collecting data over two weeks with only one device due to a limited storage and battery capacity of the accelerometer. Thus, during the first study center visit, all participants were provided with a second accelerometer that was pre-initialized to automatically start recording after one full week of assessment at the first day of week 2 (day 8, **Figure 6**). Participants were instructed to exchange both accelerometers on their own at any time of day 8 and to note the time point of exchange (see below). The second accelerometer was taken off and returned during the second study center visit. Thus, two sets of 7-day accelerometer data were obtained per participant. Both data sets were later on manually joined to have two weeks of 24h-accelerometry data per participant. During the second study center visit, participants were asked to report any burden due to the 24h wear of devices (e.g., during sleeping or while changing clothes). Participants were asked to keep a diary over the total time of assessment of two weeks to record information on their sleep/wake-rhythm and reason, beginning, and ending of any accelerometer NWT, as well as the time point of exchanging the first and second accelerometer. Based on this diary data, the participant’s total and daily length (minutes per day, min/d) and number of NWT periods was calculated.

For the analyses on a reliable assessment of PA using multiday 24h-accelerometry (RQ 1) the first and the last day of assessment (day 1 and 15, **Figure 6**), when participants visited the study center, were excluded, since PA was not representative for habitual PA on a usual day of the week. Further, the day before the metabolic measurement was excluded (day 14, **Figure 6**), since participants were instructed not to do sports on that day, which may have falsified the estimation of habitual PA; however, in sensitivity analyses that day was included. Finally, regarding RQ 1, the day of the accelerometer exchange was excluded, since data captured by the two devices had not yet been combined at the time point of analyses. Thus, six consecutive days for the first and five consecutive days for the second week were available per participant, with the first five days in each week being the same days of the week per participant.

At the time point of the analyses on detection of accelerometer NWT (RQ 2), data collected by the first and second accelerometer had been subsequently joined based on the information provided in the participants’ diary. Further, days of study center visits were not excluded for RQ 2, since capturing habitual PA levels was not relevant for NWT detection (day 1 and 15, **Figure 6**). Thus, for this analysis, two full weeks of 24h-accelerometry data were available and included for each ActivE participant.

### 3.3.2 KORA FF4 study (research question 2)

KORA participants visited the study center once at the beginning of the investigation, with visits being performed on weekdays (Monday to Friday) and participants being examined on different days of the week. At the study center, participants performed a manual anthropometric measurement assessing body height (cm) and body weight (kg) by trained personnel, with participants wearing light clothes and no shoes [168]; later on, BMI (kg/m²) was calculated (**Equation 2**). Participants were asked to report their age (years) during a personal paper-pencil questionnaire interview [291].

During the study center visit, participants were provided with the triaxial accelerometer GT3X [168] that was pre-initialized by the study personnel. This accelerometer model shows good validity and technical reproducibility for the assessment of habitual PA and is now widely used in cohort studies [66-68]. Compared to the GT3X+, the previous model GT3X (released in 2009) has a slightly different dimension (3.8 cm × 3.7 cm × 1.8 cm) and weight (27 g), uses a constant 30 Hz sampling frequency to collect data, stores only processed data, captures and records acceleration with a full-scale range magnitude of ± 3 G, and is not waterproofed [65, 220, 300]. However, both, the GT3X+ and GT3X are triaxial accelerometers being direct follow-up models, and both show good agreement in assessing PA [219, 301]. The study personnel instructed participants to start wearing the accelerometer the morning after they visited the study center. They were asked to continuously wear the device for 24h per day except for water activities, high contact sports, or sauna visits for a total time of one week at the hip on the side of the dominant hand during waking, and to move it to the wrist of the non-dominant hand for sleeping. The ActiLife software (version 6.11.2) was used to initialize the accelerometers, to download data, and to determine PA parameters. Raw accelerometer data captured by all three spatial axes was sampled at a constant 30 Hz rate and stored at a 1 Hz rate, with the filter set to default, 'normal', as recommended by the manufacturer, and the 'Idle Sleep Mode' being disabled. While downloading, triaxial accelerometer data was converted into 60-seconds epochs. Participants were asked to keep a diary over the total time of assessment for recording information on their sleep/wake-rhythm, as well as on starting, ending, and reason for any NWT period [168]. Participants' NWT was calculated based on the diary information.

### 3.3.3 Pretest 2 of the German National Cohort (research question 3)

Standard operating procedures were applied in pretest 2 of the German National Cohort, thus, the study protocol was the same across all study centers [293]. All participants of pretest 2 visited the respective study center once at the beginning of the investigation (**Figure 7**), with study center visits being performed on weekdays (Monday to Friday) [76, 167, 292]. Participants were intensively phenotypically characterized.

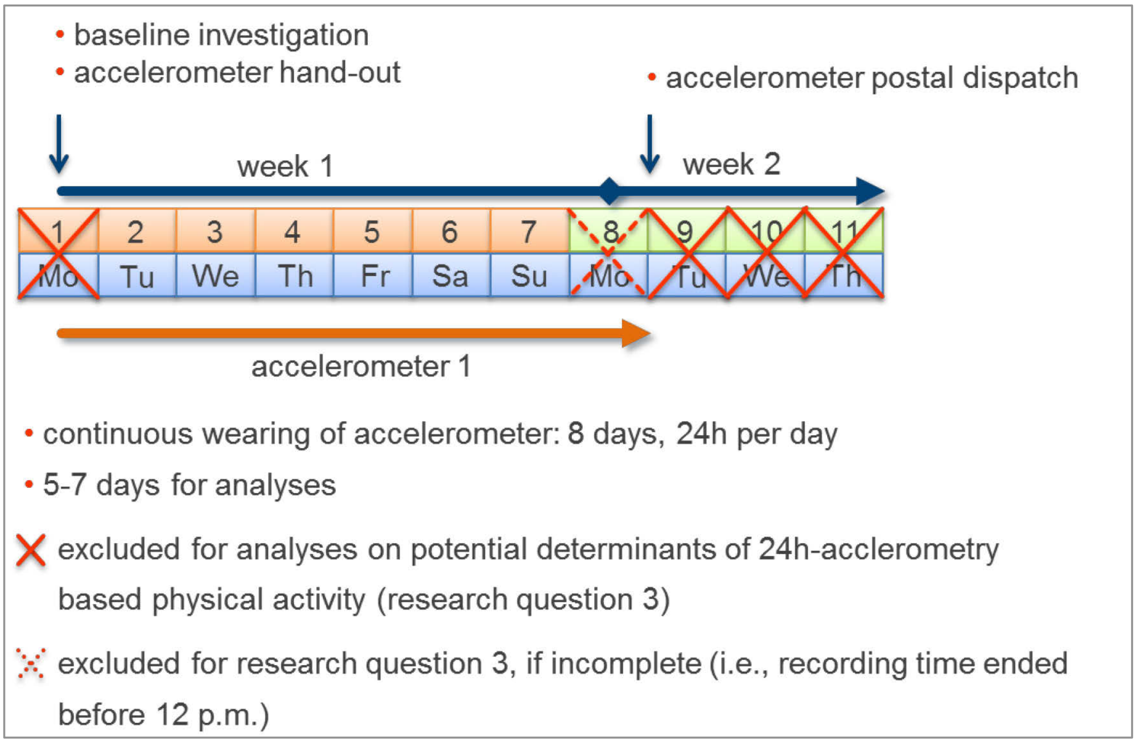


**Figure 7**: Schematic description of data collection in pretest 2 of the German National Cohort and of data selection for secondary analyses of potential determinants of physical activity using multiday 24h-accelerometry under free-living conditions (research question 3)
Participants of pretest 2 of the German National Cohort visited the study center once at the beginning of the investigation period (day 1), with study visits being performed on weekdays (Monday to Friday). At the study center, participants underwent a basic investigation (personal interview and anthropometric measurement) and started wearing the accelerometer (24h per day). Participants were instructed to wear the accelerometer continuously for one full week, to take it off after one full week (end of day 8), and to send the device back to the study center by mail afterwards. For the analyses of potential determinants of 24h-accelerometry-based PA (research question 3), day 1 (non-habitual physical behavior due to study center visit), day 8 (if incomplete), and any days exceeding day 8 (postal dispatch) were excluded. Depending on the first day of assessment, participants were assessed on different days of the week.

In accordance with the WHO guidelines, participants underwent a manual anthropometric measurement while being undressed up to the underwear [167, 290]. Body height (cm; stadiometer SECA 285 or equivalent model, Hamburg, Germany), body weight (kg; bioelectrical impedance analysis device SECA mBCA 515, Hamburg, Germany), and the waist circumference (cm; measuring tape SECA 201, Hamburg, Germany) were taken by trained personnel with an accuracy of one decimal place [293, 302]. Subsequently, BMI (kg/m²) was calculated (**Equation 2**). Furthermore, in a personal computer-assisted interview, participants were asked to report their current age (years), smoking status (never-smoker, smoker, or former smoker), alcohol consumption (never, maximal once a month, 2 to 4 times a month, 2 to 3 times a week, or 4 times a week or more frequently), school education (e.g., completed junior high school, abitur), employment status (e.g., full time employed, part time employed, not employed), net household income (e.g., <500€ per month, 8,000€ per month or more), marital status (e.g., married, single, widowed), as well as by a physician diagnosed pre-existing medical conditions (diabetes mellitus, yes or no; elevated blood lipid levels, hypercholesterolemia, and/or hypertriglyceridemia, yes or no) [76, 167, 293]; a full list of the relevant questions of the original German questionnaire and answer options are summarized in **Supplementary Table 1**, and an English translation version in **Supplementary Table 2**. Finally, accelerometers were handed-out to participants [167].

Using the triaxial accelerometer GT3X+, the appropriate ActiLife software (initialization and downloading depending on the study center: versions 6.4.5, 6.4.3, 6.5.2, 6.5.3, and 6.7.3; data processing: versions 6.12.1 to 6.13.2) was applied to initialize devices and to download and process the raw acceleration data [293]. Raw acceleration data was sampled using all three spatial axes and a 100 Hz sampling rate, with the filter set to default, 'normal' as recommended by the manufacturer [293]; the 'Idle Sleep Mode' was disabled [293]. While downloading, the raw triaxial acceleration data was converted into 10-seconds epochs [303]. Accelerometers were pre-initialized by the study personnel and participants put on the accelerometer during the study center visit, being instructed to continuously wear the accelerometer for 24h per day on the right hip for a total time of one full week except for water activities for longer than 30 minutes, sauna visits, or high contact sports [167, 293] (**Figure 7**). Depending on the day of the study center visit, participants were investigated on different days of the week. On completion of the total time of assessment, participants were instructed to send the devices back to the study center by mail within three days (**Figure 7**; at the end of day 8) [167, 293].

## 3.4 Data quality control[10]

### 3.4.1 ActivE study (research questions 1 and 2)

The study program of ActivE was performed by 50 participants.

[10] In the framework of this thesis, parts of the data quality control for the analyses on a reliable assessment of PA using multiday 24h-accelerometry have already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018); parts of the data quality control for the analyses on NWT detection in 24h-accelerometry data have already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

Two ActivE participants exchanged the first and second accelerometer on day 9 instead of day 8 (**Figure 6**). Thus, they had seven and four, instead of six and five recorded days for week 1 and week 2, respectively. Due to that week-to-week imbalance they were not comparable with the remaining participants. For the analyses on a reliable assessment of multiday 24h-accelerometry-based PA (RQ 1), these two participants were, thus, excluded from all analyses that required a week-based variable. For the analyses on NWT detection in 24h-accelerometry (RQ 2), accelerometer data for day 8 was reconstructed for both participants by combining accelerometer data of both devices based on the diary information (**Figure 6**). However, for one of both participants, accelerometer data for one waking phase was missing, while for the second one data for one waking and one sleeping phase was missing.

One further ActivE participant did not provide any diary data and was, therefore, excluded from all analyses regarding NWT detection in 24h-accelerometry data (RQ 2). Two further ActivE participants were shift workers with no or multiple sleeping phases across days and were also excluded from all analyses for RQ 2.

Therefore, finally, for most analyses on the reliable PA assessment using multiday 24h-accelerometry (RQ 1), 50 participants were included, with analyses requiring a week allocation including 48 participants (**Table 8**, **Table 10**). For analyses on NWT detection in 24h-accelerometry (RQ 2), all analyses comprised 47 participants, but analyses over the total time of assessment encompassed 658 waking and 658 sleeping phases, while for separated analyses 657 waking and 656 sleeping phases were available.

### 3.4.2 KORA FF4 cohort (research question 2)

Three of the 562 KORA participants provided incomplete or inconsistent diary or accelerometer data and were excluded from all analyses in this thesis. Thus, 559 KORA participants were finally included in the analyses on NWT detection in 24h-accelerometry data (RQ 2), encompassing a total of 7,627 waking and 7,627 sleeping phases. Due to incompletely recorded waking up and going to bed times, 3,483 waking (from 546 participants) and 3,352 sleeping phases (from 551 participants) were included for separate analyses of waking and sleeping phases in KORA for RQ 2.

### 3.4.3 Pretest 2 of the German National Cohort (research question 3)

During pretest 2 of the German National Cohort, 2,896 participants provided data on basic characteristics (i.e., demography, economy, socio-culture, lifestyle, and anthropometry, and pre-existing medical conditions) [293], 369 participants on 24h-accelerometry, and 347 participants on both according to data transferred from the central data management (**Figure 8**).

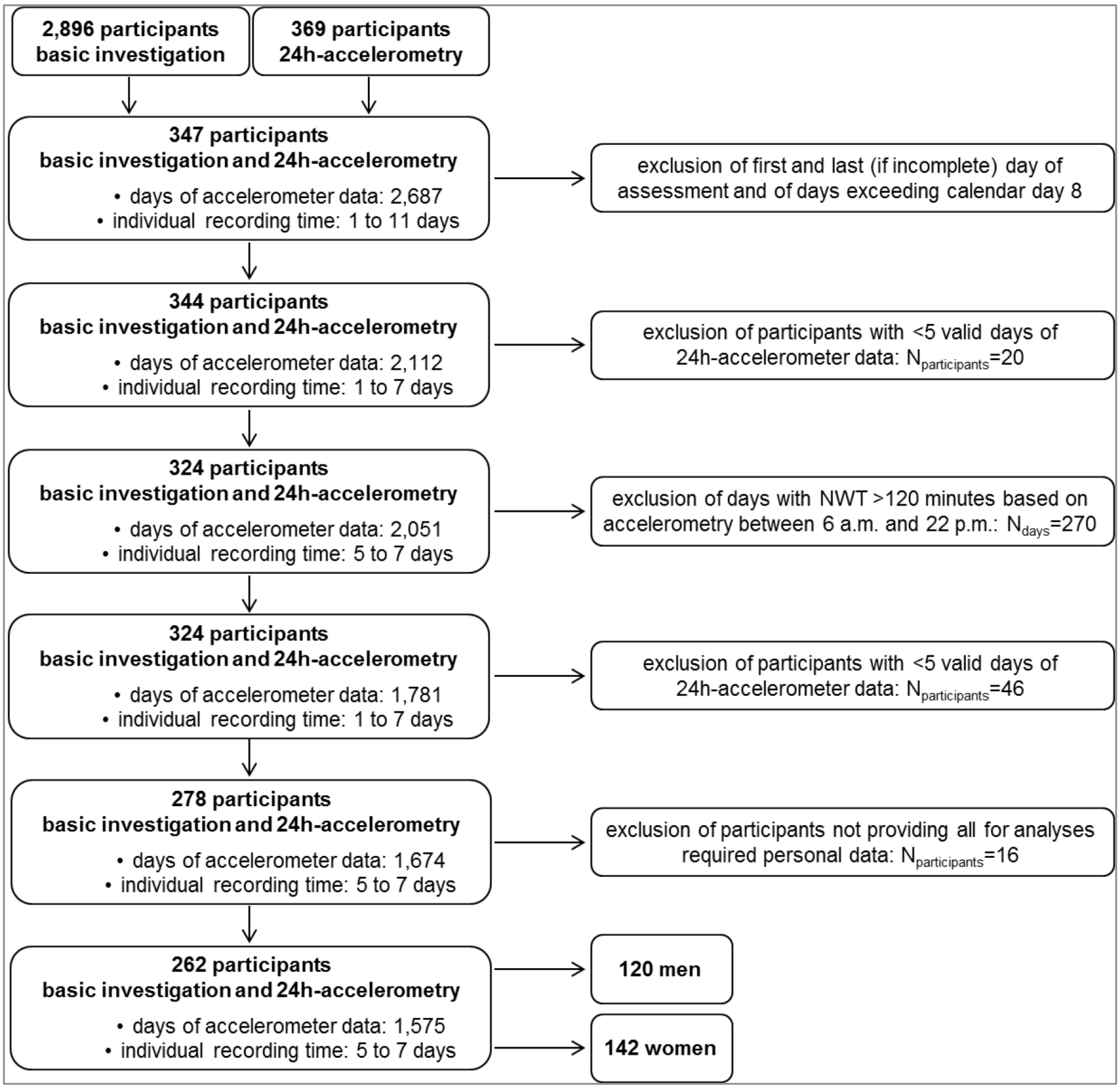


**Figure 8**: Data selection for the analyses of potential determinants of 24h-accelerometry-based physical activity in pretest 2 of the German National Cohort (research question 3)
In pretest 2 of the German National Cohort, initially, 2,869 participants provided data on basic characteristics, 369 on 24h-accelerometry, and 347 on both. After exclusion of invalid days (i.e., days with automatically detected accelerometer non-wear time (NWT) longer than 120 minutes between 6 a.m. and 10 p.m. using the ActiLife software, versions 6.12.1 to 6.13.2; ActiGraph LLC, Fort Walton Beach, FL, USA), invalid data sets (i.e., data sets with <5 valid days), and incomplete data sets, a total of 262 participants was included in the present analyses of potential determinants of multiday 24h-accelerometry-based physical activity.

In total, the 347 participants encompassed 2,687 days of accelerometry data, with the individual observation period ranging from 1 to 11 days. Since no information on the starting time of wearing the device was available, the first day of assessment was excluded (**Figure 7**). Further, participants visited the study center on the first day, and, therefore, that day did not represent habitual PA. According to the standardized study protocol, accelerometers should have been initialized by the study personnel to encompass seven complete days of PA assessment [303]; however, some devices collected data over a longer period. For the present analyses, all days exceeding day 8 were excluded (**Figure 7**), since it was unknown, whether recorded acceleration on the days after day 8 was due to participant's moving or due to postal dispatch of the accelerometer. Further, the last day of assessment was excluded (day 8, **Figure 7**) if it was incomplete (i.e., recording ended before 12 p.m.) to not bias average PA 24h estimates. Thus, data on 344 participants was available, encompassing a total of 2,112 days with accelerometry data and an observation time between 1 and 7 days per participant (**Figure 8**). Based on the results on a reliable assessment of PA using multiday 24h-accelerometry (RQ 1), a data set was defined to be valid if there were at least five days available per participant. This decision was made, since when having five days of assessment, a correlation coefficient between observed and true PA measure of ≥0.85 was observed for all PA parameters (RQ 1, **Table 9**); this was considered as suitable for the analysis on potential PA determinants. Of the 344 participants, 324 participants, including 2,051 accelerometry days, met this criterion (**Figure 8**). An initial quality check of the accelerometry data of the remaining participants using graphing tools in the ActiLife software (version 6.12.1 to 6.13.2) revealed varying participants' adherence to the study protocol regarding the continuous accelerometer wearing. Based on the results on NWT detection in 24h-accelerometry (RQ 2, see section 4.2), no NWT >120 minutes detected in accelerometry data in an assumed waking phase between 6 a.m. and 10 p.m. was defined as premise for a valid day. Consequently, 270 single days of 24h-accelerometry were excluded, resulting in 278 participants (encompassing 1,674 recorded days) still providing 24h-accelerometry data of at least five valid days (**Figure 8**). Finally, due to planned analyses, participants had to provide information on sex, age, BMI, waist circumference, smoking status, alcohol consumption, school education, employment status, net household income, and marital status as assessed during the interview (see section 3.3.3); information on the study center allocation was also required. Finally, 262 participants (120 men, 142 women), encompassing a total of 1,575 days of 24h-accelerometry, fulfilled all inclusion criteria and were included in the analyses of potential determinants of 24h-accelerometry-based PA (RQ 3). Included participants were assessed between September 2012 and January 2013.

As sensitivity analyses, suitable participants were selected using a more conservative NWT definition based on a 60-min in contrast to the 120-min NWT algorithm. Doing so, 211 participants (87 men, 124 women) provided valid data on 24h-accelerometry as well as on all variables of interest (**Supplementary Figure 2**).

## 3.5 Determination of physical activity parameters[11]

For the analyses on a reliable assessment of PA (RQ 1) as well as on potential determinants of PA using multiday 24h-accelerometry (RQ 3), the 'vector magnitude cpm', representing 'overall activity', was extracted. Further, activity intensities were determined based on the 'vector magnitude cpm' by applying the triaxial-derived cut points of the algorithm 'Freedson Adult VM3 (2011)' implemented in ActiLife (versions 6.12.1 to 6.13.3). Equivalently to METs (see section 2.1), this algorithm classifies accelerometry data of 0 to 2,690 cpm as light (<3.0 METs), 2,691 to 6,166 cpm as moderate (3.0 to 5.99 METs), 6,167 to 9,642 cpm as vigorous (6.0 to 8.99 METs), and ≥9,643 cpm as very vigorous activity (≥9.0 METs) [246] (**Figure 9**). Using this algorithm resulted in more than 90% of time to be classified as 'light' activity, which was mainly due to sleeping. Given the increasing number of studies showing light activity and sedentary behavior to be an independent risk factor (see section 2.2.1) it was aimed to separate inactivity from low intense activity. For this purpose, the 95th percentile of the 'vector magnitude cpm' was calculated, when averaged over all sleeping periods reported in ActivE. This cpm value was set as cut point to separate inactive behavior (i.e., unconscious movement comparable to sleeping) from conscious, low activity. The 95th percentile was chosen to acknowledge a 5% uncertainty to account for any misreported sleeping time or times of activity during sleeping (see section 2.5). Accordingly, time in light activity as determined by the 'Freedson Adult VM3 (2011)' algorithm was subdivided into time in 'inactivity' (0-78 cpm) and time in 'low' (79-2,690 cpm) activity, while the cut points for moderate to very vigorous activity remained unchanged (**Figure 9**).

To examine the reliable assessment of PA using multiday 24h-accelerometry (RQ 1), overall activity (cpm) and time (min/d) spent in inactivity and in low, moderate, vigorous, and very vigorous activity were determined for each ActivE participant and day using 1-second epochs (86,400 seconds or epochs per 24h per participant). Parameters were averaged over 24h over the total assessment time per participant (**Table 4**).

[11] In the framework of this thesis, parts of the determination of PA parameters for the analyses on a reliable assessment of PA using multiday 24h-accelerometry have already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018); parts of the determination of PA parameters for the analyses on NWT detection in 24h-accelerometry data have already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. Sci Rep. 7, 2227 (2017).

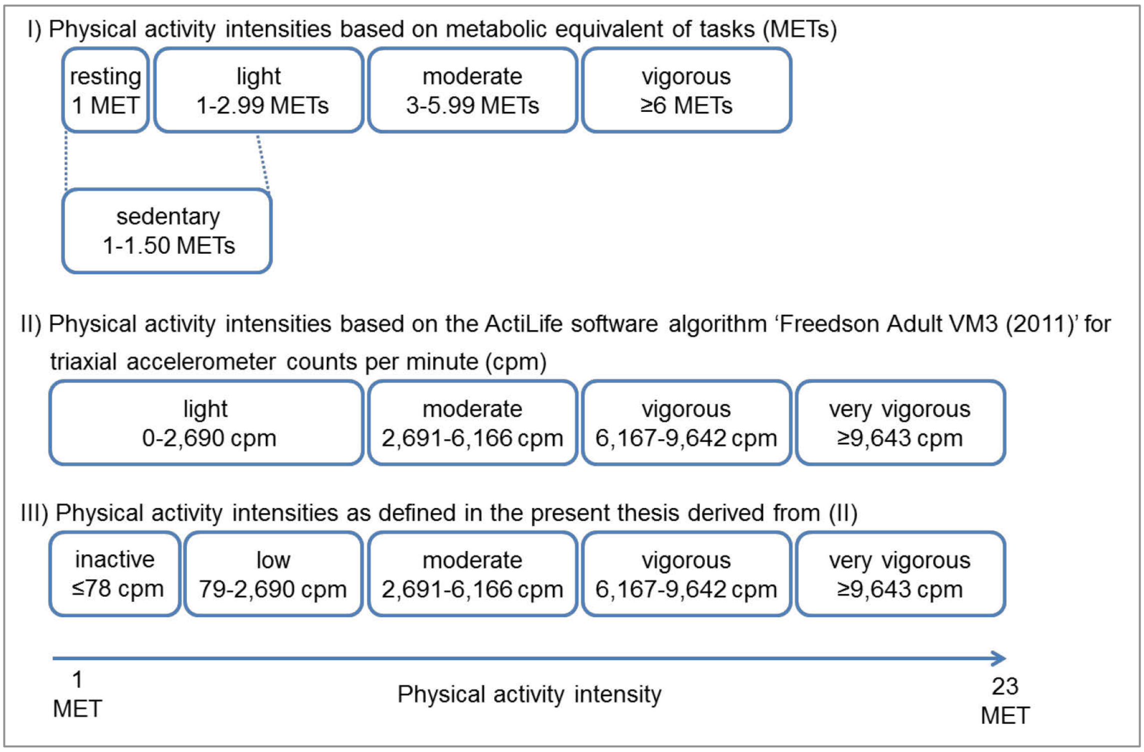


**Figure 9**: Determination of physical activity intensities as assessed using multiday 24h-accelerometry in research question 1 and 2

Referring to the physical activity intensity defined based on the 'metabolic equivalent of task' (MET; <3, 3-5.99, and ≥6.0 METs defined as light, moderate, and vigorous activity intensity, respectively [40, 100, 102]; sedentary behavior with 1 to ≤1.5 METs [99]) (panel **I**), activity intensity parameters using multiday 24h-accelerometry data were determined applying the triaxial-derived cut points of the ActiLife software algorithm 'Freedson Adult VM3 (2011)' (versions 6.12.1 to 6.13.3, ActiGraph LLC, Fort Walton Beach, FL, USA) classifying accelerometer counts 0 to 2,690 counts per minute (cpm) as light (<3 METs), 2,691 to 6,166 cpm as moderate (3 to 5.99 METs), 6,167 to 9,642 cpm as vigorous (6 to 8.99 METs), and ≥9,643 cpm as very vigorous activity (≥9.0 METs) (panel **II**) [246]. To further distinguish between inactivity and low activity, a cut point was derived based on the 95$^{th}$ percentile of the 'vector magnitude cpm' as averaged over all reported sleeping periods of participants of the ActivE study. For the analyses on a reliable assessment of PA (research question 1) and on potential determinants of physical activity using multiday 24h-accelerometry (research question 3), the 95$^{th}$ percentile was used as limit value to divide 'light' activity into 'inactivity' (0-78 cpm) and 'low activity' (79-2,690 cpm); the cut points for moderate, vigorous, and very vigorous PA remained unchanged (panel **III**).

For the analyses on NWT detection in 24h-accelerometry (RQ 2), the 'vector magnitude cpm' was extracted for each minute (60-seconds epoch; 1,440 minutes or epochs per 24h per participant) of each ActivE and KORA participant over the total time of assessment of one week (KORA) and two weeks (ActivE) (**Table 4**).

For the analyses on potential determinants of PA using multiday 24h-accelerometry (RQ 3), overall activity (cpm) and the time in overall activity (min/d) was calculated for each pretest 2 participant and day based on the 10-seconds epoch accelerometry data (8,640 epochs per 24h per participant). Time in overall activity was calculated as sum of time (min/d) spent in low, moderate, vigorous, and very vigorous activity. Further, the average daily time (min/d) spent in inactivity and in low, moderate, and vigorous-to-very-vigorous (VV) activity was determined for each participant and day. Time in VV activity represents the sum of time spent in vigorous and very vigorous activity, since the latter was found to be very short (geometric mean, GM, 0.16 min/d). Additionally, the proportion of time (% time in overall activity) spent in the activity intensities low, moderate, and VV activity was calculated as compared to the active time, i.e., compared to the time in overall activity (min/d) (**Table 4**). All parameters were averaged over 24h over the total time of assessment per participant.

**Table 4**: Determination of physical activity parameters in research questions 1 to 3

| PA parameter | unit | accelerometry criteria based on cpm[a] | energy equivalent based on MET | RQ |
|---|---|---|---|---|
| **overall activity** | cpm | ≥0 | ≥1 | 1, 2 |
| **time in overall activity** | min/d[b] | ≥79 | approx. ≥1.5[c] | 3 |
| **time in low activity** | min/d[b]<br>%[d] | 79-2.690<br>79-2.690 | approx. ≥1.5 to <3[c]<br>approx. ≥1.5 to <3[c] | 1<br>3 |
| **time in moderate activity** | min/d[b]<br>%[d] | 2.691-6.166<br>2.691-6.166 | 3 to 5.99<br>3 to 5.99 | 1<br>3 |
| **time in vigorous activity** | min/d[b]<br>%[d] | 6,167 to 9,642<br>6,167 to 9,642 | ≥6 to 8.99<br>≥6 to 8.99 | 1<br>3[e] |
| **time in very vigorous activity** | min/d[b]<br>%[d] | ≥9,643<br>≥9,643 | ≥9<br>≥9 | 1<br>3[e] |

approx., approximately; cpm, counts per minute; MET, metabolic equivalent of task; PA, physical activity; RQ, research question
[a]triaxial counts per minute based on the 'vector magnitude' as derived from the ActiLife software
[b]absolute proportion of time spent in the different activity intensities
[c]since the cut point to determine 'low activity' was derived in the context of this thesis, only an approximate estimation of the lower MET limit can be given for 'low activity' (see section 3.5)
[d]relative proportion of time in overall activity spent in the different activity intensities
[e]time in vigorous and in very vigorous activity were combined

Finally, it was determined if participants met the WHO PA recommendation [7]. For this purpose, for each participant over the total time of assessment the time spent in bouts of at least 10 minutes in moderate and at least vigorous intense activity (i.e. in VV activity) was calculated. The WHO PA recommendation is based on weekly PA amounts [7]; however, not all participants provided accelerometry data over one full week. Thus, per participant, the total time spent in bouts of at least 10 minutes in moderate or VV activity was divided by the number of days of assessment per participant and thereafter multiplied by 7 to obtain estimates for a full average week. If participants, thus, achieved at least 150 minutes of moderate activity or at least 75 minutes of VV activity per week in bouts of 10 minutes, this was classified as 'meeting the WHO PA recommendation' [7]. If participants did not fulfill both criteria, it was determined, whether they achieved an 'equivalent combination' of these. However, criteria for such an equivalent are not specified by the WHO [7]. One-hundred-fifty minutes of moderate or 75 minutes of vigorous activity per week both require an energy-equivalent of 450 METs, when multiplying by 3 and 6 METs as lower limits of moderate and vigorous activity, respectively (**Table 4**) [7, 100-102]. However, in accordance with previous research and to account for different intensities even within the moderate and vigorous intensity level [1], in this thesis, the observed weekly minutes in bouts of 10 minutes were multiplied by 4 METs for moderate and by 8 METs for vigorous activity (**Equation 3**):

$$AEE_{min} = (weekly\ time_{moderate} * 4\ METs) + (weekly\ time_{vigorous} * 8\ METs) \geq 450\ METs$$

**Equation 3**: Minimal required activity-induced energy expenditure to meet the World Health Organization physical activity recommendation based on a metabolic equivalent

$AEE_{min}$, minimal activity-induced energy expenditure; METs, metabolic equivalents of task
The World Health Organization (WHO) recommends to accumulate at least 150 minutes of moderate or 75 minutes of vigorous activity per week (which both require an energy-equivalent of 450 metabolic equivalents of task (METs), when multiplied by 3 and 6 METs as lower intensity level, respectively [7, 100-102]), or a metabolic equivalent of these. To account for different intensities within the respective intensity level, here, the minimal required activity-induced energy expenditure to meet a metabolic equivalent was defined as 450 METs based on time in at least moderate or vigorous activity per week, when multiplied by 4 and 8 METs, respectively [1].

If the individual activity-induced energy expenditure per week was greater or equal 450 METs, this was evaluated as 'meeting WHO PA recommendation' (**Equation 3**). Compared to the more conservative approach with 3 and 6 METs, choosing 4 and 8 METs as multiplier resulted in a plus of 20 participants, who fulfilled the WHO PA recommendations. Participants that neither met the WHO PA recommendation based on moderate activity nor based on vigorous activity or based on the equivalent (**Equation 3**) were categorized as 'not meeting the WHO PA recommendation'.

## 3.6 Statistical analyses

### 3.6.1 Descriptive analyses

Age, height, weight, BMI, and, if available, waist circumference are presented as mean and standard deviation (SD); categorical variables on basic characteristics, if available, as absolute and relative (%) numbers. Parameters on diary-based NWT are given as median and interquartile range (IQR), either as total length (min) and number of NWT periods over the total time of assessment, or as daily estimates averaged over the total time of assessment. If reported, PA parameters are presented as GM and 95% confidence interval (CI), and PA bout parameters as median and IQR.

For the analyses of NWT detection in 24h-accelerometry (RQ 2), NWT is reported referring to 24h, since for some KORA participants single waking and sleeping phases were excluded for analyses (see section 3.4.2). For consistency across participants and studies, the total number of waking and sleeping phases were summed up per participant in ActivE and KORA, which then was divided by 2 to consider one waking and one sleeping phase as average 24h.

Where suitable, it was tested if there were sex differences in basic characteristics, NWT, or PA parameters, or between included and excluded participants using unpaired t-tests for continuous and normally distributed variables, Mann-Whitney U tests for continuous and not normally distributed variables, and Chi-Square (or Fisher's exact tests if more than 25% of cells had expected counts less than 5) for discrete variables [227].

### 3.6.2 Reliable assessment of physical activity using multiday 24h-accelerometry under free-living conditions (research question 1)[12]

For all analyses on a reliable assessment of PA using multiday 24h-accelerometry (RQ 1) PA parameters were log-transformed.

#### 3.6.2.1 Variability of habitual physical activity using 24h-accelerometry

To investigate the intra-individual (within-person) day-to-day variability of overall activity (cpm) and of time (min/d) spent in inactivity as well as in low, moderate, vigorous, and very vigorous activity intensity over approximately two weeks, linear mixed-effects models, with sex set as fixed and subject set as random effect were used (baseline model). The proportions (%) of the within- ($s_w^2$) and between-person variance ($s_b^2$) contributing to the total variance observed were calculated for the six PA parameters.

To further assess if the PA parameters systematically differed across the days of assessment, the days of the week, or between weekdays and weekend days, geometric least square means were estimated for the PA parameters using linear mixed-effects

[12] In the framework of this thesis, parts of the analyses on a reliable assessment of PA using multiday 24h-accelerometry have already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018).

models. Three differently adjusted models were analyzed for each PA parameter as single outcome, all including sex as fixed and subject as random effect: Model 1 further included the day of assessment (1 to 11), model 2 the day of the week (Monday to Sunday) and the week (1 versus 2), and model 3 the differentiation between weekdays and weekend days (Monday to Friday, 1, versus Saturday and Sunday, 2) as well as the week (1 versus 2) as additional fixed effects. Estimated least square means and the belonging 95% CI were back-transformed and are presented graphically as GM, with error bars indicating the 95% CI for each PA parameter. *P*-values referring to the main fixed effects, i.e., the day of assessment (model 1), the day of the week (model 2), and the weekdays-versus-weekend-days distinction (model 3), as well as to the test of trend for the day of assessment (model 1) were calculated.

Finally, it was analyzed to what extent the day of the week or the distinction between weekdays and weekend days explained the total variance, assuming subject, the day of the week, and weekday-versus-weekend-day as consecutively nested random instead of fixed effects in the linear mixed-effects baseline model, model 2, or model 3, respectively.

All analyses were conducted using accelerometer data of both weeks, encompassing 11 days per participant (**Figure 6**).

#### 3.6.2.2 Number of days needed to estimate habitual physical activity using 24h-accelerometry

To calculate the number of needed consecutive days of 24h-accelerometry to estimate habitual PA, *D*, the equation proposed by Black et al. was used (**Equation 4**) [304]:

$$D = \frac{r^2}{1 - r^2} * \frac{{s_w}^2}{{s_b}^2}$$

**Equation 4**: Equation proposed by Black et al. to calculate the number of consecutive days needed to estimate habitual physical activity

This formula estimates the number of days required to assess habitual PA based on an assumed correlation, *r*, between the observed and true (unknown) mean PA parameter [304]. Thus, it estimates the number of observation days that is necessary to achieve a desired degree of concurrent validity, when estimating PA [256, 304]. The ratio of within- to between-person variance, ${s_w}^2/{s_b}^2$, was derived from the linear mixed-effects baseline model using 11 days per participant. *r* was defined to be 0.9, implying that, when PA parameters are divided into quintiles, less than 0.1% of all persons is supposed to be misclassified in the opposite extreme fraction, whereas 75% in the fifth quintile are correctly classified, when comparing the observed and true PA measure [305]. This definition of *r* was in accordance with previous studies using this formula [306, 307].

The formula by Black et al. (**Equation 4**) was derived from the nutritional epidemiology and was originally developed in infants to assess the number of 24h dietary recalls needed to estimate energy intake [304, 305]. Another approach that was used to estimate the required number of PA assessment days is the Spearman-Brown prophecy formula based on intraclass correlation coefficients (ICC) (**Equation 5**) [211]. Thus, additionally, the number of days, *N*, needed to estimate habitual PA with a desired degree of reliability was calculated using the Spearman-Brown prophecy formula [211]:

$$N = \frac{ICC_t}{1 - ICC_t} * \frac{1 - ICC_s}{ICC_s}$$

**Equation 5**: Spearman-Brown prophecy formula to calculate the number of consecutive days needed to estimate habitual physical activity

with $ICC_t$ being the desired reliability and $ICC_s$ being the single day reliability. $ICC_t$ was set to be 0.8, i.e., a desired reliability of 80% was implied, which was considered as acceptable reliability and is typically used for this formula [211]. $ICC_s$ was calculated based on the ratio of between- ($s_b^2$) to the sum of within- and between-person variance ($s_b^2 + s_w^2$), being derived from the linear mixed-effects baseline model using 11 days per participant (**Equation 6**) [211]:

$$ICC_s = \frac{{s_b}^2}{{s_b}^2 + {s_w}^2}$$

**Equation 6**: Single-day variability in the Spearman-Brown prophecy formula

To also assess the correlation between observed and true mean PA for a given number of days of assessment, $D_r$, $r_D$ was calculated for $D_r$ ranging from 1 to 11, by solving the formula by Black et al. (**Equation 4**) for *r* (**Equation 7**) [304]:

$$r_D = \sqrt{\frac{D_r}{D_r + \frac{{s_w}^2}{{s_b}^2}}}$$

**Equation 7**: Correlation between observed and true mean physical activity for a given number of consecutive days of assessment (adapted from Black et al.)

#### 3.6.2.3 Reliability of habitual physical activity using 24h-accelerometry

Finally, to assess the week-to-week reliability of overall activity and time spent different activity intensities, ICCs were calculated using the between- and within-person variance derived from a linear mixed-effects baseline model based on the mean daily PA parameters for week 1 and week 2 of each participant (analogous to **Equation 6**) [248, 257].

As sensitivity analysis, all analyses of RQ 1 were also performed by including the day before the second study center visit (day 14, **Figure 6**; see section 3.3.1).

Presented *p*-values are two-tailed and $p<0.05$ were considered statistically significant. All analyses were performed using SAS® Enterprise Guide® (version 4.3; SAS Institute Inc., Cary, NC).

### 3.6.3 Detection of accelerometer non-wear time using 24h-accelerometry under free-living conditions (research question 2)[13]

For the investigation of NWT detection in 24h-accelerometry, NWT detected in accelerometry was compared to NWT detected in diary data, with the latter set as reference. Based on the entries in the participants' diaries, for each participant was derived a) the *total time of assessment* defined as period between the first and last documented time point (waking up or going to bed time), and b) each *waking* and *sleeping* phase over the total time of assessment defined as period between waking up and going to bed, or vice versa, respectively. NWT detection based on 24h-accelerometry and diary data was then compared over the total time of assessment, as well as separately for waking and sleeping phases (**Figure 10**, **Figure 11**).

To investigate the suitability of different algorithms to detect NWT in 24h-accelerometry data, three different approaches were applied to compare 24h-accelerometry- and diary-based NWT.

#### 3.6.3.1 Sensitivity and specificity of non-wear time algorithms of >60 to >180 minutes based on accelerometry compared to diary data

First, based on the diary, for each participant all periods of reported NWT >60, >90, >120, >150, and >180 minutes were identified (**Figure 10**, panel I). Similarly, to determine NWT based on 24h-accelerometry data, the extracted data of the 'vector magni-

[13]In the framework of this thesis, parts of the analyses on NWT detection in 24h-accelerometry data have already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

tude cpm' was used to identify consecutive zero-acceleration readings in periods >60, >90, >120, >150, and >180 minutes, without allowing for interruptions due to non-zero-accelerations.

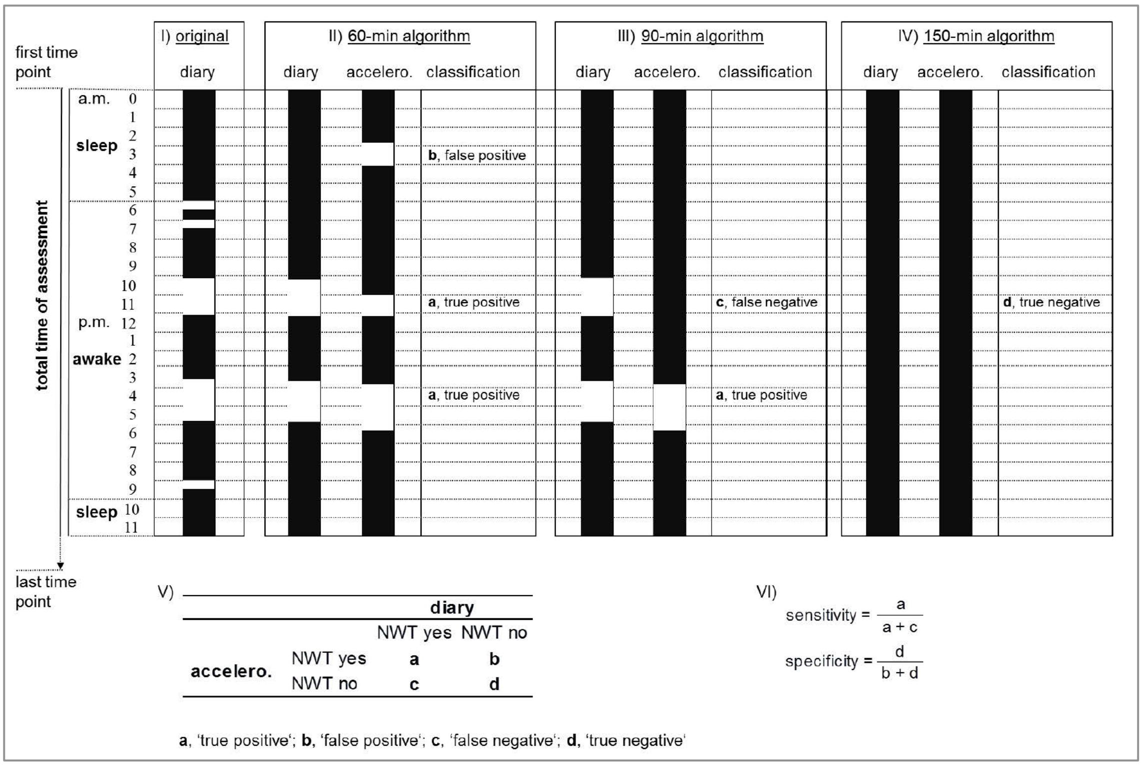


**Figure 10**: Exemplary description of non-wear time validation using consecutive time periods for calculation of sensitivity and specificity of NWT detection by algorithms >60, >90, >120, >150, and >180 minutes based on accelerometry and diary data (research question 2)[14]

As an example, based on the original diary data (panel I) five non-wear time (NWT) periods were reported with lengths of 30, 30, 115, 130, and 30 minutes, respectively (white rectangles, NWT based on diary or accelerometry, respectively; black rectangles, wear time based on diary or accelerometry, respectively). These NWT periods were included for analyses over the total time of assessment and during waking; no NWT was reported during sleeping. Applying a 60-min NWT algorithm (panel II), two of all reported NWT periods (115 and 130 minutes, respectively) were detected in the diary. Based on accelerometry data (accelero.), two NWT periods during waking (65 and 140 minutes, respectively) and one NWT during sleeping (75 minutes) were identified using the 60-min algorithm. When using a 90-min algorithm (panel III), two of all reported NWT periods (115 and 130 minutes, respectively) were detected in the diary, while in accelerometry data, one NWT was identified (140 minutes). Applying a 150-min algorithm (panel IV) resulted in no NWT detected in diary or accelerometry data. With the diary set as reference, for each algorithm and for the total time of assessment, waking, and sleeping, identified NWT periods were then classified according to the fourfold table in panel V, and sensitivity (true positive NWT detection) and specificity (true negative NWT detection) were calculated using the formulas in panel VI [26].

[14] In the framework of this thesis, this figure has already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

With the diary set as reference, for all NWT algorithms, each NWT period detected (either based on diary or accelerometry) was compared between accelerometry and diary. NWT detection based on accelerometry was categorized as true positive if there was an overlap of ≥50% in length (minutes) of NWT periods between accelerometry and diary (**Figure 10**, panel II–V, classification ‘a, true positive’); if the overlap was <50%, the according period was classified as ‘not assigned’ and was excluded from the analyses of sensitivity and specificity of NWT detection. If a NWT period was detected in accelerometry, but not in diary, this was coded as false positive NWT detection based on accelerometry (**Figure 10**, panel II–V, classification ‘b, false positive’). Identifying a NWT period in diary, but not detecting a corresponding NWT based on the accelerometry data, this was categorized as false negative NWT detection based on accelerometry (**Figure 10,** panel II–V, classification ‘c, false negative’). If both, accelerometry and diary data did not show any NWT during the period analyzed (i.e., the total time of assessment, waking, or sleeping), this was defined as true negative NWT detection based on accelerometry (**Figure 10**, panel II–V, classification ’d, true negative’). According to the classifications above that were summarized according to the fourfold table in panel V in **Figure 10**, sensitivity (proportion of true positive NWT detection) and specificity (proportion of true negative NWT detection) for each algorithm were then calculated using the formulas in panel VI in **Figure 10**, taking into account the total number of NWT periods identified in either accelerometry, diary, or both [269].

#### 3.6.3.2 Overlap of accelerometry and diary non-wear time periods identified using algorithms of >60 to >180 minutes

Secondly, NWT periods >60, >90, >120, >150, and >180 minutes based on accelerometry and diary were identified on a minute-by-minute basis, with a continuous outcome representing the length of NWT periods (min) (**Figure 11**, panel I). Based on this information, the overlap in length of NWT was calculated, when applying the 60-min to 180-min NWT algorithms to both, accelerometry and diary (**Figure 11**, panel II). For this purpose, for each algorithm the minutes were calculated in (1) NWT periods >60 to >180 minutes identified in both, *accelerometry and diary* (**Figure 11**, panel II, case ‘accelero. + diary’), (2) NWT periods >60 to >180 minutes identified in *diary only*, not in accelerometry (**Figure 11**, panel II, case ‘diary only’), and, (3) NWT periods >60 to >180 minutes identified in *accelerometry only*, not in diary (**Figure 11**, panel II, case ‘accelero. only’). Then, the proportion of total NWT minutes detected by both, *accelerometry and diary*, (i.e., overlap, case 1), by *diary only* (case 2), or by *accelerometry only* (case 3) was calculated referring to the potential total NWT. The potential total NWT was defined as NWT minutes identified in either diary, accelerometry, or both.

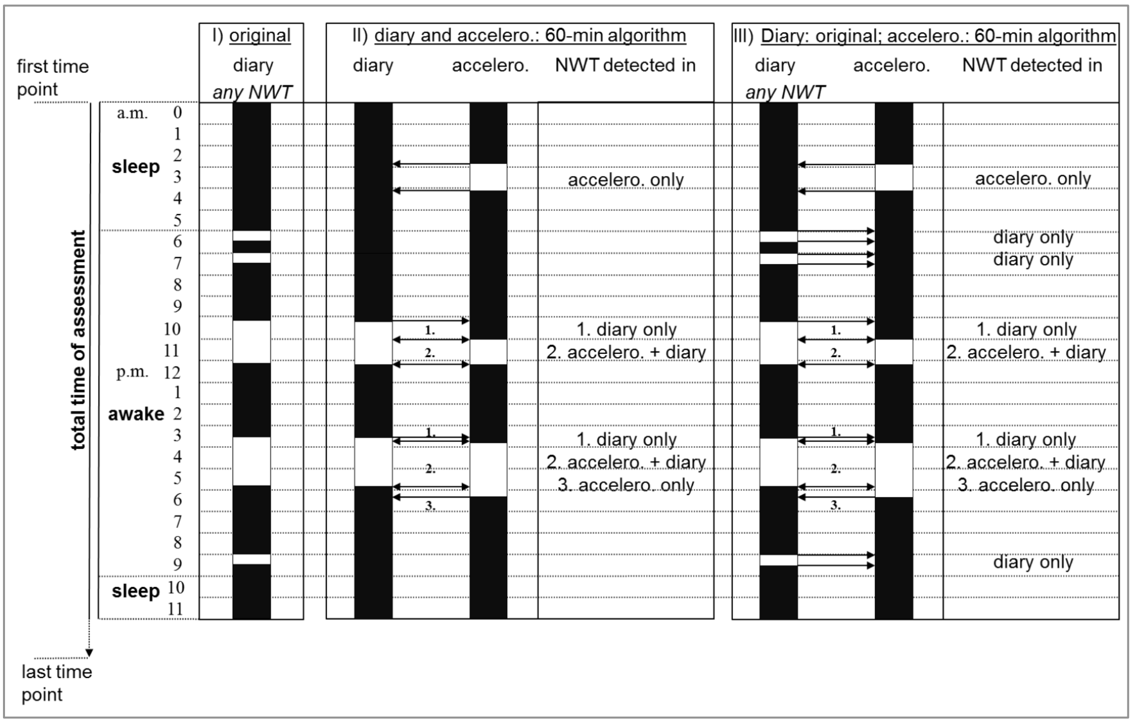


**Figure 11**: Exemplary description of non-wear time validation using a minute-by-minute evaluation for calculation of overlap in length of NWT detected by algorithms >60, >90, >120, >150, and >180 minutes based on accelerometry and diary data (research question 2)[15]

As an example, based on the original diary data (panel I) five non-wear time (NWT) periods were reported with lengths of 30, 30, 115, 130, and 30 minutes, respectively (white rectangles, NWT based on diary or accelerometry, respectively; black rectangles, wear time based on diary or accelerometry, respectively). These NWT periods were included for analyses over the total time of assessment and during waking; no NWT was reported during sleeping. Applying a 60-min NWT algorithm (panel II), two of all reported NWT periods were identified (115 and 130 minutes, respectively). Based on accelerometry data, two NWT periods during waking (65 and 140 minutes, respectively) and one NWT during sleeping (75 minutes) were identified using a 60-min algorithm. When using a 60-min NWT algorithm in accelerometry data only and comparing the identified NWT with diary-based NWT of *any* length (panel III), all five 'original' NWT periods in diary data (30, 30, 115, 130, and 30 minutes, respectively, panel I) were detected, while three NWT periods were identified based on accelerometry data (75, 65, and 140 minutes, respectively). For each algorithm and for the total time of assessment, waking, and sleeping, minutes of NWT were categorized as NWT detected in *accelerometry only* ('accelero. only'), *diary only* ('diary only'), or both ('accelero. + diary'). Then, the proportion of each to the potential total NWT (sum of NWT identified in *accelerometry only*, *diary only*, or both) was calculated. With the diary set as reference, NWT minutes identified in both, *accelerometry and diary* were defined as overlap in length of NWT (true positive NWT detection).

[15]In the framework of this thesis, this figure has already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

#### 3.6.3.3 Overlap of any diary non-wear time with accelerometry non-wear time identified using algorithms of >60 to >180 minutes

Finally, it was assessed, if an algorithm defining consecutive zero-acceleration readings as NWT enables NWT detection in 24h-accelerometry at all, and to what extent NWT periods >60 minutes contribute to total NWT (**Figure 11**, panel III). For this purpose, the same respective analyses as used for the previous approach (see section 3.6.3.2) were conducted, now comparing *any* NWT reported in the diary (regardless of a minimal NWT length) with NWT >60 to >180 minutes based on accelerometry.

Analyses were performed using SAS® Enterprise Guide® (version 4.3; SAS Institute Inc., Cary, NC) or the R Statistical Programming Language for Windows (version 3.2.0) [308], and MS Access 2010/SQL via Microsoft Visual Basic for Application 7.0.

### 3.6.4 Potential determinants of physical activity using multiday 24h-accelerometry under free-living conditions (research question 3)

In this thesis, factors investigated regarding their association with 24h-accelerometry-based time in overall activity and in different activity intensities are referred to as 'potential determinants', with this term encompassing factors that are actual determinants, correlates, or not related to PA [30].

For the analyses of potential determinants of 24h-accelerometry-based PA, linear and logistic regression analyses using robust variance estimates were performed [309, 310]. For this purpose, available discrete variables (**Supplementary Table 1**, **Supplementary Table 2**) were re-categorized to obtain evaluable group sizes by combining equivalent categories. Information on the highest acquired school education was categorized as 'university entrance qualification' encompassing persons reporting to have an advanced technical college certificate ('Fachhochschulreife', 'Abschluss einer Fachoberschule') or a general or subject-related qualification for university entrance ('Allgemeine Hochschulreife', 'fachgebundene Hochschulreife', 'Abitur'), or as 'no university entrance qualification', encompassing persons, who left school without having completed junior high school (no 'Hauptschulabschluss', no 'Volksschulabschluss') and persons reporting to have completed junior high school ('Hauptschulabschluss', 'Volksschulabschluss'), to have a secondary school certificate ('Realschulabschluss', 'Mittlere Reife'), or to have completed eight to ten grades of a polytechnic secondary school in the German Democratic Republic ('Polytechnische Oberschule'). If persons selected the category 'other' degree, it was checked, whether the reported degree is equivalent to having a university entrance qualification, or not. The employment status was assigned to 'full time employed' (including full time employment and in vocational training/apprenticeship, ‘in einer beruflichen Ausbildung/Lehre’), ‘part time employed’ (including part time employment, partial retirement, and persons reporting to have a 400-Euro-job or 'mini-job', or to be marginally, occasionally, or sporadically employed), or ‘not employed’ including unemployed persons and those on maternity leave, parental leave (’Erziehungsurlaub’, ‘Elternzeit’), or those reporting other leave of absence (‘Beurlaubung’). The net household income was categorized as '<2,500 €/month’, ‘2,500-3,999 €/month’, ‘≥4,000 €/month’, or ‘not available’ (n. a.). Information on the marital status was classified as ‘married’ (encompassing persons reporting to be married and to live together with the partner) or ‘not married’ (encompassing persons answering to be married, but to live apart from spouse, to be unmarried, divorced, or widowed). The information on whether persons have ever been diagnosed by a physician with diabetes mellitus was assigned to ‘diabetes mellitus’ if men reported to have ever been diagnosed, or if women reported to have ever been diagnosed independent of being pregnant or to have a manifest diagnosis since pregnancy. ‘No diabetes mellitus’ was given if men or women reported to have never been diagnosed with diabetes mellitus, or if women were initially diagnosed during pregnancy, but after pregnancy, symptoms did not persist. Finally, participants were categorized as ever have been diagnosed with ‘dyslipidemia’ if they reported to have ever been diagnosed with elevated blood lipid levels, hypercholesterolemia, and/or hypertriglyceridemia (assessed as one category); otherwise, persons were classified as ‘no dyslipidemia’. Information on sex (‘men’ versus ‘women’), smoking status (‘never-smoker’, ‘smoker’, or ‘former smoker’), and alcohol consumption (‘never’, ‘maximal 1x/month’, ‘2-4x/month’, ‘2-3x/week’, or ‘≥4x/week’) was included in the analyses as queried (**Supplementary Table 1**, **Supplementary Table 2**). Finally, the study center was included as assessed representing the different study centers. Similarly, BMI and waist circumference were used as continuous measures as calculated or measured, respectively, and the effect of age on PA measures was assessed for each 5-years increase.

BMI and waist circumference are highly correlated (present analyses, Pearson correlation coefficient, $r=0.83$, $p<.0001$; age-adjusted $r=0.81$, $p<.0001$) [311]. Including both together in one regression model could pose problems in the effect estimation of the collinear predictors BMI and waist circumference, since holding one variable constant, while changing the other one is hardly possible due to the strong correlation of both [312, 313]. To avoid collinearity, the residuals of waist circumference adjusted for BMI were determined by running a linear regression model with the waist circumference as outcome and the BMI as only independent variable. The resulting residuals were stored and used as independent variable to be included in the regression analyses. As the correlation between BMI and waist circumference was now adjusted for (Pearson correlation coefficient, r=0.02, p=0.76; age-adjusted r=-0.02, p=0.72), it was possible to analyze the effect of BMI as well as the effect of the BMI-adjusted waist circumference, i.e., the additional effect of waist circumference if BMI is held constant.

For discrete, ordinal data the lowest category was set as reference, as done for the net household income. However, the lowest category for alcohol consumption represented those, who reported to never drink alcohol. As these included few people, the second lowest category was chosen as reference group for the alcohol consumption variable to not attenuate estimates of effect sizes of the regression analyses. For discrete variables on a nominal scale (i.e., sex, smoking status, employment status, marital status, diabetes mellitus, and dyslipidemia) categories showing most counts were set as reference group for the regression analyses on potential determinants of 24h-accelerometry-based PA.

According to the ecological and *'Analysis Grid for Environments Linked to Obesity'* approaches, assessed potential determinants of 24h-accelerometry-based habitual PA all belong to the intrapersonal and homes level of influence (see **Table 2**) [77, 78, 271].

#### 3.6.4.1 Potential determinants of time spent in overall activity and in activity intensities

To investigate potential determinants of PA using 24h-accelerometry, the time spent in overall activity (min/d) as well as the proportion of active time (% overall activity min/d) spent in low, moderate, and VV activity were used. The latter allow to assess if there were relative shifts in active time spent in different activity intensities depending on potential PA determinants. Time in inactivity was not examined, as it had an almost perfect inverse correlation with time in overall activity (Pearson correlation coefficient, r=-0.82, p<.0001; age-adjusted r=-0.82, p<.0001). Four separate linear regression models were used, including each PA measure as single outcome and the following predictors [310]: self-reported sex (men; reference: women), age (per 5 years), measured BMI (kg/m²), waist circumference (cm, residually adjusted for BMI), smoking status (current or former smokers; reference: never-smokers), alcohol consumption (never, 2-4x/month, 2-3x/week, or ≥4x/week; reference: maximal 1x/month), university entrance qualification (yes; reference: no), employment status (part time or not employed; reference: full time), net household income (2,500-3,999 €/month, ≥4,000 €/month, or n. a.; reference: <2,500 €/month), marital status (not married, reference: married), diabetes mellitus (yes; reference: no), and dyslipidemia (yes; reference: no). Further, to account for the multicentric study design, models were adjusted for the study center as done in previous studies analyzing data collected in several study centers [120].

First, univariable models were performed for each PA outcome and each potential determinant. Secondly, a multivariable linear regression model was analyzed, including as predictors sex, age, BMI, waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, as well as the study center allocation (model 1). Finally, a multivariable model additionally including diabetes mellitus and dyslipidemia as potential PA determinants was assessed (model 2).

Then, it was tested for interactions with sex using F-tests for all potential determinants in model 1 and 2 [26, 227, 310]. If a significant interaction was found, the respective linear regression model was conducted stratified by sex to evaluate sex differences in the association of the potential determinants with the PA outcomes.

Finally, it was tested if the assumption of linearity was fulfilled by creating scatter plots, showing the PA outcome on the y-axis and the continuous variables, i.e., age, BMI, and waist circumference (residually adjusted for BMI) on the x-axis. A non-random dispersion in the scatter plots indicates that assuming a non-linear association may be more suitable to describe the relationship between the potential determinant and PA [227, 310].

#### 3.6.4.2 Potential determinants of meeting the physical activity recommendation of the World Health Organization

To assess potential determinants of PA using 24h-accelerometry, further, logistic regression analyses with the binary outcome ‘meeting the WHO PA recommendation’ (yes versus no) were performed, using the same respective univariable and multivariable (model 1 and 2) models as ran for the linear regression analyses (see section 3.6.4.1) [310]. It was also tested for interactions with sex, using F-tests and, where necessary, separated analyses were performed for sexes [26, 227, 310].

The linear as well as logistic regression analyses were repeated as sensitivity analyses, when using the more conservatively defined study sample regarding NWT, i.e. when allowing for less than 60 instead of 120 NWT minutes during an assumed waking period between 6 a.m. and 10 p.m. (see section 3.4.3).

Presented *p*-values are two-tailed and $p<0.05$ were considered statistically significant. All analyses were performed using SAS® Enterprise Guide® (version 4.3; SAS Institute Inc., Cary, NC).

# 4 Results

## 4.1 Reliable assessment of physical activity using multiday 24h-accelerometry under free-living conditions (research question 1)[16]

### 4.1.1 Study Population

**Table 5** summarizes the demographic and medical history characteristics of the ActivE population as included for RQ 1. On average, participants were 45.0 years old (SD, 14.9). Men were older, taller, heavier, and had a larger waist circumference than women. Based on the WHO classifications for BMI and waist circumference, participants were preobese (WHO limit values; BMI, 25 kg/m²; waist circumference, 94.0 and 80.0 cm in men and women, respectively) [289]. The majority (56%) of men and women reported to be full time employed. Differences were found in the distribution of categories of employment between men and women (p=0.04); while proportion of full time employment was the same between sexes, more men than women were not employed, while for part time employment the opposite was true. None of the participants reported to have ever been diagnosed with diabetes mellitus, 10% to have been diagnosed with hypertension, and 2% each to have been diagnosed with coronary artery disease or cancer. There were no significant differences in the medical history between sexes.

Averaged over 11 days of assessment and the total study population, overall activity was 437.0 cpm (95% CI; 404.8, 471.6) (**Table 6**). Of the 1,440 minutes encompassed in 24h, on average, participants spent 1,186.8 min/d (1,169.9, 1,204.0) in inactivity, and 127.1 min/d (118.1, 136.9), 95.7 min/d (89.3, 102.6), 14.4 min/d (12.3, 16.8), and 3.8 min/d (3.1, 4.8) in low, moderate, vigorous, and very vigorous activity, respectively. Sex differences in these PA parameters were only small and non-significant. When returning the accelerometer, none of the participants reported complaints during waking or sleeping phases that prevented to continuously wear the accelerometer.

[16] In the framework of this thesis, parts of the results on a reliable assessment of PA using multiday 24h-accelerometry have already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018).

**Table 5**: Demographic and disease history characteristics of the study population, ActivE study, 2012-2014[17]

| | **total** (N=50) | | **men** (n=25) | | **women** (n=25) | | **test for sex differences**[a] |
|---|---|---|---|---|---|---|---|
| | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | **p** |
| age, years | 45.0 | (14.9) | 49.9 | (13.7) | 40.0 | (14.6) | 0.02 |
| height, cm | 174.3 | (9.2) | 181.0 | (6.0) | 167.5 | (6.5) | <.0001 |
| body weight, kg | 80.2 | (14.5) | 87.8 | (12.1) | 72.5 | (12.7) | <.0001 |
| BMI, kg/m² | 26.4 | (4.1) | 26.8 | (3.5) | 25.9 | (4.6) | 0.42 |
| waist circumference, cm | 90.0 | (12.4) | 95.8 | (9.9) | 84.3 | (12.0) | 0.0005 |
| | **n** | % | **n** | % | **n** | % | **p** |
| employment status | | | | | | | 0.04 |
| full time | 28 | 56 | 14 | 56 | 14 | 56 | |
| part time | 10 | 20 | 2 | 8 | 8 | 32 | |
| not employed | 12 | 24 | 9 | 36 | 3 | 12 | |
| medical conditions | | | | | | | |
| diabetes mellitus | 0 | 0 | 0 | 0 | 0 | 0 | - |
| hypertension | 5 | 10 | 4 | 16 | 1 | 4 | 0.34 |
| coronary artery disease | 1 | 2 | 1 | 4 | 0 | 0 | 1.00 |
| cancer | 1 | 2 | 1 | 4 | 0 | 0 | 1.00 |

BMI, body mass index; n, number; SD, standard deviation
[a]continuous variables, normally distributed: t-test; discrete variables: Chi-Square test/Fisher's exact test

Averaged over the total time of assessment and the total study population, participants reported 215.0 NWT minutes (IQR; 120.0, 338.0) spent in 9.0 (7.0, 12.0) NWT periods (**Table 6**). Per day, participants reported to have taken the accelerometer off on median 1.0 time (0.0, 1.0) for a medium NWT duration of 13.0 minutes (0.0, 25.0) (**Table 6**). There were only slight, non-significant differences in NWT parameters between men and women. NWT periods reported in the diaries were visually checked against software graphs on the according accelerometer data and occurrence, length, and daytime of NWT periods were generally comparable between diary and accelerometer data (data not shown). Since only few and short NWT periods were reported, NWT was included in all analyses. Further, since there were no substantial differences in PA or NWT parameters between sexes, men and women were combined for the following analyses (**Table 6**).

[17]In the framework of this thesis, a modified version of this table has already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018).

**Table 6**: Physical activity based on 24h-accelerometry and non-wear time based on diary of the study population, ActivE study[18]

| | **total** (N=50) | | **men** (n=25) | | **women** (n=25) | | **test for sex differences**[a] |
|---|---|---|---|---|---|---|---|
| **PA parameter**[b] | **GM** | **95% CI** | **GM** | **95% CI** | **GM** | **95% CI** | **p** |
| overall activity, cpm | 437.0 | (404.8, 471.6) | 426.8 | (382.8, 475.8) | 447.4 | (401.3, 498.8) | 0.54 |
| time in inactivity, min/d | 1,186.8 | (1,169.9, 1,204.0) | 1,196.3 | (1,172.3, 1,220.7) | 1,177.5 | (1,153.9, 1,201.5) | 0.27 |
| time in low activity, min/d | 127.1 | (118.1, 136.9) | 118.6 | (107.0, 131.3) | 136.4 | (123.1, 151.0) | 0.06 |
| time in moderate activity, min/d | 95.7 | (89.3, 102.6) | 93.3 | (84.5, 102.9) | 98.2 | (89.0, 108.4) | 0.46 |
| time in vigorous activity, min/d | 14.4 | (12.3, 16.8) | 14.7 | (11.8, 18.4) | 14.1 | (11.3, 17.5) | 0.76 |
| time in very vigorous activity, min/d | 3.8 | (3.1, 4.8) | 4.0 | (2.9, 5.6) | 3.6 | (2.6, 5.0) | 0.62 |
| **NWT parameter**[c] | **median** | **IQR** | **median** | **IQR** | **median** | **IQR** | **p** |
| average NWT per participant, min | 215.0 | (120.0, 338.0) | 254.5 | (124.0, 392.0) | 205.0 | (115.0, 270.0) | 0.23 |
| number of NWT periods per participant | 9.0 | (7.0, 12.0) | 8.0 | (6.5, 11.5) | 10.0 | (7.0, 12.0) | 0.53 |
| NWT per day, min | 13.0 | (0.0, 25.0) | 15.0 | (0.0, 30.0) | 13.0 | (4.0, 23.0) | 0.90 |
| number of NWT periods per day | 1.0 | (0.0, 1.0) | 1.0 | (0.0, 1.0) | 1.0 | (1.0, 1.0) | 0.22 |

cpm, counts per minute; GM, geometric mean; IQR, interquartile range; min, minutes; min/d, minutes per day; NWT, non-wear time; PA, physical activity; 95% CI, 95% confidence interval

[a]continuous variables, normally distributed (physical activity parameters): t-test; continuous variables, not normally distributed (NWT parameters): Mann-Whitney U test

[b]analyses were performed using log-transformed physical activity data

[c]derived from participants' diaries over 11 days for N=49

[18]In the framework of this thesis, a modified version of this table has already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018).

### 4.1.2 Day-to-day variability of habitual physical activity using multiday 24h-accelerometry

The results for the within- and between-person variance in 24h-accelerometry PA are summarized in **Table 7**. For overall activity, the between-person variance accounted for 39.7% of total variance, whereas within-person (day-to-day) variance accounted for 60.3%. Regarding the time in activity intensities, the between-person variance accounted for 34.4% of total variance for time in moderate activity to 45.5% for time in low activity, whereas, vice versa, within-person variance ranged from 54.5 to 65.6%.

**Table 7**: Physical activity within- and between-person variance and number of days needed to assess habitual physical activity using 24h-accelerometry, total (N=50)[19]

| | | | % of total variance | | |
|---|---|---|---|---|---|
| **PA parameter[a]** | **within-person variance** | **between-person variance** | **within-person variance** | **between-person variance** | **number of days** |
| | $s_w^2$ | $s_b^2$ | $s_w^2$ | $s_b^2$ | **D[b]** |
| overall activity, cpm | 0.09593 | 0.06317 | 60.3 | 39.7 | **7** |
| time in inactivity, min/d | 0.00273 | 0.00225 | 54.9 | 45.1 | **6** |
| time in low activity, min/d | 0.06727 | 0.05627 | 54.5 | 45.5 | **6** |
| time in moderate activity, min/d | 0.09604 | 0.05033 | 65.6 | 34.4 | **9** |
| time in vigorous activity, min/d | 0.28890 | 0.21890 | 56.9 | 43.1 | **6** |
| time in very vigorous activity, min/d | 0.57190 | 0.34590 | 62.3 | 37.7 | **8** |

cpm, counts per minute; D, number of days to assess physical activity based on a given r (with r as assumed correlation between observed and true mean of physical activity parameter) [304]; min/d, minutes per day; PA, physical activity; $s_b^2$, between-person variance over 11 days of 24h-accelerometry-based physical activity; $s_w^2$, within-person variance over 11 days of 24h-accelerometry-based physical activity

[a]analyses were performed using log-transformed physical activity data

[b]D is calculated based on an assumed correlation between observed and true mean physical activity of r=0.9 and is rounded up to the nearest full number of days

Then, it was investigated, whether overall PA and time in the different intensities systematically differed across the days of assessment (1 to 11), the days of the week (Monday to Sunday), or between weekdays and weekend days (1 vs. 2) (**Figure 12**). In these analyses, in general, only small differences were observed in the PA parameters.

[19]In the framework of this thesis, this table has already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018).

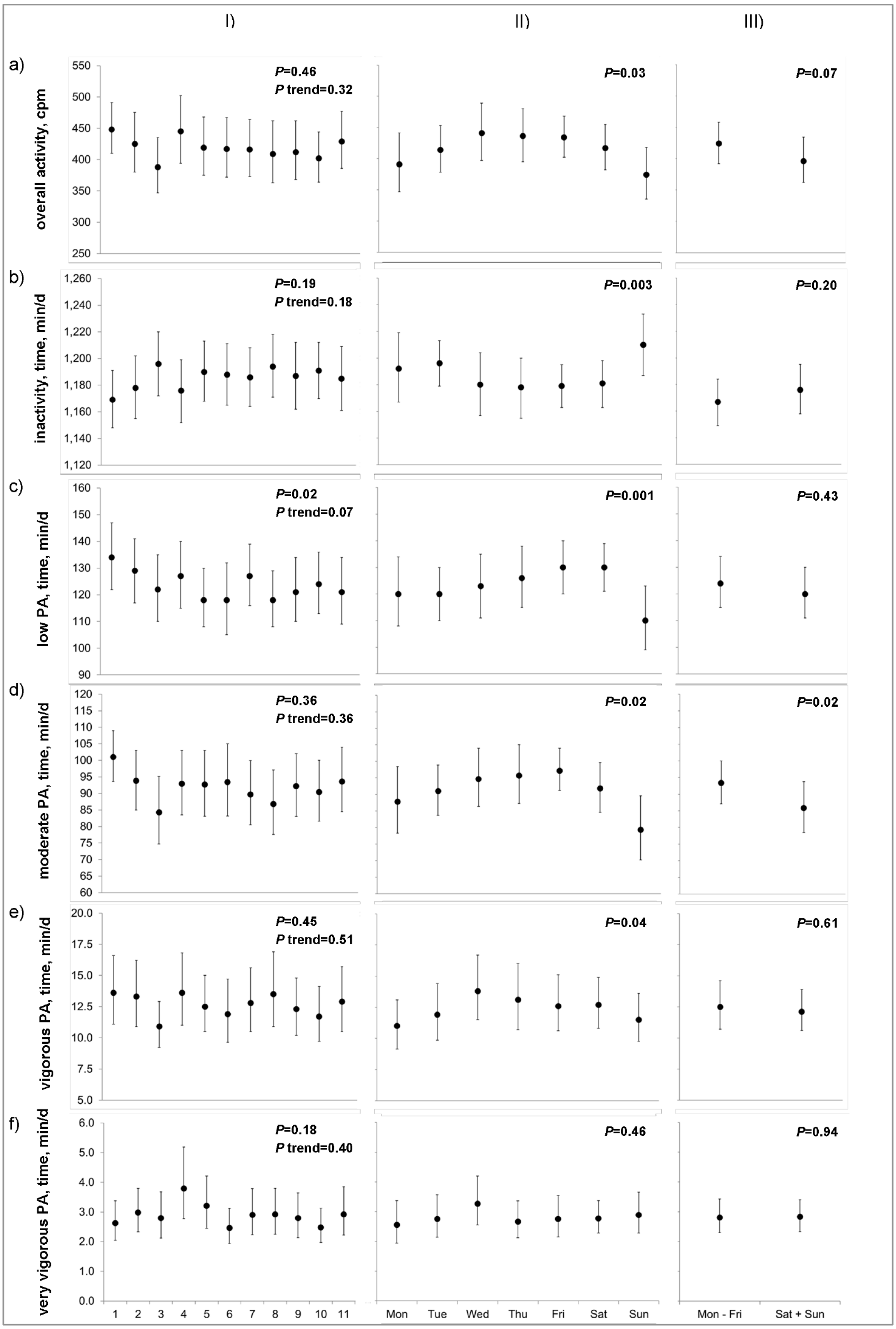


**Figure 12**: Physical activity based on 24h-accelerometry across the days of assessment, the days of the week, or between weekend days and weekdays, total (N=50)[20]

[20] In the framework of this thesis, this figure has already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018).

Results of linear mixed-effects models with adjustment for sex (panel I) or week and sex (panels II and III). Dots indicate geometric least square means and error bars represent 95% confidence intervals for overall physical activity (PA; triaxial counts per minute, cpm, panel a), time in minutes per day (min/d) spent in inactivity (panel b), and in low (panel c), moderate (panel d), vigorous (panel e), and very vigorous activity (panel f). *P*-values presented refer to the main fixed effects, i.e., the day of assessment (panel I; overall *p*-value and *p*-value for trend analyses), the day of the week (panel II), or weekdays versus weekend days (panel III). Results for analyses depicted in panel II and III are based on 48 participants. Note that for the sake of graphic representability, in panel a) to panel e) the lower end of the y-axes is hidden and y-axes, thus, do not begin with 0.

Across the days of assessment, overall activity and the time in low, moderate, and vigorous activity were highest at the first day, decreased in first three days to a lowest level on the third day (except for time in low activity), and were similar across the remaining days of assessment at a mean level compared to the first three days (**Figure 12**, panel I); however, differences were significant only for time in low activity (p=0.02). In contrast, for time in inactivity the opposite (non-significant) pattern was observed across the days of assessment, while time in very vigorous activity only slightly differed across days, tending to be slightly higher on the fourth day than on the other days. There was no significant trend of the PA parameters across the days of assessment.

Across the days of the week, significant differences were found for overall activity (p=0.03) and the time spent in low (p=0.001), moderate (p=0.02), and vigorous activity (p=0.04) (**Figure 12**, panel II). These PA measures were highest on Wednesday (overall activity and time in vigorous activity) and Friday (time in low and moderate activity), and were lowest on Monday (time in vigorous activity) and Sunday (overall activity and time in low and moderate activity). There were apparent differences between Saturday and Sunday, with Saturday showing PA amounts like weekdays and Sunday showing considerable lower PA levels. For time in inactivity, the pattern across the days of the week was complementary to the results found for overall activity and time in activity intensities (p=0.003); it was lowest on Thursday and highest on Sunday. Again, Saturday was more comparable to weekdays, while time in inactivity was substantially higher on Sunday compared to the remaining days. Time in very vigorous activity was quite constant across the days of the week, being slightly higher on Wednesday (p=0.46).

Time in moderate activity was significantly lower on weekend days than on weekdays (p=0.02) (**Figure 12**, Panel III). Similarly, overall activity tended to be lower on weekend days as compared to weekdays; however, these differences were only small and not significant (0.07). The time spent in inactivity and in low, vigorous, and very vigorous activity was quite similar between weekdays and weekend days.

Then, it was investigated to what extent the day of the week or the distinction between weekdays and weekend days explained the total observed variance of PA (**Table 8**). For overall activity, the day of the week explained 2.1% of total variance. For time in inactivity and in the different activity intensities, the day of the week accounted for 0.0% (time in very vigorous activity) to 9.6% (time in low activity) of total observed variance. The weekday-versus-weekend-day effect accounted for 13.9% of total variance of overall activity and explained 5.7% (time in vigorous activity) to 18.8% (time in moderate activity) of total variance of time spent in the different activity intensities.

**Table 8**: Explanation of variance of habitual physical activity using 24h-accelerometry, total (N=48)

| **PA parameter**[a] | **sex** | **subject** | **week** (1 vs. 2) | **day of the week** (Mon-Sun) | **weekday vs. week-end day** | **residual** |
|---|---|---|---|---|---|---|
| | | | **% of total variance** | | | |
| overall activity, cpm | 0.0 | 40.0 | - | 2.1 | - | 57.9 |
| | 0.0 | 37.5 | 0.0 | - | 13.9 | 48.5 |
| time in inactivity, min/d | 2.2 | 44.3 | - | 3.8 | - | 49.7 |
| | 2.2 | 42.1 | 0.0 | - | 11.9 | 43.7 |
| time in low activity, min/d | 8.5 | 40.9 | - | 9.6 | - | 41.0 |
| | 8.1 | 38.3 | 0.0 | - | 17.5 | 36.1 |
| time in moderate activity, min/d | 0.0 | 33.9 | - | 9.4 | - | 56.7 |
| | 0.0 | 31.4 | 0.0 | - | 18.8 | 49.8 |
| time in vigorous activity, min/d | 0.0 | 43.6 | - | 0.3 | - | 56.1 |
| | 0.0 | 42.5 | 0.0 | - | 5.7 | 51.8 |
| time in very vigorous activity, min/d | 0.0 | 38.2 | - | 0.0 | - | 61.8 |
| | 0.0 | 37.1 | 0.0 | - | 7.2 | 55.8 |

cpm, counts per minute; min/d, minutes per day; PA, physical activity; vs., versus
[a]analyses were performed using log-transformed data

### 4.1.3 Number of days needed to estimate habitual physical activity using 24h-accelerometry

Based on the results for the within- (day-to-day) and between-person variance, further, the number of days, *D*, needed for a valid estimation of habitual PA based on 24h-accelerometry was calculated using the formula by Black et al. (**Table 7**, **Equation 4**). *D* was lowest for time spent in inactivity, and in low and vigorous activity (*D*=6), while for time in moderate activity, *D* was highest (*D*=9). Applying the Spearman-Brown prophecy formula showed similar results on days being required to achieve a reliability of 0.8 (**Supplementary Table 3**); the number of days needed, *N*, was lowest for time in inactivity and in low activity (*N*=5), and was highest for time in moderate activity (*N*=8).

When calculating the correlation between observed and true PA measure, $r_D$, depending on the number of days of repeated PA assessments, $D_r$, measurement over a period of approximately one week was found to be suitable for estimating habitual PA with a given confidence of $r_D$=0.90 (**Table 9**).

### 4.1.4 Reliability of habitual physical activity using 24h-accelerometry

Finally, the week-to-week reliability of PA based on 24h-accelerometry was investigated, when comparing PA averaged over an approximately 1-week period (**Table 10**). Mean daily overall activity was lower and time spent in low to very vigorous activity were slightly shorter in the second than in the first week, whereas for time in inactivity the opposite was true. As compared to the day-to-day variability (**Table 7**), the week-to-week within-person variance was considerably lower, being 25.3% for overall activity and being in the range of 18.2% (time in vigorous activity) to 33.3% (time in moderate activity) for the time spent in the different activity intensities. The ICC based on the comparison of the mean daily PA parameters in week 1 and week 2 was 0.75 for overall activity and ranged from 0.68 (time moderate activity) to 0.82 (time in vigorous activity) for the time spent in the different activity intensities, indicating good to excellent week-to-week reliability [248].

### 4.1.5 Sensitivity analyses

The day before the second study center visit was deleted from all previous analyses on RQ 1, since participants were instructed not to perform PA on that day due to a planned metabolic measurement. When including the day before the last day (day 14, **Figure 6**), i.e., including six days in each week, results for all analyses regarding the variability and reliability were not substantially different to the findings reported in the main analyses (**Supplementary Table 4**, **Supplementary Table 5**, **Supplementary Table 6**, **Supplementary Table 7**; **Supplementary Figure 1**).

**Table 9**: Correlations between observed and true physical activity based on a given number of days of assessment of 24h-accelerometry, total (N=50)[21]

| PA parameter[a] | within-person variance | between-person variance | | $r_D$ | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $s_w^2$ | $s_b^2$ | $s_w^2/s_b^2$ | $D_r$=1 | $D_r$=2 | $D_r$=3 | $D_r$=4 | $D_r$=5 | $D_r$=6 | $D_r$=7 | $D_r$=8 | $D_r$=9 | $D_r$=10 | $D_r$=11 |
| overall activity, cpm | 0.09593 | 0.06317 | 1.52 | 0.63 | 0.75 | 0.81 | 0.85 | 0.88 | 0.89 | 0.91 | 0.92 | 0.93 | 0.93 | 0.94 |
| time in inactivity, min/d | 0.00273 | 0.00225 | 1.22 | 0.67 | 0.79 | 0.84 | 0.88 | 0.90 | 0.91 | 0.92 | 0.93 | 0.94 | 0.94 | 0.95 |
| time in low activity, min/d | 0.06727 | 0.05627 | 1.20 | 0.67 | 0.79 | 0.85 | 0.88 | 0.90 | 0.91 | 0.92 | 0.93 | 0.94 | 0.95 | 0.95 |
| time in moderate activity, min/d | 0.09604 | 0.05033 | 1.91 | 0.59 | 0.72 | 0.78 | 0.82 | 0.85 | 0.87 | 0.89 | 0.90 | 0.91 | 0.92 | 0.92 |
| time in vigorous activity, min/d | 0.28890 | 0.21890 | 1.32 | 0.66 | 0.78 | 0.83 | 0.87 | 0.89 | 0.91 | 0.92 | 0.93 | 0.93 | 0.94 | 0.94 |
| time in very vigorous activity, min/d | 0.57190 | 0.34590 | 1.65 | 0.61 | 0.74 | 0.80 | 0.84 | 0.87 | 0.89 | 0.90 | 0.91 | 0.92 | 0.93 | 0.93 |

cpm, counts per minute; $D_r$, number of days of physical activity assessment; min/d, minutes per day; PA, physical activity; $r_D$, correlation between observed and true mean of physical activity parameter based on a given $D_r$, adapted from [304]; $s_b^2$, between-person variance over 11 days of 24h-accelerometry-based physical activity; $s_w^2$, within-person variance over 11 days of 24h-accelerometry-based physical activity

[a]analyses were performed using log-transformed data

[21]In the framework of this thesis, this table has already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018).

**Table 10**: Within- and between-person variance and week-to-week reliability of habitual physical activity using 24h-accelerometry, total (N=48)[22]

| PA parameter[a] | week 1 | week 2 | % of total variance: within-person variance | % of total variance: between-person variance | ICC week 1 vs. week 2 | |
|---|---|---|---|---|---|---|
| | GM | GM | $s_w^2$ | $s_b^2$ | ICC | 95% CI |
| overall activity, cpm | 438.0 | 421.3 | 25.3 | 74.7 | 0.75 | (0.60, 0.85) |
| time in inactivity, min/d | 1,186.0 | 1,192.1 | 25.3 | 74.7 | 0.76 | (0.61, 0.86) |
| time in low activity, min/d | 127.2 | 124.3 | 25.0 | 75.0 | 0.78 | (0.64, 0.87) |
| time in moderate activity, min/d | 96.2 | 91.9 | 33.3 | 66.7 | 0.68 | (0.49, 0.80) |
| time in vigorous activity, min/d | 14.0 | 13.8 | 18.2 | 81.8 | 0.82 | (0.70, 0.89) |
| time in very vigorous activity, min/d | 3.7 | 3.4 | 32.0 | 68.0 | 0.69 | (0.51, 0.81) |

cpm, counts per minute; ICC, intraclass correlation coefficient; GM, geometric mean; min/d, minutes per day; PA, physical activity; $s_b^2$, between-person variance of 24h-accelerometry-based physical activity between week 1 and week 2; $s_w^2$, within-person variance of 24h-accelerometry-based physical activity between week 1 and 2; vs., versus; 95% CI, 95% confidence interval
[a]analyses were performed using log-transformed data

## 4.2 Detection of accelerometer non-wear time using multiday 24h-accelerometry under free-living conditions (research question 2)[23]

### 4.2.1 Study Population

**Table 11** summarizes the characteristics of the 47 ActivE (men, 51.1%) and 559 KORA (men, 46.9%) participants included in the analyses on NWT detection in 24h-accelerometry data. Since KORA initially included older ages than ActivE and, further, data from the second KORA follow-up was used, participants in KORA seemed to be slightly older compared to the cross-sectional baseline characteristics in ActivE. According to the WHO categorization, both study populations were slightly obese, particularly in KORA (WHO limit values; BMI, 25 kg/m [289]).

[22]In the framework of this thesis, this table has already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health.* 18, 530 (2018).

[23]In the framework of this thesis, parts of the results on NWT detection in 24h-accelerometry data have already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

**Table 11**: Characteristics of the study populations, ActivE study, 2012-2014, and KORA FF4 study, 2013-2014[24]

| | ActivE study | | KORA FF4 study | |
|---|---|---|---|---|
| number of participants | 47 | | 559 | |
| men, % | 51.1 | | 46.9 | |
| | **median** | **IQR** | **median** | **IQR** |
| age, years | 43 | (32, 59) | 58 | (53, 63) |
| height, cm | 175.6 | (165.8, 180.1) | 168.8 | (162.0, 176.8) |
| body weight, kg | 78.3 | (70.9, 88.0) | 78.9 | (68.6, 91.1) |
| BMI, kg/m² | 25.4 | (23.2, 28.7) | 27.2 | (24.5, 30.6) |
| waist circumference, cm | 89.0 | (80.4, 95.7) | n. a. | n. a. |
| **NWT based on diary** | | | | |
| NWT/24h[a], min | 20.8 | (12.4, 30.3) | 23.9 | (13.6, 44.5) |
| number of NWT periods/24h[a] | 0.8 | (0.6, 1.0) | 0.9 | (0.6, 1.0) |
| | **distribution of NWT periods, %** | | | |
| | ***total time of assessment***[b] | | | |
| >60 min | 9.1 | | 15.4 | |
| >90 min | 4.5 | | 8.7 | |
| >120 min | 3.3 | | 6.4 | |
| >150 min | 2.0 | | 5.1 | |
| >180 min | 1.5 | | 4.3 | |
| | ***waking***[c] | | | |
| >60 min | 8.6 | | 13.1 | |
| >90 min | 4.0 | | 7.6 | |
| >120 min | 2.6 | | 5.2 | |
| >150 min | 1.3 | | 4.0 | |
| >180 min | 0.5 | | 3.2 | |
| | ***sleeping***[c] | | | |
| >60 min | 50.0 | | 88.0 | |
| >90 min | 50.0 | | 84.0 | |
| >120 min | 50.0 | | 84.0 | |
| >150 min | 50.0 | | 84.0 | |
| >180 min | 50.0 | | 80.0 | |

BMI, body mass index; IQR, interquartile range; n. a., not available; NWT, non-wear time

[a]the total number of waking and sleeping phases were summed up per participant and divided by two to consider one waking and one sleeping phase as average 24h

[b]analyses were conducted from the first to the last recorded time point of assessment in the diary

[c]waking and sleeping phases were derived from participants' diary entries

Based on the diary, ActivE and KORA participants reported a similar median NWT length (20.8 min and 23.9 min, respectively) and number of NWT periods in 24h (0.8

[24]In the framework of this thesis, this table has already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

and 0.9, respectively) (**Table 11**). There were no significant differences in NWT parameters between age groups of 20 to 39 years, 40 to 59 years, and ≥60 years in ActivE, or between ages <60 years and ≥60 years in KORA (**Table 12**).

**Table 12**: Non-wear time in the different age groups in ActivE and KORA

| | 20-39 years | | 40-59 years | | ≥60 years | | test for age differences[a] |
|---|---|---|---|---|---|---|---|
| **NWT based on diary** | **Median (IQR)** | | | | | | **p** |
| | **ActivE study (N=47)** | | | | | | |
| number of NWT periods/24h | 20.8 | (11.5,29.8) | 20.9 | (12.0,30.3) | 22.1 | (16.4,30.4) | 0.88 |
| NWT/24h, min | 0.8 | (0.5,1.0) | 0.9 | (0.7,1.1) | 0.7 | (0.4,0.9) | 0.36 |
| | **KORA FF4 study (N=559)** | | | | | | |
| number of NWT periods/24h | - | | 0.9 | (0.6,1.0) | 0.9 | (0.4,1.0) | 0.96 |
| NWT/24h, min | - | | 23.0 | (13.7,41.3) | 24.9 | (13.3,46.7) | 0.54 |

h, hours, IQR, interquartile range; min, minutes; NWT, non-wear time
[b]Wilcoxon rank sum test

Considering all reported NWT regardless of length, over the total time of assessment, 9.1% and 15.4% of all NWT minutes were spent in periods >60 min in ActivE and KORA, respectively (**Table 11**). Consequently, around 85 to 90% of the total diary NWT was <60 minutes. In ActivE, showering, personal care, and changing clothes were mostly reported as NWT reasons, particularly for NWT <60 minutes. As expected, the longer the NWT algorithm, the less NWT periods were reported, and NWT periods >180 minutes accounted for 1.5% and 4.3% of all NWT based on diary in ActivE and KORA, respectively. Slightly lower, but similar proportions of NWT periods >60 to >180 minutes occurred during waking in both studies, whereas during sleeping, NWT was typically longer than 180 minutes (50% in ActivE, 80% in KORA). Thus, during sleeping, the proportions of NWT >60 to >180 minutes were quite similar, and proportions of NWT in periods >60 to >180 minutes were considerably larger than for the total time of assessment or waking. However, generally, few NWT periods were reported during sleeping with only 3 and 22 periods during sleeping in ActivE and KORA, respectively, being >60 minutes (**Table 13**).

**Table 13**: Sensitivity and specificity: non-wear time algorithms >60 to >180 minutes using 24h-accelerometry versus diary[25]

| NWT algorithm[a] | ActivE study (N=47) | | | | KORA FF4 study (N=559) | | | |
|---|---|---|---|---|---|---|---|---|
| | number of NWT periods | | sensitivity[b] | specificity[b] | number of NWT periods | | sensitivity[b] | specificity[b] |
| | diary | accelerometry | | | diary | accelerometry | | |
| ***total time of assessment*[c]** | | | | | | | | |
| >60 min | 50 | 378 | 0.72 | 0.00 | 476 | 1,535 | 0.64 | 0.08 |
| >90 min | 25 | 81 | 0.80 | 0.16 | 269 | 420 | 0.70 | 0.57 |
| >120 min | 18 | 34 | 0.83 | 0.54 | **199** | **284** | **0.76** | **0.74** |
| >150 min | 11 | 17 | 0.82 | 0.78 | 156 | 223 | 0.72 | 0.79 |
| >180 min | **8** | **10** | **0.88** | **0.92** | 134 | 192 | 0.72 | 0.82 |
| ***waking*[d]** | | | | | | | | |
| >60 min | 47 | 75 | 0.70 | 0.93 | 369 | 531 | 0.65 | 0.91 |
| >90 min | **22** | **34** | **0.76** | **0.97** | 214 | 257 | 0.70 | 0.97 |
| >120 min | 14 | 17 | 0.71 | 0.99 | **145** | **178** | **0.76** | **0.98** |
| >150 min | 7 | 8 | 0.57 | 0.99 | 112 | 132 | 0.68 | 0.98 |
| >180 min | 3 | 3 | 0.67 | 1.00 | 91 | 108 | 0.68 | 0.99 |
| ***sleeping*[d]** | | | | | | | | |
| >60 min | 3 | 299 | 1.00 | 0.59 | 22 | 868 | 0.90 | 0.77 |
| >90 min | **3** | **44** | **1.00** | **0.94** | **21** | **130** | **0.86** | **0.97** |
| >120 min | **3** | **16** | **1.00** | **0.98** | **21** | **81** | **0.86** | **0.98** |
| >150 min | **3** | **9** | **1.00** | **0.99** | **21** | **75** | **0.86** | **0.98** |
| >180 min | **3** | **6** | **1.00** | **1.00** | **20** | **66** | **0.85** | **0.99** |

min, minutes; NWT, non-wear time
[a]algorithms were applied to diary and accelerometry data to check for self-reported NWT periods >60, >90, >120, >150, and >180 minutes or NWT periods based on consecutive acceleration zero-counts >60, >90, >120, >150, and >180 minutes, respectively
[b]periods with an overlap between NWT according to diary and accelerometry of ≥50% were included in this analysis; number of epochs with an overlap of <50% was: ActivE, waking, 90-min algorithm: 1; KORA FF4, total time, 60- to 180-min algorithm: 30, 7, 8, 5, and 4, respectively; KORA FF4, waking, 60- to 180-min algorithm: 14, 4, 5, 2, and 1, respectively; KORA FF4, sleeping, 60-min algorithm: 1
[c]analyses were conducted from the first to the last time point of assessment recorded in the diary
[d]waking and sleeping phases were derived from participants' diary entries
**bold**: algorithms showing high sensitivity and specificity in ActivE and KORA FF4, respectively

[25]In the framework of this thesis, this table has already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

### 4.2.2 Sensitivity and specificity of non-wear time algorithms >60 to >180 minutes based on accelerometry compared to diary data

The results for the number of NWT periods >60 to >180 minutes based on diary and accelerometry, as well as the resulting sensitivity and specificity of NWT detection, when comparing accelerometry with diary data, are shown in **Table 13**. Over the total time of assessment, 50 NWT periods >60 minutes, encompassing 7,891 NWT minutes, were reported in the diaries of the 47 ActivE participants, while the 559 KORA participants reported 476 NWT periods >60 minutes, including 83,642 NWT minutes (**Table 14**, **Table 15)**. Overall, in both studies sensitivity and specificity of NWT detection based on 24h-accelerometry data were low, when applying the 60-min algorithm over the total time of assessment as well as for waking and sleeping phases (**Table 13**). Generally, higher sensitivity and specificity were found for longer NWT algorithms. Particularly over the total time of assessment, sensitivity and specificity were lowest for the 60-min algorithm in ActivE (0.72 and 0.00) and KORA (0.64 and 0.08), while sensitivity and specificity increased with length of NWT; the increase with length of NWT algorithm was lower for sensitivity than for specificity. Further, in both studies, specificity was lowest for the 60-min algorithm during waking (ActivE, 0.93; KORA, 0.91) and, especially, during sleeping (ActivE, 0.59; KORA, 0.77) compared to longer algorithms. During waking, sensitivity was also lowest for the 60-min algorithm compared to longer algorithms in KORA. During sleeping, a maximal sensitivity was already achieved using the 60-min algorithm (ActivE, 1.00; KORA, 0.90), being similar or slightly lower for longer NWT algorithms.

Over the total time of assessment, sensitivity and specificity of NWT detection were both high for the 180-min and 120-min algorithm in ActivE (sensitivity, 0.88; specificity, 0.92) and KORA (sensitivity, 0.76; specificity, 0.74), respectively (**Table 13**). However, these algorithms allowed to detect at maximum 1.5% and 6.4% of all reported NWT (**Table 11**).

When analyzing waking phases, sensitivity and specificity were both high for the 90-min algorithm in ActivE (sensitivity, 0.76; specificity, 0.97) and the 120-min algorithm in KORA (sensitivity, 0.76; specificity, 0.98) (**Table 13**). Using these algorithms, at maximum 4.0% and 5.2% of all reported NWT were assessable based on accelerometry data in ActivE and KORA, respectively (**Table 11**).

During sleeping, in both studies sensitivity and specificity were generally high (sensitivity, >0.85; specificity,>0.94) for the 90-min to 180-min algorithms (**Table 13**). Differences between algorithms were, if at all, small, since NWT during sleeping was mainly longer than all algorithms assessed (**Table 11, Table 13**). Thus, the majority of reported NWT is detectable during sleeping, when applying any of the algorithms.

### 4.2.3 Overlap of accelerometry and diary non-wear time periods identified using the >60 min to >180-min algorithms

**Table 14** and **Table 15** summarize the minutes in and the number of NWT periods >60 to >180 minutes based on diary and accelerometry data, as well as the resulting NWT minutes detected in both, *accelerometry and diary* (i.e., the overlap in length of NWT), and NWT minutes detected in either *diary only* or *accelerometry only*. Overall, in both studies, overlap was lowest for the 60-min algorithm for the total time of assessment (ActivE, 18.0%; KORA 28.4%), as well as during waking (ActivE, 40.1%; KORA 41.3%) and, particularly, during sleeping (ActivE, 5.0%; KORA 9.0%). At the same time, NWT minutes false positively detected in *accelerometry only* were highest for the 60-min algorithms over the total time of assessment (ActivE, 77.8%; KORA 60.7%), during waking (ActivE, 45.4%; KORA 42.7%) and, most pronounced, during sleeping, where NWT minutes detected in accelerometry, but not in diary contributed 94.9% and 89.4% to the potential total NWT in ActivE and KORA, respectively.

For the total time of assessment, applying the 180-min and 120-min algorithm that were most sensitive and specific in ActivE and KORA, respectively (**Table 13**), resulted in the highest overlap in length of NWT among all algorithms assessed (ActivE, 63.5%; KORA, 42.1%; **Table 14**, **Table 15**). At the same time, NWT minutes false positively detected in *accelerometry only* were lowest for these algorithms (ActivE, 26.7%; KORA, 43.7%).

For waking, when using the algorithms with high sensitivity and specificity in ActivE and KORA, i.e., the 90-min and 120-min algorithm (**Table 13**), respectively, NWT overlap was higher than for the 60-min algorithm (ActivE, 44.4%; KORA, 45.2%; **Table 14**, **Table 15**). At the same time, proportion of NWT minutes reported in *diary only* was lowest for the 90-min and 120-min algorithm (ActivE, 13.8%; KORA, 16.0%), while in both studies around 40% of the potential total NWT was detected in *accelerometry only*.

During sleeping, applying the 90-min to 180-min algorithms that had high sensitivity and specificity for NWT detection (**Table 13**) resulted in higher degrees of overlap in length of NWT and lower degrees of NWT detected in *accelerometry only* the longer the algorithm was: in ActivE, overlap increased from 18.2 to 50.1% and false positive NWT detection decreased from 81.3 to 48.4%, while in KORA differences between algorithms were smaller, with the overlap increasing from 21.3 to 26.0% and NWT detected in *accelerometry only* decreasing from 74.7 to 69.0% (**Table 14**, **Table 15**).

**Table 14**: Overlap: non-wear time algorithms >60 to >180 minutes using 24h-accelerometry versus diary; ActivE study[26]

| NWT algorithm[a] | diary | | accelerometry | | diary or accelerometry | | | |
|---|---|---|---|---|---|---|---|---|
| | total NWT | NWT periods | total NWT | NWT periods | potential total NWT[b] | NWT diary and accelerometry | NWT diary only | NWT accelerometry only |
| | min | n | min | n | min | % | % | % |
| ***total time of assessment***[c] | | | | | | | | |
| >60 min | 7,891 | 50 | 34,127 | 378 | 35,612 | 18.0 | 4.2 | 77.8 |
| >90 min | 6,133 | 25 | 13,243 | 81 | 14,170 | 36.7 | 6.5 | 56.7 |
| >120 min | 5,400 | 18 | 8,301 | 34 | 9,156 | 49.6 | 9.3 | 41.0 |
| >150 min | 4,463 | 11 | 6,065 | 17 | 6,759 | 55.8 | 10.3 | 34.0 |
| >180 min | 3,983 | 8 | 4,903 | 10 | 5,436 | 63.5 | 9.8 | 26.7 |
| ***waking***[d] | | | | | | | | |
| >60 min | 5,079 | 47 | 7,956 | 75 | 9,302 | 40.1 | 14.5 | 45.4 |
| >90 min | 3,321 | 22 | 4,914 | 34 | 5,702 | 44.4 | 13.8 | 41.8 |
| >120 min | 2,470 | 14 | 3,123 | 17 | 3,815 | 46.6 | 18.1 | 35.3 |
| >150 min | 1,533 | 7 | 1,934 | 8 | 2,465 | 40.6 | 21.5 | 37.8 |
| >180 min | 873 | 3 | 1,119 | 3 | 1,309 | 52.2 | 14.5 | 33.3 |
| ***sleeping***[d] | | | | | | | | |
| >60 min | 1,257 | 3 | 24,382 | 299 | 24,418 | 5.0 | 0.1 | 94.9 |
| >90 min | 1,257 | 3 | 6,676 | 44 | 6,712 | 18.2 | 0.5 | 81.3 |
| >120 min | 1,257 | 3 | 3,832 | 16 | 3,868 | 31.6 | 0.9 | 67.5 |
| >150 min | 1,257 | 3 | 2,926 | 9 | 2,962 | 41.2 | 1.2 | 57.6 |
| >180 min | 1,257 | 3 | 2,401 | 6 | 2,437 | 50.1 | 1.5 | 48.4 |

min, minutes; n, number; NWT, non-wear time
[a]algorithms were applied to diary and accelerometry data to check for self-reported NWT periods >60, >90, >120, >150, and >180 minutes or NWT periods based on consecutive acceleration zero-counts>60, >90, >120, >150, and >180 minutes, respectively
[b]potential total NWT includes NWT which is NWT detected by either *diary*, *accelerometry*, or *both*
[c]analyses were conducted from the first to the last time point of assessment recorded in the diary
[d]waking and sleeping phases were derived from participants' diary entries

[26]In the framework of this thesis, a modified version of this table has already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

**Table 15**: Overlap: non-wear time algorithms >60 to >180 minutes using 24h-accelerometry versus diary; KORA FF4 study[27]

| NWT algorithm[a] | diary | | accelerometry | | diary or accelerometry | | | |
|---|---|---|---|---|---|---|---|---|
| | total NWT | NWT periods | total NWT | NWT periods | potential total NWT[b] | NWT diary and accelerometry | NWT diary only | NWT accelerometry only |
| | min | n | min | n | min | % | % | % |
| ***total time of assessment***[c] | | | | | | | | |
| >60 min | 83,642 | 476 | 189,666 | 1,535 | 212,912 | 28.4 | 10.9 | 60.7 |
| >90 min | 69,810 | 269 | 110,560 | 420 | 128,642 | 40.2 | 14.1 | 45.7 |
| >120 min | 62,806 | 199 | 95,794 | 284 | 111,616 | 42.1 | 14.2 | 43.7 |
| >150 min | 57,396 | 156 | 87,262 | 223 | 103,171 | 40.2 | 15.4 | 44.4 |
| >180 min | 53,933 | 134 | 81,623 | 192 | 96,786 | 40.1 | 15.7 | 44.3 |
| ***waking***[d] | | | | | | | | |
| >60 min | 56,004 | 369 | 82,091 | 531 | 97,708 | 41.3 | 16.0 | 42.7 |
| >90 min | 45,447 | 214 | 61,874 | 257 | 74,082 | 44.9 | 16.5 | 38.7 |
| >120 min | 38,529 | 145 | 52,835 | 178 | 62,915 | 45.2 | 16.0 | 38.8 |
| >150 min | 34,359 | 112 | 46,430 | 132 | 56,822 | 42.2 | 18.3 | 39.5 |
| >180 min | 31,009 | 91 | 42,257 | 108 | 51,776 | 41.5 | 18.4 | 40.1 |
| ***sleeping***[d] | | | | | | | | |
| >60 min | 9,331 | 22 | 86,690 | 868 | 88,080 | 9.0 | 1.6 | 89.4 |
| >90 min | 9,270 | 21 | 35,146 | 130 | 36,605 | 21.3 | 4.0 | 74.7 |
| >120 min | 9,270 | 21 | 30,204 | 81 | 31,663 | 24.7 | 4.6 | 70.7 |
| >150 min | 9,270 | 21 | 29,411 | 75 | 30,870 | 25.3 | 4.7 | 70.0 |
| >180 min | 9,108 | 20 | 27,923 | 66 | 29,381 | 26.0 | 5.0 | 69.0 |

min, minutes; n, number; NWT, non-wear time
[a]algorithms were applied to diary and accelerometry data to check for self-reported NWT periods >60, >90, >120, >150, and >180 minutes or NWT periods based on consecutive acceleration zero-counts>60, >90, >120, >150, and >180 minutes, respectively
[b]potential total NWT includes NWT which is NWT detected by either *diary*, *accelerometry*, or *both*
[c]analyses were conducted from the first to the last time point of assessment recorded in the diary
[d]waking and sleeping phases were derived from participants' diary entries

[27]In the framework of this thesis, a modified version of this table has already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

### 4.2.4 Overlap of any diary non-wear time with accelerometry non-wear time identified using the >60 min to >180-min algorithms

Further, overlap and deviation in NWT minutes was assessed, when comparing accelerometry-based NWT based on the 60-min to 180-min algorithms with any NWT based on diary regardless of a minimal length (**Table 16**, **Table 17**). Across the 47 ActivE participants, 551 NWT periods of any length were reported, including 17,231 minutes, while the 559 KORA participants reported 3,089 NWT periods, encompassing 142,640 minutes. Overall, in both studies, overlap between accelerometry- and diary-based NWT was low, being mainly about 20%. Applying the 60-min algorithm to accelerometry over the total time of assessment resulted in an overlap with any diary NWT of 14.7% in ActivE and 22.8% in KORA, respectively, whereas NWT detected in *accelerometry only* accounted for 61.5% and 47.3%, respectively, of the potential total NWT. Interestingly, when focusing on waking, the overlap was highest among the tested algorithms, when applying the 60-min algorithm to accelerometry, and overlap decreased with length of NWT algorithm from 20.8% to 4.8% in ActivE and from 27.3% to 17.0% in KORA. However, at the same time, false positive NWT detection, i.e., NWT detected in *accelerometry only*, was also highest for the 60-min algorithm (ActivE, 22.2%; KORA, 26.5%) compared to the longer algorithms. For sleeping, overlap with diary-based NWT minutes was extremely low (ActivE, 5.0%; KORA, 9.1%) and false positive NWT detection based on accelerometry was very high (ActivE, 94.7%; KORA, 89.2%), when applying the 60-min algorithm to accelerometry.

Due to considering all diary-based NWT (resulting in a constant amount of total NWT minutes based on diary across algorithms) versus taking into account only NWT >60 to >180 minutes based on accelerometry (resulting in a decrease in total NWT minutes based on accelerometry across algorithms), NWT detected in *diary only* increased with length of the NWT algorithm in both studies over the total time of assessment and during waking and sleeping (**Table 16**, **Table 17**). Thus, over the total time of assessment, false negative NWT detection was high reaching a maximum for the 180-min algorithm of 73.7% and 55.7% in ActivE and KORA, respectively. Separated analyses showed that false negative NWT detection was most pronounced during waking, with up to 92.4% (ActivE) and 68.0% (KORA) being detected in *diary only*, whereas during sleeping it was only 3.2% and 6.0%, respectively. In contrast, proportion of NWT minutes detected in *accelerometry only* decreased in both studies with increasing length of the algorithms over the total time of assessment as well as during waking and sleeping.

**Table 16**: Overlap: non-wear time algorithms >60 to >180 minutes using 24h-accelerometry versus any diary-based non-wear time, ActivE study[28]

| NWT algorithm[a] | diary | | accelerometry | | diary or accelerometry | | | |
|---|---|---|---|---|---|---|---|---|
| | total NWT | NWT periods | total NWT | NWT periods | potential total NWT[b] | NWT diary and accelerometry | NWT diary only | NWT accelerometry only |
| | min | n | min | n | min | % | % | % |
| ***total time of assessment***[c] | | | | | | | | |
| >60 min | 17,231 | 551 | 34,127 | 378 | 44,782 | 14.7 | 23.8 | 61.5 |
| >90 min | 17,231 | 551 | 13,243 | 81 | 25,136 | 21.2 | 47.3 | 31.4 |
| >120 min | 17,231 | 551 | 8,301 | 34 | 20,949 | 21.9 | 60.4 | 17.7 |
| >150 min | 17,231 | 551 | 6,065 | 17 | 19,404 | 20.1 | 68.7 | 11.2 |
| >180 min | 17,231 | 551 | 4,903 | 10 | 18,662 | 18.6 | 73.7 | 7.7 |
| ***waking***[d] | | | | | | | | |
| >60 min | 14,390 | 546 | 7,956 | 75 | 18,496 | 20.8 | 57.0 | 22.2 |
| >90 min | 14,390 | 546 | 4,914 | 34 | 16,671 | 15.8 | 70.5 | 13.7 |
| >120 min | 14,390 | 546 | 3,123 | 17 | 15,697 | 11.6 | 80.1 | 8.3 |
| >150 min | 14,390 | 546 | 1,934 | 8 | 15,199 | 7.4 | 87.3 | 5.3 |
| >180 min | 14,390 | 546 | 1,119 | 3 | 14,804 | 4.8 | 92.4 | 2.8 |
| ***sleeping***[d] | | | | | | | | |
| >60 min | 1,302 | 6 | 24,382 | 299 | 24,462 | 5.0 | 0.3 | 94.7 |
| >90 min | 1,302 | 6 | 6,676 | 44 | 6,756 | 18.1 | 1.2 | 80.7 |
| >120 min | 1,302 | 6 | 3,832 | 16 | 3,912 | 31.3 | 2.0 | 66.7 |
| >150 min | 1,302 | 6 | 2,926 | 9 | 3,006 | 40.8 | 2.7 | 56.7 |
| >180 min | 1,302 | 6 | 2,401 | 6 | 2,481 | 49.4 | 3.2 | 47.5 |

min, minutes; n, number; NWT, non-wear time
[a]algorithms were applied only to accelerometry data to check for periods based on consecutive acceleration zero-counts >60, >90, >120, >150, and >180 minutes, respectively; from diary, all NWT regardless of a minimal length is shown, thus, NWT is constant across all NWT algorithms
[b]potential total NWT includes NWT which is NWT detected by either *diary*, *accelerometry*, or *both*
[c]analyses were conducted from the first to the last time point of assessment recorded in the diary
[d]waking and sleeping phases were derived from participants' diary entries

[28]In the framework of this thesis, a modified version of this table has already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

**Table 17**: Overlap: non-wear time algorithms >60 to >180 minutes using 24h-accelerometry versus any diary-based non-wear time, KORA FF4 study[29]

| NWT algorithm[a] | diary | | accelerometry | | diary or accelerometry | | | |
|---|---|---|---|---|---|---|---|---|
| | total NWT | NWT periods | total NWT | NWT periods | potential total NWT[b] | NWT diary and accelerometry | NWT diary only | NWT accelerometry only |
| | min | n | min | n | min | % | % | % |
| | ***total time of assessment***[c] | | | | | | | |
| >60 min | 142,640 | 3,089 | 189,666 | 1,535 | 270,588 | 22.8 | 29.9 | 47.3 |
| >90 min | 142,640 | 3,089 | 110,560 | 420 | 199,817 | 26.7 | 44.7 | 28.6 |
| >120 min | 142,640 | 3,089 | 95,794 | 284 | 190,185 | 25.4 | 49.6 | 25.0 |
| >150 min | 142,640 | 3,089 | 87,262 | 223 | 186,905 | 23.0 | 53.3 | 23.7 |
| >180 min | 142,640 | 3,089 | 81,623 | 192 | 184,194 | 21.8 | 55.7 | 22.6 |
| | ***waking***[d] | | | | | | | |
| >60 min | 112,233 | 2,811 | 82,091 | 531 | 152,628 | 27.3 | 46.2 | 26.5 |
| >90 min | 112,233 | 2,811 | 61,874 | 257 | 139,417 | 24.9 | 55.6 | 19.5 |
| >120 min | 112,233 | 2,811 | 52,835 | 178 | 135,672 | 21.7 | 61.1 | 17.3 |
| >150 min | 112,233 | 2,811 | 46,430 | 132 | 133,561 | 18.8 | 65.2 | 16.0 |
| >180 min | 112,233 | 2,811 | 42,257 | 108 | 131,995 | 17.0 | 68.0 | 15.0 |
| | ***sleeping***[d] | | | | | | | |
| >60 min | 9,488 | 25 | 86,690 | 868 | 88,166 | 9.1 | 1.7 | 89.2 |
| >90 min | 9,488 | 25 | 35,146 | 130 | 36,752 | 21.4 | 4.4 | 74.2 |
| >120 min | 9,488 | 25 | 30,204 | 81 | 31,810 | 24.8 | 5.0 | 70.2 |
| >150 min | 9,488 | 25 | 29,411 | 75 | 31,017 | 25.4 | 5.2 | 69.4 |
| >180 min | 9,488 | 25 | 27,923 | 66 | 29,691 | 26.0 | 6.0 | 68.0 |

min, minutes; n, number; NWT, non-wear time
[a]algorithms were applied only to accelerometry data to check for periods based on consecutive acceleration zero-counts >60, >90, >120, >150, and >180 minutes, respectively; from diary, all NWT regardless of a minimal length is shown, thus, NWT is constant across all NWT algorithms
[b]potential total NWT includes NWT which is NWT detected by either *diary*, *accelerometry*, or *both*
[c]analyses were conducted from the first to the last time point of assessment recorded in the diary
[d]waking and sleeping phases were derived from participants' diary entries

[29]In the framework of this thesis, a modified version of this table has already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. *Sci Rep. 7, 2227* (2017).

Over the total time of assessment, applying the most sensitive and specific 180-min (ActivE) and 120-min NWT algorithm (KORA) (**Table 13**) to accelerometry data resulted in an overlap with length of any diary-based NWT of 18.6% and 25.4%, respectively (**Table 16**, **Table 17**). In contrast, NWT reported in *diary only* made up 73.7% in ActivE and 49.6% in KORA.

Focusing on waking and applying the algorithms with high sensitivity and specificity in ActivE (90-min algorithm) and KORA (120-min algorithm) to accelerometry only (**Table 13**), overlap with any diary-based NWT was 15.8% and 21.7%, respectively (**Table 16**, **Table 17**). However, NWT false negatively detected in *diary only* was high, being 70.5% in ActivE and 61.1% in KORA.

During sleeping, the overlap in NWT minutes increased and false positive NWT detection in *accelerometry only* decreased with length of the algorithm applied to accelerometry. Using the algorithms with high sensitivity and specificity, i.e., the 90-min to 180-min algorithms, resulted in a maximal overlap of 49.4% and 26.0% and a minimal false positive NWT detection of 47.5% and 68.0%, in ActivE and KORA, respectively, for the 180-min algorithm. Since mainly long (i.e., >180 minutes) NWT periods were reported during sleeping, results for overlap and deviation in NWT minutes detected based on accelerometry and diary were very similar, when comparing accelerometry-based NWT >60 to >180 minutes with diary-based NWT >60 to >180 minutes (**Table 14**, **Table 15**) or with any diary-based NWT (**Table 16**, **Table 17**).

## 4.3 Potential determinants of physical activity using multiday 24h-accelerometry under free-living conditions (research question 3)

### 4.3.1 Study Population

There were no significant differences in basic characteristics between participants providing accelerometry data that were included or excluded from the following analyses on potential determinants of 24h-accelerometry-based PA, with exception of the net household income that, at borderline, significantly differed between both groups (**Supplementary Table 8**); more included than excluded participants reported a net household income belonging to the highest income group.

In total, 262 participants (men, 45.8%) from 16 of the 18 nationwide study centers of pretest 2 of the German National Cohort were included. Regarding the total study population, the majority (26.4%) of participants came from Berlin and its catchment area (**Table 18**); in contrast, the study center Saarbrücken provided the least participants (1.5%).

**Table 18**: Participants per study center providing valid 24-accelerometry data, pretest 2 German National Cohort, 2012

| | total | | men | | women | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| all study centers | 262 | 100.0 | 120 | 100.0 | 142 | 100.0 |
| Augsburg | 21 | 8.0 | 7 | 5.8 | 14 | 9.9 |
| Berlin-Center | 23 | 8.8 | 9 | 7.5 | 14 | 9.9 |
| Berlin-North | 13 | 5.0 | 4 | 3.3 | 9 | 6.3 |
| Berlin-South/Brandenburg | 33 | 12.6 | 12 | 10.0 | 21 | 14.8 |
| Hannover | 15 | 5.7 | 9 | 7.5 | 6 | 4.2 |
| Bremen | 22 | 8.4 | 8 | 6.7 | 14 | 9.9 |
| Düsseldorf | 13 | 5.0 | 7 | 5.8 | 6 | 4.2 |
| Freiburg | 7 | 2.7 | 3 | 2.5 | 4 | 2.8 |
| Halle | 19 | 7.3 | 12 | 10.0 | 7 | 4.9 |
| Hamburg | 13 | 5.0 | 10 | 8.3 | 3 | 2.1 |
| Heidelberg | 23 | 8.8 | 8 | 6.7 | 15 | 10.6 |
| Kiel | 10 | 3.8 | 6 | 5.0 | 4 | 2.8 |
| Münster | 6 | 2.3 | 3 | 2.5 | 3 | 2.1 |
| Neubrandenburg | 26 | 9.9 | 15 | 12.5 | 11 | 7.7 |
| Regensburg | 14 | 5.3 | 5 | 4.2 | 9 | 6.3 |
| Saarbrücken | 4 | 1.5 | 2 | 1.7 | 2 | 1.4 |

n, number

Characteristics of the study population are summarized in **Table 19**. Most participants reported to have never smoked (41.2%), to moderately consume alcoholic beverages (2 to 4 times a month, 30.2%), to not have a university entrance qualification (51.9%), and to be full time employed (54.6%). A net household income of 2,500 to 3,999 € per month was most frequently reported (37.0%) and most participants reported to be married (62.6%). Haven been diagnosed with manifest diabetes mellitus reported 6.9% of all participants, while 28.2% reported to have ever been diagnosed with dyslipidemia.

As compared to the aimed age distribution of pretest 2 [295], the younger age groups of 20 to 29 and 30 to 39 years were underrepresented (4.2% and 8.8%, respectively, compared to the predefined proportion of 10%), while the age group of 40 to 49 years was overrepresented (32.1% compared to the predefined proportion of 26.7%). The age groups of 50 to 59 years and 60 to 69 years both made up 27.5% of the study population and were, thus, close to the predefined proportion of 26.7%.

**Table 19**: Characteristics of the study population, pretest German National Cohort, 2012

| | **total** (N=262) | | **men** (n=120) | | **women** (n=142) | | **test for sex differences**[a] |
|---|---|---|---|---|---|---|---|
| | **n** | **%** | **n** | **%** | **n** | **%** | **p** |
| smoking status | | | | | | | 0.35 |
| never-smokers | 108 | 41.2 | 45 | 37.5 | 63 | 44.4 | |
| smokers | 59 | 22.5 | 26 | 21.7 | 33 | 23.2 | |
| former smokers | 95 | 36.3 | 49 | 40.8 | 46 | 32.4 | |
| alcohol consumption | | | | | | | 0.0009 |
| never | 8 | 3.1 | 3 | 2.5 | 5 | 3.5 | |
| max. 1x/month | 59 | 22.5 | 17 | 14.2 | 42 | 29.6 | |
| 2 - 4x/month | 79 | 30.2 | 32 | 26.7 | 47 | 33.1 | |
| 2 - 3x/week | 66 | 25.2 | 34 | 28.3 | 32 | 22.5 | |
| ≥4x/week | 50 | 19.1 | 34 | 28.3 | 16 | 11.3 | |
| school education | | | | | | | 0.02 |
| university entrance qualification | 126 | 48.1 | 67 | 55.8 | 59 | 41.5 | |
| no university entrance qualification | 136 | 51.9 | 53 | 44.2 | 83 | 58.5 | |
| employment status | | | | | | | <.0001 |
| full time | 143 | 54.6 | 87 | 72.5 | 56 | 39.4 | |
| part time | 65 | 24.8 | 12 | 10.0 | 53 | 37.3 | |
| not employed | 54 | 20.6 | 21 | 17.5 | 33 | 23.2 | |
| net household income per month | | | | | | | 0.25 |
| <2,500 € | 89 | 34.0 | 41 | 34.2 | 48 | 33.8 | |
| 2,500-3,999 € | 97 | 37.0 | 42 | 35.0 | 55 | 38.7 | |
| ≥4,000 € | 61 | 23.3 | 33 | 27.5 | 28 | 19.7 | |
| n. a. | 15 | 5.7 | 4 | 3.3 | 11 | 7.7 | |
| marital status | | | | | | | 0.21 |
| not married | 98 | 37.4 | 40 | 33.3 | 58 | 40.8 | |
| married | 164 | 62.6 | 80 | 66.7 | 84 | 59.2 | |
| diabetes mellitus[b] | 18 | 6.9 | 11 | 9.2 | 7 | 4.9 | 0.21 |
| dyslipidemia[b] | 74 | 28.2 | 41 | 34.2 | 33 | 23.2 | 0.08 |
| | **mean** | **SD** | **mean** | **SD** | **mean** | **SD** | |
| age, years | 51.0 | 10.9 | 50.7 | 11.3 | 51.3 | 10.6 | 0.65 |
| height, cm | 170.9 | 9.4 | 178.2 | 6.8 | 164.8 | 6.5 | <.0001 |
| weight, kg | 76.8 | 14.4 | 86.4 | 12.5 | 68.7 | 10.4 | <.0001 |
| BMI, kg/m² | 26.2 | 4.0 | 27.3 | 4.0 | 25.4 | 3.8 | <.0001 |
| waist circumference, cm | 90.1 | 13.0 | 98.1 | 12.0 | 83.4 | 9.6 | <.0001 |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; n, number; n. a., not available; SD, standard deviation
[a]continuous variables, normally distributed: t-test; discrete variables: Chi-Square test/Fisher's exact test
[b]data for 249 out of the total 262 participants available

The study population, on average, was 51.0 years old (SD, 10.9 years) and, as measured by the mean BMI and waist circumference, preobese according to WHO classifications (limit value; BMI, 25 kg/m²; waist circumference, 94.0 and 80.0 cm in men and women, respectively) (**Table 19**) [289]. Men were taller, heavier, and had a higher BMI and waist circumference than women (all p<.0001). Further, there were significant differences between sexes in the alcohol consumption (p=0.0009), the highest school education (p=0.02), and the employment status (p<.0001); men, on average, tended to consume more alcohol than women, and having a university entrance qualification as well as part time employment was more prevalent in women than in men.

Sixty participants provided valid 24h-accelerometry data for 5 days, 139 participants for 6 days, and 63 participants for 7 days. **Table 20** summarizes the 24h-accelerometry-based PA estimates averaged over an approximately 1-week period and over all participants. Overall activity of participants was 431.3 cpm (95% CI; 416.3, 446.9), which is comparable to the results found in ActivE (see section 4.1.1). A full day encompasses 1,440 minutes and participants spent, on average, most time in inactivity (1,010.2 min/d; 999.4, 1,021.0), while 416.9 min/d (406.3, 427.7) were spent in activity. Men spent more time in inactivity than women, while, consequently, for time in activity the opposite was true (difference between sexes, p=0.01 for time in inactivity and time in activity). Average time in low, moderate, and VV activity was 327.0 min/d (318.6, 335.6), 79.4 min/d (75.6, 83.4), and 2.8 min/d (2.4, 3.2), respectively, or, compared to the time in overall activity (min/d), made up 78.7% (78.0, 79.5), 18.9% (18.2, 19.6), and 0.7% (0.6, 0.8), respectively. There were only slight, non-significant differences between men and women in the time in activity intensities with exception of the absolute time in low activity (min/d) that was longer in women than in men (p=0.001). Regarding time in 10-minutes bouts in moderate or VV activity that was used to determine, whether participants met the WHO PA recommendation, or not, on average (median), participants spent 6.2 min/d (IQR, 1.8. 14.3) in 10-minutes bouts in moderate activity, with 0.4 (0.2, 1.0) median bouts per day and a median length of 13.1 min/d (11.4, 15.3) per bout. Few bouts in VV activity occurred on average, but length of bouts in VV activity tended to be longer than for moderate activity, being 20.5 min/d (14.2, 30.3).

More than two thirds of all participants (67.9%) did not meet the WHO PA recommendation [7]. Of those meeting the recommendation (n=84, 32.1%), 58 participants met it either based on the time in 10-minutes bouts of moderate or VV activity per week, or based on both, while 28 participants were sufficiently active based on a metabolic equivalent (**Equation 3**) (**Supplementary Figure 3**) [1, 7]. Women tended to more likely meet the WHO PA recommendation than men (p=0.05).

**Table 20**: 24h-accelerometry-based physical activity parameter of the study population

| **PA parameter** | **total** (N=262) | | **men** (n=120) | | **women** (n=142) | | **test for sex differences**[a] |
|---|---|---|---|---|---|---|---|
| | **GM** | **95% CI** | **GM** | **95% CI** | **GM** | **95% CI** | **p** |
| overall activity, cpm | 431.3 | (416.3, 446.9) | 422.2 | (400.6, 444.9) | 439.2 | (418.5, 460.8) | 0.30 |
| time in inactivity, min/d | 1,010.2 | (999.4, 1,021.0) | 1024.9 | (1,008.9, 1,041.1) | 997.9 | (983.6, 1,012.4) | **0.01** |
| **time in activity** | | | | | | | |
| time in overall activity, min/d | 416.9 | (406.3, 427.7) | 402.2 | (387.4, 417.7) | 429.6 | (415.0, 444.8) | **0.01** |
| *absolute proportions* | | | | | | | |
| time in low activity, min/d | 327.0 | (318.6, 335.6) | 312.5 | (300.9, 324.5) | 339.8 | (328.2, 351.8) | **0.001** |
| time in moderate activity, min/d | 79.4 | (75.6, 83.4) | 79.5 | (73.9, 85.4) | 79.3 | (74.2, 84.8) | 0.99 |
| time in VV activity, min/d | 2.8 | (2.4, 3.2) | 3.0 | (2.4, 3.8) | 2.5 | (2.1, 3.1) | 0.20 |
| *relative proportions* | | | | | | | |
| time in low activity, % of time in overall activity | 78.7 | (78.0, 79.5) | 78.0 | (76.9, 79.1) | 79.3 | (78.3, 80.4) | 0.07 |
| time in moderate activity, % of time in overall activity | 18.9 | (18.2, 19.6) | 19.5 | (18.4, 20.6) | 18.3 | (17.4, 19.2) | 0.11 |
| time in VV activity, % of time in overall activity | 0.7 | (0.6, 0.8) | 0.7 | (0.6, 0.9) | 0.6 | (0.5, 0.7) | 0.08 |
| **10-min bouts of activity** | **median** | **IQR** | **median** | **IQR** | **median** | **IQR** | |
| time in bouts in moderate activity, min/d | 6.2 | (1.8. 14.3) | 5.0 | (1.8, 11.2) | 7.4 | (1.8, 17.0) | 0.18 |
| number of bouts in moderate activity, n/d | 0.4 | (0.2, 1.0) | 0.4 | (0.2, 0.9) | 0.5 | (0.2, 1.2) | 0.25 |
| duration of bouts in moderate activity, min/d | 13.1 | (11.4, 15.3) | 12.8 | (11.2, 14.9) | 13.8 | (11.8, 15.5) | 0.05 |
| time in bouts in VV activity, min/d | 0.0 | (0.0, 0.0) | 0.0 | (0.0, 0.0) | 0.0 | (0.0, 0.0) | 0.72 |
| number of bouts in VV activity, n/d | 0.0 | (0.0, 0.0) | 0.0 | (0.0, 0.0) | 0.0 | (0.0, 0.0) | 0.78 |
| duration of bouts in VV activity, min/d | 20.5 | (14.2, 30.3) | 26.0 | (12.1, 33.8) | 19.8 | (15.3, 21.9) | 0.66 |
| **meeting WHO physical activity recommendation**[b] | **n** | **%** | **n** | **%** | **n** | **%** | |
| yes | 84 | 32.1 | 31 | 25.8 | 53 | 37.3 | **0.05** |
| no | 178 | 67.9 | 89 | 74.2 | 89 | 62.7 | |

cpm, counts per minute; GM, geometric mean; IQR, interquartile range; min/d, minutes per day; n, number; VV, vigorous to very vigorous; WHO, World Health Organization; 95% CI, 95% confidence interval

[a]continuous variables, normally distributed: t-test; continuous variables, not normally distributed (absolute and relative proportion in vigorous to very vigorous activity, bout parameters): Mann-Whitney U test; discrete variables: Chi-Square test

[b]meeting World Health Organization physical activity recommendation: ≥150 minutes of moderate activity/week, or ≥75 minutes of vigorous activity/week, or an equivalent of these [7]

## 4.3.2 Potential determinants of time spent in overall activity and in activity intensities

### 4.3.2.1 Univariable linear regression analyses

**Table 21** and **Table 22** summarize the results of the univariable linear regression analyses for the total study population for the four PA outcomes. Regarding time in overall activity, in unadjusted models including only the respective potential determinant, men were 27.3 min/d (95% CI; 6.2, 48.3; p=0.01) less active than women, and persons having a university entrance qualification were 42.8 min/d (22.3, 63.3; p<.0001) less overall active than persons without this qualification (**Table 21**). In contrast, persons who reported to never drink alcohol were found to be 68.7 min/d (1.3, 136.1; p=0.05; *p*-valued not rounded: 0.046) more overall active than participants drinking alcohol maximal once a month. Persons reporting to be part time employed spent 28.7 min/d (3.1, 54.2; p=0.03) more in overall activity and employment status was also found to be generally associated with time in overall activity (p=0.003). Regarding the proportion of time of overall activity that was spent in different activity intensities, per 5-years higher age, participants spent 0.5% (0.2, 0.8; p=0.004) more active time per day in low activity, but 0.2% (0.1, 0.3; p<.0001) less active time in VV activity (**Table 22**). Further, smoking status was associated with active time spent in low (p<.0001), moderate (p=0.007), and VV activity (p=0.02), with current smokers spending 3.4% (1.5, 5.4; p=0.0006) more active time per day in low activity, but 2.6% (0.8, 4.4; p=0.005) and 0.9% (0.3, 1.5; p=0.006) less active time in moderate and VV activity, respectively, compared to never-smokers. Having a university entrance qualification (in contrast to not having one) was associated with 0.6% (0.1, 1.0; p=0.02) more active time per day spent in VV activity. Additionally, employment status was associated with active time spent in low (p=0.04) and in VV activity (p=0.0002), and not being employed resulted in 2.5% (0.6, 4.5; p=0.01) more active time per day spent in low activity, but in 1.0% (0.5, 1.4; p<.0001) less active time spent in VV activity as compared to full time employed persons. Finally, persons, who reported to have ever been diagnosed with dyslipidemia spent 0.6% (0.1, 1.0; p=0.02) less active time per day in VV activity than persons without this diagnosis.

**Table 21**: Univariable association of potential physical activity determinants and time in overall activity[1], total (N=262)

| **potential determinant** | **time in overall activity**, min/d | | | |
|---|---|---|---|---|
| | **β** | **95% CI** | **p[a]** | |
| sex (men vs. women) | -27.3 | (-48.3, -6.2) | **0.01** | |
| age, years (5 years) | 1.1 | (-3.6, 5.7) | 0.65 | |
| BMI, kg/m² | -2.5 | (-5.5, 0.5) | 0.10 | |
| waist circumference, cm[b] | -0.1 | (-2.8, 0.0) | 0.06 | |
| smoking status | | | | |
| never-smokers | 0 | (reference) | | 0.14 |
| smokers | 18.0 | (-13.3, 49.2) | 0.26 | |
| former smokers | -13.3 | (-35.3, 8.7) | 0.23 | |
| alcohol consumption | | | | |
| never | 68.7 | (1.3, 136.1) | **0.05** | 0.37 |
| max. 1x/month | 0 | (reference) | | |
| 2 - 4x/month | 1.9 | (-25.9, 29.6) | 0.90 | |
| 2 - 3x/week | 8.4 | (-22.0, 38.9) | 0.59 | |
| ≥4x/week | 8.4 | (-24.0, 40.9) | 0.61 | |
| university entrance qualification (yes vs. no) | -42.8 | (-63.3, -22.3) | **<.0001** | |
| employment status | | | | |
| full time | 0 | (reference) | | **0.003** |
| part time | 28.7 | (3.1, 54.2) | **0.03** | |
| not employed | -22.9 | (-47.9, 2.1) | 0.07 | |
| net household income per month | | | | |
| <2,500 € | 0 | (reference) | | 0.68 |
| 2,500-3,999 € | 3.1 | (-21.5, 27.6) | 0.81 | |
| ≥4,000 € | -5.4 | (-35.2, 24.4) | 0.72 | |
| n. a. | 23.9 | (-21.1, 68.9) | 0.30 | |
| marital status (married, no vs. yes) | -14.5 | (-37.3, 8.2) | 0.21 | |
| diabetes mellitus (yes vs. no)[c] | -1.3 | (-50.7, 48.2) | 0.96 | |
| dyslipidemia (yes vs. no)[c] | -19.5 | (-43.2, 4.2) | 0.11 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; min/d, minutes per day; n. a., not available; vs., versus; 95% CI, 95% confidence interval
[1]Results were derived from a univariable linear regression analysis with the potential determinants included as independent and time in overall activity included as dependent variable. β-coefficients can be interpreted as change in minutes in overall activity per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, men spent 27.3 minutes per day less time in overall activity compared to women.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
[c]data for 249 out of the total 262 participants available
**bold**: *p*-value <0.05 (bold p=0.05 for never drinking alcohol: *p*-valued not rounded=0.046)

**Table 22**: Univariable association of potential physical activity determinants and proportion of active time in different activity intensities[1], total (N=262)

| **potential determinant** | **time in low activity**, % of time in overall activity | | | | **time in moderate activity**, % of time in overall activity | | | | **time in VV activity**, % of time in overall activity | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **β** | **95% CI** | **p[a]** | | **β** | **95% CI** | **p[a]** | | **β** | **95% CI** | **p[a]** | |
| sex (men vs. women) | -1.4 | (-2.8, 0.1) | 0.07 | | 1.1 | (-0.2, 2.4) | 0.11 | | 0.3 | (-0.2, 0.8) | 0.24 | |
| age, years (5 years) | 0.5 | (0.2, 0.8) | **0.004** | | -0.3 | (-0.6, 0.0) | 0.07 | | -0.2 | (-0.3, -0.1) | **<.0001** | |
| BMI, kg/m² | -0.1 | (-0.3, 0.1) | 0.25 | | 0.2 | (0.0, 0.4) | 0.08 | | -0.1 | (-0.1, 0.0) | 0.05 | |
| waist circumference, cm[b] | 0.0 | (-0.1, 0.1) | 0.40 | | 0.0 | (-0.1, 0.0) | 0.38 | | 0.0 | (0.0, 0.0) | 0.89 | |
| smoking status | | | | | | | | | | | | |
| never-smokers | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| smokers | 3.4 | (1.5, 5.4) | **0.0006** | **<.0001** | -2.6 | (-4.4, -0.8) | **0.005** | **0.007** | -0.9 | (-1.5, -0.3) | **0.006** | **0.02** |
| former smokers | 0.3 | (-1.3, 1.9) | 0.72 | | 0.2 | (-1.3, 1.6) | 0.84 | | -0.4 | (-1.0, 0.1) | 0.12 | |
| alcohol consumption | | | | | | | | | | | | |
| never | -4.3 | (-10.0, 1.3) | 0.13 | | 4.3 | (-1.1, 9.8) | 0.12 | | 0.0 | (-1.2, 1.2) | 0.98 | |
| max. 1x/month | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| 2 - 4x/month | 0.7 | (-1.5, 2.9) | 0.54 | 0.39 | -0.5 | (-2.4, 1.4) | 0.59 | 0.26 | -0.2 | (-1.0, 0.6) | 0.65 | 0.60 |
| 2 - 3x/week | 0.4 | (-1.9, 2.6) | 0.75 | | -0.4 | (-2.4, 1.6) | 0.69 | | 0.0 | (-0.8, 0.9) | 0.91 | |
| ≥4x/week | -0.4 | (-2.8, 2.0) | 0.73 | | 0.8 | (-1.3, 3.0) | 0.44 | | -0.4 | (-1.2, 0.4) | 0.29 | |
| university entrance qualification (yes vs. no) | -1.3 | (-2.8, 0.2) | 0.08 | | 0.8 | (-0.6, 2.1) | 0.26 | | 0.6 | (0.1, 1.0) | **0.02** | |
| employment status | | | | | | | | | | | | |
| full time | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| part time | 0.7 | (-1.0, 2.4) | 0.42 | **0.04** | -0.2 | (-1.8, 1.4) | 0.78 | 0.23 | -0.5 | (-1.0, 0.1) | 0.08 | **0.0002** |
| not employed | 2.5 | (0.6, 4.5) | **0.01** | | -1.6 | (-3.4, 0.2) | 0.09 | | -1.0 | (-1.4, -0.5) | **<.0001** | |
| net household income per month | | | | | | | | | | | | |
| <2,500 € | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| 2,500-3,999 € | -0.5 | (-2.3, 1.3) | 0.59 | 0.29 | 0.1 | (-1.6, 1.7) | 0.95 | 0.32 | 0.4 | (0.0, 0.9) | 0.06 | 0.09 |
| ≥4000 € | -0.2 | (-2.1, 1.7) | 0.84 | | -0.4 | (-2.0, 1.2) | 0.60 | | 0.6 | (-0.1, 1.4) | 0.11 | |
| n. a. | -3.3 | (-6.8, 0.1) | 0.06 | | 2.6 | (-0.6, 5.7) | 0.11 | | 0.8 | (-0.2, 1.7) | 0.13 | |
| marital status (married, no vs. yes) | 0.1 | (-1.4, 1.6) | 0.92 | | 0.0 | (-1.3, 1.4) | 0.99 | | -0.1 | (-0.6, 0.4) | 0.73 | |
| diabetes mellitus (yes vs. no)[c] | -0.3 | (-3.0, 2.4) | 0.82 | | 0.5 | (-1.9, 2.9) | 0.67 | | -0.2 | (-0.8, 0.4) | 0.50 | |
| dyslipidemia (yes vs. no)[c] | 1.3 | (-0.4, 3.0) | 0.14 | | -0.7 | (-2.3, 0.8) | 0.35 | | -0.6 | (-1.0, -0.1) | **0.02** | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; n. a., not available; vs., versus; VV, vigorous to very vigorous; 95% CI, 95% confidence interval
[1]Results were derived from three different univariable linear regression analyses with the potential determinants included as independent and proportion of active time spent in the three different activity intensities included as single dependent variable. β-coefficients can be interpreted as relative change (%) in the proportion of time in overall activity spent in the different activity intensities per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, with each 5-years higher age, persons spent 0.5% more active time in low activity.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
[c]data for 249 out of the total 262 participants available
**bold**: *p*-value <0.05

#### 4.3.2.2 Multivariable linear regression analyses

Then, multivariable linear regression analyses were performed, assessing a model including sex, age, BMI, waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, and study center (model 1, **Table 23** and **Table 24**), as well as a model further including diabetes mellitus and dyslipidemia (model 2, **Table 25** and **Table 26**). Results of both models were quite similar. As both is possible, a pre-existing diagnosis of diabetes mellitus or dyslipidemia to influence PA (i.e., the direction of association that was aimed to investigate) as well as PA to influence the likelihood of the diagnoses (reverse causality), model 2 including diabetes mellitus and dyslipidemia was evaluated. Accordingly, regarding time in overall activity, with each 1-unit higher BMI (i.e., per 1 kg/m²), persons were 3.9 min/d (0.6, 7.3; p=0.02) less active (**Table 25**). Furthermore, persons with a university entrance qualification were 35.9 min/d (13.0, 58.8; p=0.002) less overall active than persons not having this degree. Similarly, employment status was associated with time in overall activity (p<.0001) and not being employed versus being full time employed was associated with 66.2 min/d (34.7, 97.7; p<.0001) less time in overall activity. For the proportion of time in overall activity spent in different activity intensities, men compared to women spent 2.5% (0.1, 5.0; p=0.04) less active time in low, but 2.2% (0.1, 4.4; p=0.04) more active time in moderate activity (**Table 26**). Per 5-years higher age, participants spent 0.6% (0.2, 1.0; p=0.007) more active time in low activity at the expense of VV activity (-0.2% (-0.4, -0.1; p=0.007)); active time spent in moderate activity also tended to increase, but this association was at borderline not statistically significant (-0.4% (-0.7, 0.0; p=0.05)). Similarly, waist circumference (residually adjusted for BMI) was associated with 0.2% (0.0, 0.3; p=0.03) more active time spent in low at the expense of moderate activity (-0.2% (-0.3, 0.0; p=0.02)). Further, smoking status was associated with active time spent in low (p=0.0007), moderate (p=0.004), and VV activity (p=0.003), with current smokers spending 3.2% (1.4, 5.1; p=0.0006) more active time in low activity, but 2.3% (0.6, 4.0; p=0.008) and 1.0% (0.4, 1.5; p=0.0008) less active time in moderate and VV activity, respectively, compared to never-smokers. Former smokers spent 0.6% (0.0, 1.1; p=0.04) less active time in VV activity compared to current smokers. Alcohol consumption was associated with the proportion of active time spent in low activity (p=0.03) and persons reporting to never drink alcohol spent 4.3% (0.1, 8.5, p=0.04) less active time in low activity compared to persons drinking alcohol maximal once a month; active time spent in moderate activity tended to be increased (3.9%, (-0.3, 8.0; p=0.07)). Finally, persons not reporting their net household income spent 4.2% (0.7, 7.8; p=0.02) less active time in low, but 3.5% (0.0, 7.1; p=0.05; *p*-valued not rounded=0.049) more active time in moderate activity compared to persons reporting an income of <2,500 €. *P*-values regarding the study center were statistically significant for proportion of active time spent in low (p=0.03), moderate (p=0.01), and VV activity (p=0.007).

**Table 23**: Multivariable association of potential physical activity determinants and time in overall activity, model 1[1], total (N=262)

| **potential determinant** | **time in overall activity**, min/d | | | |
|---|---|---|---|---|
| | **β** | **95% CI** | **p[a]** | |
| sex (men vs. women) | -10.7 | (-37.8, 16.4) | 0.44 | |
| age, years (5 years) | 6.3 | (0.0, 12.5) | **0.05** | |
| BMI, kg/m² | -3.8 | (-7.4, -0.3) | **0.03** | |
| waist circumference, cm[b] | -1.4 | (-3.2, 0.4) | 0.12 | |
| smoking status | | | | |
| never-smokers | 0 | (reference) | | |
| smokers | 20.5 | (-6.3, 47.4) | 0.13 | 0.16 |
| former smokers | -6.0 | (-26.7, 14.6) | 0.56 | |
| alcohol consumption | | | | |
| never | 51.2 | (-6.9, 109.3) | 0.08 | |
| max. 1x/month | 0 | (reference) | | |
| 2 - 4x/month | 1.7 | (-25.9, 29.3) | 0.91 | 0.15 |
| 2 - 3x/week | 14.6 | (-14.6, 43.8) | 0.33 | |
| ≥4x/week | 29.1 | (-2.2, 60.5) | **0.07** | |
| university entrance qualification (yes vs. no) | -39.2 | (-61.4, -17.1) | **0.0006** | |
| employment status | | | | |
| full time | 0 | (reference) | | |
| part time | 3.8 | (-21.0, 28.6) | 0.76 | **<.0001** |
| not employed | -65.9 | (-96.1, -35.6) | **<.0001** | |
| net household income per month | | | | |
| <2,500 € | 0 | (reference) | | |
| 2,500-3,999 € | -8.0 | (-30.5, 14.5) | 0.48 | 0.47 |
| ≥4,000 € | -9.5 | (-39.1, 20.0) | 0.53 | |
| n. a. | 18.6 | (-16.8, 53.9) | 0.30 | |
| marital status (married, no vs. yes) | -22.3 | (-46.6, 1.9) | 0.07 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel

BMI, body mass index; min/d, minutes per day; n. a., not available; vs., versus; 95% CI, 95% confidence interval

[1]Results were derived from a multivariable linear regression analysis with the potential determinants included as independent and time in overall activity included as dependent variable. β-coefficients can be interpreted as change in minutes in overall activity per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, with each 1-unit higher body mass index (BMI), persons spent 3.8 minutes per day less time in overall activity. Model includes sex, age, BMI, waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, and study center.

[a]*p*-values presented are raw values

[b]residually adjusted for body mass index

**bold**: *p*-value <0.05 (bold p=0.05 for age: *p*-valued not rounded=0.0498)

**Table 24**: Multivariable association of potential physical activity determinants and proportion of active time in different activity intensities, model 1[1], total (N=262)

| **potential determinant** | **time in low activity**, % of time in overall activity | | | | **time in moderate activity**, % of time in overall activity | | | | **time in VV activity**, % of time in overall activity | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **β** | **95% CI** | **p[a]** | | **β** | **95% CI** | **p[a]** | | **β** | **95% CI** | **p[a]** | |
| sex (men vs. women) | -2.4 | (-4.7, -0.1) | **0.04** | | 2.1 | (0.0, 4.1) | **0.04** | | 0.3 | (-0.5, 1.2) | 0.44 | |
| age, years (5 years) | 0.6 | (0.2, 1.0) | **0.002** | | -0.4 | (-0.7, -0.1) | **0.02** | | -0.2 | (-0.3, -0.1) | **0.005** | |
| BMI, kg/m² | -0.1 | (-0.4, 0.1) | 0.27 | | 0.2 | (0.0, 0.4) | 0.11 | | 0.0 | (-0.1, 0.0) | 0.18 | |
| waist circumference, cm[b] | 0.2 | (0.0, 0.3) | **0.02** | | -0.2 | (-0.3, 0.0) | **0.01** | | 0.0 | (-0.1, 0.0) | 0.53 | |
| smoking status | | | | | | | | | | | | |
| never-smokers | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| smokers | 3.3 | (1.5, 5.1) | **0.0004** | **0.0008** | -2.4 | (-4.1, -0.8) | **0.005** | **0.004** | -0.9 | (-1.4, -0.3) | **0.002** | **0.007** |
| former smokers | 0.2 | (-1.3, 1.7) | 0.79 | | 0.3 | (-1.0, 1.7) | 0.63 | | -0.5 | (-1.0, 0.0) | **0.04** | |
| alcohol consumption | | | | | | | | | | | | |
| never | -5.2 | (-9.3, -1.2) | **0.01** | | 5.0 | (0.9, 9.1) | **0.02** | | 0.2 | (-0.8, 1.3) | 0.65 | |
| max. 1x/month | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| 2 - 4x/month | 1.1 | (-1.0, 3.3) | 0.30 | **0.01** | -0.8 | (-2.6, 1.0) | 0.40 | **0.02** | -0.4 | (-1.1, 0.4) | 0.36 | 0.69 |
| 2 - 3x/week | 0.3 | (-1.8, 2.4) | 0.81 | | -0.1 | (-1.9, 1.7) | 0.93 | | -0.2 | (-1.0, 0.7) | 0.66 | |
| ≥4x/week | -0.9 | (-3.4, 1.5) | 0.44 | | 1.2 | (-1.0, 3.4) | 0.27 | | -0.3 | (-1.1, 0.6) | 0.53 | |
| university entrance qualification (yes vs. no) | -0.9 | (-2.3, 0.6) | 0.23 | | 0.6 | (-0.7, 1.8) | 0.35 | | 0.3 | (-0.2, 0.8) | 0.26 | |
| employment status | | | | | | | | | | | | |
| full time | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| part time | 0.1 | (-1.6, 1.9) | 0.88 | 0.96 | 0.2 | (-1.4, 1.7) | 0.82 | 0.95 | -0.3 | (-0.9, 0.3) | 0.31 | 0.60 |
| not employed | 0.3 | (-1.9, 2.5) | 0.79 | | -0.1 | (-2.2, 1.9) | 0.89 | | -0.2 | (-0.8, 0.5) | 0.63 | |
| net household income per month | | | | | | | | | | | | |
| <2,500 € | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| 2,500-4,000 € | -0.1 | (-1.8, 1.6) | 0.92 | 0.09 | 0.0 | (-1.6, 1.5) | 0.96 | 0.14 | 0.1 | (-0.4, 0.6) | 0.63 | 0.72 |
| >4,000 € | 0.2 | (-1.7, 2.2) | 0.80 | | -0.4 | (-2.0, 1.3) | 0.67 | | 0.1 | (-0.6, 0.8) | 0.75 | |
| n. a. | -3.7 | (-6.7, -0.6) | **0.02** | | 3.2 | (0.1, 6.2) | **0.04** | | 0.5 | (-0.4, 1.3) | 0.27 | |
| marital status (married, no vs. yes) | 0.8 | (-1.0, 2.5) | 0.38 | | -0.3 | (-1.8, 1.2) | 0.68 | | -0.5 | (-1.0, 0.1) | 0.11 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; n. a., not available; vs., versus; VV, vigorous to very vigorous; 95% CI, 95% confidence interval

[1]Results were derived from three different multivariable linear regression analyses with the potential determinants included as independent and proportion of active time spent in the three different activity intensities included as single dependent variable. β-coefficients can be interpreted as relative change (%) in the proportion of time in overall activity spent in the different activity intensities per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, with each 5-years higher age, persons spent 0.6% more active time in low activity. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, and study center.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
**bold**: *p*-value <0.05

**Table 25**: Multivariable association of potential physical activity determinants and time in overall activity, model 2[1], total (N=249)

| potential determinant | time in overall activity, min/d | | | |
|---|---|---|---|---|
| | **β** | **95% CI** | **p[a]** | |
| sex (men vs. women) | -9.1 | (-37.9, 19.6) | 0.53 | |
| age (5 years) | 6.1 | (-0.7, 13.0) | 0.08 | |
| BMI, kg/m² | -3.9 | (-7.3, -0.6) | **0.02** | |
| waist circumference, cm[b] | -1.6 | (-3.5, 0.3) | 0.10 | |
| smoking status | | | | |
| never-smokers | 0 | (reference) | | |
| smokers | 19.8 | (-7.9, 47.5) | 0.16 | 0.13 |
| former smokers | -9.0 | (-30.3, 12.2) | 0.40 | |
| alcohol consumption | | | | |
| never | 44.9 | (-16.6, 106.3) | 0.15 | |
| max. 1x/month | 0 | (reference) | | |
| 2 - 4x/month | 4.1 | (-24.6, 32.7) | 0.78 | 0.24 |
| 2 - 3x/week | 13.3 | (-17.5, 44.1) | 0.40 | |
| ≥4x/week | 32.4 | (-1.6, 66.3) | 0.06 | |
| university entrance qualification (yes vs. no) | -35.9 | (-58.8, -13.0) | **0.002** | |
| employment status | | | | |
| full time | 0 | (reference) | | |
| part time | 3.4 | (-22.4, 29.2) | 0.57 | **<.0001** |
| not employed | -66.2 | (-97.7, -34.7) | **<.0001** | |
| net household income per month | | | | |
| <2,500 € | 0 | (reference) | | |
| 2,500-3,999 € | -6.8 | (-30.4, 16.7) | 0.57 | 0.64 |
| ≥4,000 € | -11.8 | (-42.5, 18.8) | 0.45 | |
| n. a. | 15.6 | (-24.8, 56.1) | 0.45 | |
| marital status (married, no vs. yes) | -21.3 | (-46.3, 3.6) | 0.09 | |
| diabetes mellitus (yes vs. no) | 18.3 | (-36.2, 72.7) | 0.51 | |
| dyslipidemia (yes vs. no) | 2.6 | (-22.9, 28.1) | 0.84 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; min/d, minutes per day; n. a., not available; vs., versus; 95% CI, 95% confidence interval
[1]Results were derived from a multivariable linear regression analysis with the potential determinants included as independent and time in overall activity included as dependent variable. β-coefficients can be interpreted as change in minutes in overall activity per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, with each 1-unit higher body mass index (BMI), persons spent 3.9 minutes per day less time in overall activity. Model includes sex, age, BMI, waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
**bold**: *p*-value <0.05

**Table 26**: Multivariable association of potential physical activity determinants and proportion of active time in different activity intensities, model 2[1], total (N=249)

| potential determinant | time in low activity, % of time in overall activity | | | | time in moderate activity, % of time in overall activity | | | | time in VV activity, % of time in overall activity | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | β | 95% CI | p[a] | | β | 95% CI | p[a] | | β | 95% CI | p[a] | |
| sex (men vs. women) | -2.5 | (-5.0, -0.1) | **0.04** | | 2.2 | (0.1, 4.4) | **0.04** | | 0.3 | (-0.6, 1.2) | 0.51 | |
| age (5 years) | 0.6 | (0.2, 1.0) | **0.007** | | -0.4 | (-0.7, 0.0) | 0.05 | | -0.2 | (-0.4, -0.1) | **0.007** | |
| BMI, kg/m² | -0.1 | (-0.4, 0.1) | 0.29 | | 0.2 | (0.0, 0.4) | 0.11 | | -0.1 | (-0.1, 0.0) | 0.16 | |
| waist circumference, cm[b] | 0.2 | (0.0, 0.3) | **0.03** | | -0.2 | (-0.3, 0.0) | **0.02** | | 0.0 | (-0.1, 0.0) | 0.53 | |
| smoking status | | | | | | | | | | | | |
| never-smokers | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| smokers | 3.2 | (1.4, 5.1) | **0.0006** | **0.0007** | -2.3 | (-4.0, -0.6) | **0.008** | **0.004** | -1.0 | (-1.5, -0.4) | **0.0008** | **0.003** |
| former smokers | 0.0 | (-1.6, 1.6) | 0.98 | | 0.5 | (-0.9, 2.0) | 0.46 | | -0.6 | (-1.1, 0.0) | **0.04** | |
| alcohol consumption | | | | | | | | | | | | |
| never | -4.3 | (-8.5, -0.1) | **0.04** | | 3.9 | (-0.3, 8.0) | 0.07 | | 0.5 | (-0.5, 1.5) | 0.36 | |
| max. 1x/month | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| 2 - 4x/month | 1.3 | (-1.0, 3.6) | 0.26 | **0.03** | -0.9 | (-2.8, 1.1) | 0.39 | 0.08 | -0.4 | (-1.3, 0.4) | 0.29 | 0.35 |
| 2 - 3x/week | 0.4 | (-1.9, 2.6) | 0.75 | | -0.2 | (-2.1, 1.7) | 0.86 | | -0.2 | (-1.1, 0.7) | 0.65 | |
| ≥4x/week | -0.9 | (-3.5, 1.8) | 0.51 | | 1.1 | (-1.2, 3.5) | 0.34 | | -0.3 | (-1.1, 0.6) | 0.57 | |
| university entrance qualification (yes vs. no) | -0.9 | (-2.4, 0.5) | 0.21 | | 0.7 | (-0.6, 2.0) | 0.31 | | 0.3 | (-0.2, 0.8) | 0.29 | |
| employment status | | | | | | | | | | | | |
| full time | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| part time | 0.1 | (-1.7, 1.9) | 0.85 | 0.93 | 0.2 | (-1.4, 1.8) | 0.87 | 0.93 | -0.3 | (-0.9, 0.3) | 0.90 | 0.63 |
| not employed | 0.4 | (-1.9, 2.7) | 0.72 | | -0.2 | (-2.3, 1.9) | 0.86 | | -0.2 | (-0.9, 0.4) | 0.49 | |
| net household income per month | | | | | | | | | | | | |
| <2,500 € | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| 2,500-3,999 € | -0.2 | (-2.0, 1.6) | 0.85 | 0.09 | 0.1 | (-1.5, 1.8) | 0.87 | 0.17 | 0.0 | (-0.5, 0.6) | 0.90 | 0.55 |
| ≥4,000 € | 0.3 | (-1.7, 2.3) | 0.74 | | -0.4 | (-2.1, 1.3) | 0.65 | | 0.1 | (-0.7, 0.8) | 0.86 | |
| n. a. | -4.2 | (-7.8, -0.7) | **0.02** | | 3.5 | (0.0, 7.1) | **0.05** | | 0.7 | (-0.3, 1.6) | 0.16 | |
| marital status (married, no vs. yes) | 0.9 | (-0.9, 2.8) | 0.32 | | -0.4 | (-1.9, 1.2) | 0.66 | | -0.6 | (-1.2, 0.0) | 0.06 | |
| diabetes mellitus (yes vs. no) | -0.1 | (-2.5, 2.4) | 0.95 | | 0.0 | (-2.3, 2.3) | 1.00 | | 0.1 | (-0.6, 0.7) | 0.81 | |
| dyslipidemia (yes vs. no) | -0.1 | (-1.8, 1.6) | 0.93 | | 0.0 | (-1.6, 1.5) | 0.98 | | 0.1 | (-0.3, 0.5) | 0.65 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; n. a., not available; vs., versus; VV, vigorous to very vigorous; 95% CI, 95% confidence interval
[1]Results were derived from three different multivariable linear regression analyses with the potential determinants included as independent and proportion of active time spent in the three different activity intensities included as single dependent variable. β-coefficients can be interpreted as relative change (%) in the proportion of time in overall activity spent in the different activity intensities per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, with each 5-years higher age, persons spent 0.6% more active time in low activity. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
**bold**: *p*-value <0.05 (bold p=0.05 for not reported net household income and time in moderate activity: *p*-valued not rounded=0.049)

A linear regression analyses using robust variance estimates was performed [309]. Nevertheless, as active time spent in VV activity visually showed deviations from a normal distribution and, in the linear regression analyses, the residuals also visually showed a skewed distribution (and, thus, may not fulfill assumptions underlying linear regression analyses), active time spent in VV activity was further log-transformed and the linear regression analyses for model 2 were repeated using the log-transformed PA measure (**Supplementary Table 9**). Effect sizes (i.e., change in % of active time spent in VV activity) did not substantially differed and *p*-values tended to be smaller compared to results found for the non-log-transformed data. Sex (p=0.04) and waist circumference (residually adjusted for BMI) (p=0.03) were now borderline significant, while former smoking was not associated with active time spent in VV activity anymore. Nevertheless, robustness of the linear regression analyses is considered as fulfilled.

#### 4.3.2.3 Test for interaction with sex

Then, it was investigated if there were sex differences in the association of potential determinants and PA, when assessing regression model 2 (**Table 27**). There were significant interactions with sex for the association of net household income with time in overall activity (p=0.02), waist circumference (residually adjusted for BMI) with active time spent in low (p=0.01) and moderate activity (p=0.03), as well as for smoking status with active time spent in low (p=0.02) and moderate activity (p=0.02). Thus, analyses for the multivariable linear regression model 2 were conducted separately for men and women (**Table 28**). Accordingly, having a net household income of 4,000 € or more compared to <2,500 € per month was associated with 48.8 min/d (9.6, 88.0; p=0.02) less time in overall activity in men, whereas women (non-significantly) tended to be more overall active (40.2 min/d (-8.4, 88.9); p=0.10). Regarding activity intensities, with each 1-cm higher waist circumference (residually adjusted for BMI), men spent 0.4% (0.2, 0.5; p=0.0004) more active time in low at the expense of moderate activity (-0.3% (-0.5, -0.1); p=0.002); in women, no association was present (p=0.44 and 0.71, respectively). Finally, smoking status was associated with active time spent in low (p<.0001) and moderate (p<.0001) activity in women, but not in men (p=0.71 and p=0.88, respectively). Female current smokers compared to never-smokers spent 5.5% (3.2, 7.9; p<.0001) more active time in low, but 4.4% (2.2, 6.6; p=0.0001) less active time in moderate activity (men, 0.0% (-3.1, 0.3; p=0.98) and 0.6% (-2.2, 3.4; p=0.67), respectively).

**Table 27**: P-values for the test for interaction of the multivariable association of potential physical activity determinant and time in physical activity with sex, model 2[1], total (N=249)

| potential determinant | time in **overall activity**, min/d | time in **low activity**, % of time in overall activity | time in **moderate activity**, % of time in overall activity | time in **VV activity**, % of time in overall activity |
|---|---|---|---|---|
| | **p for interaction[a]** | **p for interaction[a]** | **p for interaction[a]** | **p for interaction[a]** |
| age (years) | 0.16 | 0.59 | 0.40 | 0.45 |
| BMI (kg/m²) | 0.85 | 0.98 | 0.69 | 0.32 |
| waist circumference (cm)[b] | 0.31 | **0.01** | **0.03** | 0.08 |
| smoking status | 0.29 | **0.02** | **0.02** | 0.90 |
| alcohol consumption | 0.11 | 0.53 | 0.67 | 0.27 |
| university entrance qualification | 0.27 | 0.23 | 0.39 | 0.20 |
| employment status | 0.59 | 0.23 | 0.15 | 0.68 |
| net household income | **0.02** | 0.59 | 0.56 | 0.87 |
| marital status | 0.87 | 0.21 | 0.28 | 0.32 |
| diabetes mellitus | 0.21 | 0.49 | 0.34 | 0.75 |
| dyslipidemia | 0.63 | 0.62 | 0.65 | 0.80 |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; min/d, minutes per day; VV, vigorous to very vigorous
[1]Results were derived from four different multivariable linear regression analyses with the potential determinants and a single sex interaction term for each potential determinant included as independent and time in overall activity and proportion of active time spent in the three different activity intensities independent as single dependent variable. p-values <0.05 indicate a significant interaction with sex for the respective potential determinant and the respective physical activity measures, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
**bold**: *p*-value <0.05

**Table 28**: Sex-stratified multivariable association of potential physical activity determinants and time in overall activity or the proportion of active time in different activity intensities, model 2[1]

| **potential determinant** | **men** (n=117) | | | | **women** (n=132) | | | |
|---|---|---|---|---|---|---|---|---|
| | **time in overall activity**, min/d | | | | **time in overall activity**, min/d | | | |
| | **β** | **95% CI** | **p** | | **β** | **95% CI** | **p** | |
| net household income per month | | | | | | | | |
| <2,500 € | 0 | (reference) | | | 0 | (reference) | | |
| 2,500-3,999 € | -30.1 | (-67.2, 7.0) | 0.11 | 0.10 | 17.4 | (-13.9, 48.6) | 0.27 | 0.38 |
| ≥4,000 € | -48.8 | (-88.0, -9.6) | **0.02** | | 40.2 | (-8.4, 88.9) | 0.10 | |
| n. a. | -20.9 | (-74.7, 32.9) | 0.44 | | 33.5 | (-25.0, 91.9) | 0.26 | |
| | **time in low activity**, % of time in overall activity | | | | **time in low activity**, % of time in overall activity | | | |
| | **β** | **95% CI** | **p** | | **β** | **95% CI** | **p** | |
| waist circumference, cm[b] | 0.4 | (0.2, 0.5) | **0.0004** | | -0.1 | (-0.3, 0.1) | 0.44 | |
| smoking status | | | | | | | | |
| never-smokers | 0 | (reference) | | | 0 | (reference) | | |
| smokers | 0.0 | (-3.1, 0.3) | 0.98 | 0.71 | **5.5** | **(3.2, 7.9)** | **<.0001** | **<.0001** |
| former smokers | 0.8 | (-1.4, 0.3) | 0.48 | | -0.6 | (-2.7, 1.4) | 0.54 | |
| | **time in moderate activity**, % of time in overall activity | | | | **time in moderate activity**, % of time in overall activity | | | |
| | **β** | **95% CI** | **p** | | **β** | **95% CI** | **p** | |
| waist circumference, cm[b] | -0.3 | (-0.5, -0.1) | **0.002** | | 0.0 | (-0.2, 0.2) | 0.71 | |
| smoking status | | | | | | | | |
| never-smokers | 0 | (reference) | | | 0 | (reference) | | |
| smokers | 0.6 | (-2.2, 3.4) | 0.67 | 0.88 | **-4.4** | **(-6.6, -2.2)** | **0.0001** | **<.0001** |
| former smokers | 0.0 | (-2.0, 2.1) | 0.98 | | 0.9 | (-1.0, 2.7) | 0.35 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
min/d, minutes per day; n. a., not available; 95% CI, 95% confidence interval
[1]Results were derived from six different multivariable linear regression analyses with the potential determinants included as independent and time in overall activity or proportion of active time spent in the three different activity intensities included as single dependent variable. β-coefficients can be interpreted as change in time in overall activity or relative change (%) in the proportion of time in overall activity spent in the different activity intensities per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, with each 1-unit higher waist circumference (residually adjusted for body mass index, BMI), men spent 0.4% more active time in low activity. Model includes sex, age, BMI, waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
**bold**: *p*-value <0.05

#### 4.3.2.4 Sensitivity linear regression analyses

Results for the sensitivity analyses on the linear regression analyses using a more strictly defined study sample regarding NWT (60-min instead of 120-min NWT algorithm), encompassing 211 participants, are summarized for regression model 2 (N=201) in **Supplementary Table 10** and **Supplementary Table 11**. Overall, *p*-values tended to be smaller and effect sizes tended to be slightly larger as compared to the results in the main analyses. Results for age, smoking, university entrance qualification, and not reporting the net household income were still and in the same order of magnitude significant, with effect sizes being slightly higher. In contrast to the main results, for time in overall activity (min/d), persons, who reported to never drink alcohol (70.7 min/d (7.3, 134.0); p=0.03) or to drink alcohol 4 times per week or more frequently (47.5 min/d (10.8, 84.1; p=0.01) were more physically active compared to persons drinking alcohol maximal once a month. BMI was no longer associated with time in overall activity. The associations of sex, waist circumference (residually adjusted for BMI), and alcohol consumption with active time spent in low or moderate activity were no longer present. In contrast, each 1-unit higher BMI was now associated with 0.3% (0.0, 0.5; p=0.04) less active time spent in low at the expense of moderate activity (0.3% (0.1, 0.6), p=0.005). *P*-values regarding the study center were similar as compared to the main analyses (active time spent in low activity, p=0.01; in moderate activity, p=0.02; in VV activity, p=0.007).

#### 4.3.2.5 Test for linearity

To test, whether the assumption of linearity that is a precondition for performing linear regression analyses holds true for the models assessed here, scatter plots were created, displaying the relationship between the PA parameters and the potential continuous determinants, i.e., age, BMI, and waist circumference (residually adjusted for BMI) (**Supplementary Figure 4**, **Supplementary Figure 5**). Visually, there were no substantial deviations from a random dispersion of data across the range of the variables, indicating that using a linear regression analyses to describe the association of PA with the potential determinants as assessed here is suitable.

### 4.3.3 Potential determinants of meeting the physical activity recommendation of the World Health Organization

#### 4.3.3.1 Univariable logistic regression analyses

Further, logistic regression analyses were conducted with meeting the WHO PA recommendation as binary outcome (yes versus no). In univariable logistic regression analyses, men compared to women (OR: 0.59; 95% CI: 0.34, 1.00; p=0.05, *p*-valued not rounded=0.048) and current smokers compared to never-smokers (0.26; 0.12, 0.59; p=0.001) less likely met the WHO criteria (**Table 29**); smoking status was generally associated with the OR of meeting the WHO criteria (p=0.005).

#### 4.3.3.2 Multivariable logistic regression analyses

Logistic regression analyses were the same respective models as performed for the linear regression analyses. Again, model 2 including pre-existing medical conditions was evaluated (**Table 30**), but results for the analyses excluding diabetes mellitus and dyslipidemia were very similar (**Supplementary Table 12**). In the multivariable logistic regression analyses model 2, smoking status was significantly associated with the likelihood of meeting the WHO PA recommendation (p=0.004) (**Table 30**). For persons, who reported to be current smokers, the OR was 0.21 (0.08, 0.53, p=0.001) to meet the WHO PA recommendation as compared to never-smokers. *P*-value for the study center was not statistically significant (p=0.80).

#### 4.3.3.3 Test for interaction with sex

Then, it was tested for interactions with sex for the association of the potential determinants and the likelihood of meeting the WHO PA recommendation for logistic regression model 2. There were sex differences in the association of waist circumference (residually adjusted for BMI) (p=0.03) and smoking status (p=0.03) with the OR of meeting the WHO criteria (**Table 31**). Per 1-unit higher waist circumference (residually adjusted for BMI), OR for meeting the WHO criteria was 0.79 (0.65, 0.97; p=0.02) in men, while in women, the OR was 1.11 (1.01, 1.23; p=0.03) (**Table 32**). In men, the OR of meeting the WHO PA recommendation was further decreased for current (0.08; 0.01, 0.83; p=0.03) as well as for former smokers (0.05; 0.01, 0.47; p=0.01) compared to never-smokers. In women, only being a current smoker was associated with a decreased OR of 0.22 (0.05, 0.93; p=0.04) compared to never-smokers.

#### 4.3.3.4 Sensitivity logistic regression analyses

Results for the sensitivity logistic regression analyses based on a more conservatively defined study population (60-min instead of a 120-min NWT algorithm) are shown in **Supplementary Table 13** for regression model 2 (N=201). Overall, *p*-values and OR were very similar compared to the results found in the main analyses. Smoking status was associated with the OR of meeting the WHO PA recommendation (p=0.02). The OR for current smokers was in the same order of magnitude decreased (OR=0.21 (0.07, 0.65); p=0.01) compared to never-smokers.

**Table 29**: Univariable association of potential physical activity determinants and fulfillment of the physical activity recommendation of the World Health Organization[1], total (N=262)

| **potential determinant** | **meeting WHO recommendation**[a] (yes vs. no) | | | |
|---|---|---|---|---|
| | **OR** | **95% CI** | **p**[b] | |
| sex (men vs. women) | 0.59 | (0.34, 1.00) | **0.05** | |
| age, years (5 years) | 0.98 | (0.87, 1.11) | 0.78 | |
| BMI, kg/m² | 0.94 | (0.87, 1.00) | 0.06 | |
| waist circumference, cm[c] | 0.98 | (0.94, 1.01) | 0.18 | |
| smoking status | | | | |
| never-smokers | 1 | (reference) | | |
| smokers | 0.26 | (0.12, 0.59) | **0.001** | **0.005** |
| former smokers | 0.71 | (0.40, 1.25) | 0.23 | |
| alcohol consumption | | | | |
| never | 0.76 | (0.14, 4.13) | 0.75 | |
| max. 1x/month | 1 | (reference) | | |
| 2 - 4x/month | 1.18 | (0.57, 2.44) | 0.65 | 0.91 |
| 2 - 3x/week | 1.22 | (0.58, 2.58) | 0.61 | |
| ≥4x/week | 0.89 | (0.39, 2.03) | 0.77 | |
| university entrance qualification (no vs. yes) | 1.38 | (0.83, 2.33) | 0.22 | |
| employment status | | | | |
| full time | 1 | (reference) | | |
| part time | 1.11 | (0.60, 2.08) | 0.73 | 0.94 |
| not employed | 1.00 | (0.51, 1.96) | 1.00 | |
| net household income per month | | | | |
| <2,500 € | 1 | (reference) | | |
| 2,500-3,999 € | 1.08 | (0.58, 2.01) | 0.81 | 0.36 |
| ≥4,000 € | 0.96 | (0.47, 1.96) | 0.91 | |
| n. a. | 2.62 | (0.86, 7.96) | 0.09 | |
| marital status (married, no vs. yes) | 0.66 | (0.39, 1.13) | 0.13 | |
| diabetes mellitus (yes vs. no)[d] | 0.59 | (0.19, 1.84) | 0.36 | |
| dyslipidemia (yes vs. no)[d] | 0.85 | (0.47, 1.54) | 0.60 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; n. a., not available; OR, odds ratio; vs., versus; WHO, World Health Organization; 95% CI, 95% confidence interval
[1]Results were derived from a univariable logistic regression analysis with the potential determinants included as independent and fulfillment of the World Health Organization (WHO) physical activity (PA) recommendation included as dependent variable [7]. β-coefficients can be interpreted as change in the likelihood (odds ratio, OR) of meeting the WHO PA recommendation, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, the likelihood for meeting the WHO PA recommendation was decreased by 41% in men compared to women.
[a]meeting WHO physical activity recommendation: ≥150 minutes of moderate activity/week, or ≥75 minutes of vigorous activity/week, or an equivalent of these [7]
[b]*p*-values presented are raw values
[c]residually adjusted for body mass index
[d]data for 249 out of the total 262 participants available
**bold**: *p*-value <0.05 (bold p=0.05 for not reported net household income: *p*-valued not rounded=0.048)

**Table 30**: Multivariable association of potential physical activity determinants and fulfillment of the physical activity recommendation of the World Health Organization, model 2[1], total (N=249)

| potential determinant | meeting WHO recommendation[a] (yes vs. no) | | | |
|---|---|---|---|---|
| | OR | 95% CI | p[b] | |
| sex (men vs. women) | 0.95 | (0.35, 2.53) | 0.91 | |
| age (5 years) | 1.09 | (0.89, 1.32) | 0.41 | |
| BMI, kg/m² | 0.96 | (0.87, 1.05) | 0.36 | |
| waist circumference, cm[c] | 0.97 | (0.91, 1.04) | 0.42 | |
| smoking status | | | | |
| never-smokers | 1 | (reference) | | |
| smokers | 0.21 | (0.08, 0.53) | **0.001** | **0.004** |
| former smokers | 0.59 | (0.30, 1.16) | 0.12 | |
| alcohol consumption | | | | |
| never | 0.32 | (0.02, 4.72) | 0.41 | |
| max. 1x/month | 1 | (reference) | | |
| 2 - 4x/month | 1.51 | (0.62, 3.69) | 0.36 | 0.68 |
| 2 - 3x/week | 1.59 | (0.62, 4.09) | 0.34 | |
| ≥4x/week | 1.30 | (0.44, 3.87) | 0.64 | |
| university entrance qualification (yes vs. no) | 1.29 | (0.66, 2.51) | 0.46 | |
| employment status | | | | |
| full time | 1 | (reference) | | |
| part time | 0.89 | (0.38, 2.08) | 0.79 | 0.95 |
| not employed | 1.04 | (0.38, 2.85) | 0.94 | |
| net household income per month | | | | |
| <2,500 € | 1 | (reference) | | |
| 2,500-3,999 € | 1.09 | (0.49, 2.43) | 0.83 | 0.85 |
| ≥4,000 € | 0.86 | (0.34, 2.17) | 0.75 | |
| n. a. | 1.67 | (0.39, 7.09) | 0.49 | |
| marital status (married, no vs. yes) | 1.67 | (0.77, 3.62) | 0.20 | |
| diabetes mellitus (yes vs. no) | 0.58 | (0.15, 2.28) | 0.44 | |
| dyslipidemia (yes vs. no) | 0.96 | (0.44, 2.11) | 0.93 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel

BMI, body mass index; n. a., not available; OR, odds ratio; vs., versus; WHO, World Health Organization; 95% CI, 95% confidence interval

[1]Results were derived from a multivariable logistic regression analysis with the potential determinants included as independent and fulfillment of the World Health Organization (WHO) physical activity (PA) recommendation included as dependent variable [7]. β-coefficients can be interpreted as change in the likelihood (odds ratio, OR) of meeting the WHO PA recommendation, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, the likelihood of meeting the WHO PA recommendation was decreased by 79% in smokers compared to never-smokers. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.

[a]meeting World Health Organization physical activity recommendation: ≥150 minutes of moderate activity/week, or ≥75 minutes of vigorous activity/week, or an equivalent of these [7]

[b]*p*-values presented are raw values

[c]residually adjusted for body mass index

**bold**: *p*-value <0.05

**Table 31**: P-values for the test for interaction of the multivariable association of potential physical activity determinants and fulfillment of the physical activity recommendation of the World Health Organization with sex, model 2[1], total (N=249)

| potential determinant | meeting WHO recommendation[a] (yes vs. no) |
|---|---|
| | **P for interaction[b]** |
| age (years) | 0.09 |
| BMI (kg/m²) | 0.30 |
| waist circumference (cm)[c] | **0.03** |
| smoking status | **0.03** |
| alcohol consumption | 0.93 |
| qualification for university entrance | 0.22 |
| employment status | 0.20 |
| net household income | 0.64 |
| marital status | 0.34 |
| diabetes mellitus | 0.12 |
| dyslipidemia | 0.53 |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; vs., versus; WHO, World Health Organization
[1]Results were derived from a multivariable logistic regression analysis with the potential determinants included as independent and fulfillment of the World Health Organization (WHO) physical activity (PA) recommendation included as dependent variable [7]. β-coefficients can be interpreted as change in the likelihood (odds ratio, OR) of meeting the WHO PA recommendation, referring to a 1-unit increment for continuous variables or the respective reference category for categorical variables; for example, the likelihood of meeting the WHO PA recommendation was decreased by 79% in smokers compared to never-smokers. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.
[a]meeting World Health Organization physical activity recommendation: ≥150 minutes of moderate activity/week, or ≥75 minutes of vigorous activity/week, or an equivalent of these [7]
[b]*p*-values presented are raw values
[c]residually adjusted for body mass index
**bold**: *p*-value <0.05

**Table 32**: Sex-stratified multivariable association of potential physical activity determinants and fulfillment of the physical activity recommendation of the World Health Organization, model 2[1]

| potential determinant | men (n=117) meeting WHO recommendation[a] (yes vs. no) | | | | women (n=132) meeting WHO recommendation[a] (yes vs. no) | | | |
|---|---|---|---|---|---|---|---|---|
| | **OR** | **95% CI** | **p[b]** | | **OR** | **95% CI** | **p[b]** | |
| waist circumference, cm[c] | 0.79 | (0.65, 0.97) | **0.02** | | 1.11 | (1.01, 1.23) | **0.03** | |
| smoking status | | | | | | | | |
| never-smokers | 1 | (reference) | | | 1 | (reference) | | |
| smokers | 0.08 | (0.01, 0.83) | **0.03** | **0.03** | 0.22 | (0.05, 0.93) | **0.04** | **0.03** |
| former smokers | 0.05 | (0.01, 0.47) | **0.01** | | 1.67 | (0.59, 4.72) | 0.33 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken
OR, odds ratio; vs., versus; WHO, World Health Organization; 95% CI, 95% confidence interval
[1]Results were derived from a multivariable logistic regression analysis with the potential determinants included as independent and fulfillment of the World Health Organization (WHO) physical activity (PA) recommendation included as dependent variable [7]. β-coefficients can be interpreted as change in the likelihood (odds ratio, OR) of meeting the WHO PA recommendation, referring to a 1-unit increment for continuous variables or the respective reference category for categorical variables; for example, the likelihood of meeting the WHO PA recommendation was decreased by 92% in male smokers compared to male never-smokers. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.
[a]meeting World Health Organization physical activity recommendation: ≥150 minutes of moderate activity/week, or ≥75 minutes of vigorous activity/week, or an equivalent of these [7]
[b]*p*-values presented are raw values
[c]residually adjusted for body mass index
**bold**: *p*-value <0.05

# 5 Discussion[30]

In this thesis, the application of multiday 24h-accelerometry in epidemiology to study habitual overall activity, activity intensities, and potential activity determinants was examined in the general adult population by addressing three objectives, building on one another (RQ 1 to 3).

## 5.1 Reliable assessment of physical activity using multiday 24h-accelerometry under free-living conditions (research question 1)

The first aim was to investigate the reliable estimation of habitual PA using multiday 24h-accelerometry under free-living conditions in the general adult population (RQ 1). For this purpose, the day-to-day within-person variability, the number of days needed, and the reliability of 24h-accelerometry-assessed overall activity and time spent in different activity intensities was examined over approximately two weeks. Day-to-day within-person variability was high in overall activity and in time in low, moderate, vigorous, and very vigorous activity. Across participants, PA parameters systematically differed across the days of the week and between weekdays and weekend days, whereas the day of assessment was not related to PA. However, overall, differences in 24h-accelerometry-based PA between days were small, resulting in a low proportion of the total variance of PA being attributable to the day of assessment, the day of the week, or the distinction between weekdays and weekend days. Further, around one week of 24h-accelerometry was found to be suitable for assessing overall activity and time in different activity intensities. When using 24h-accelerometry-assessed PA averaged over an approximately 1-week period, its week-to-week reliability was good to excellent. Therefore, the present data indicates that around one week of evaluable data is appropriate for a reliable characterization of habitual overall activity and time in different activity intensities using 24h-accelerometry over a single period in an epidemiological study.

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[30]In the framework of this thesis, parts of the discussion on a reliable assessment of PA using multiday 24h-accelerometry have already been published by the author, [288] Jaeschke L, Steinbrecher A, Jeran S, Konigorski S, Pischon T. Variability and reliability study of overall physical activity and activity intensity levels using 24h-accelerometry-assessed data. *BMC Public Health*. 18, 530 (2018); parts of the discussion on the ability of NWT detection in 24h-accelerometry data have already been published by the author, [242] Jaeschke L, Luzak A, Steinbrecher A, Jeran S, Ferland M, Linkohr B, Schulz H, Pischon T. 24 h-accelerometry in epidemiological studies: automated detection of non-wear time in comparison to diary information. Sci Rep. 7, 2227 (2017).

None of the ActivE participants reported any burden from 24h-accelerometry, indicating a high acceptance and feasibility of wearing the accelerometer continuously 24h per day. Further, few NWT periods were reported by participants, indicating that accelerometry data in the present analyses allows for sound deductions on variability and reliability of 24h-accelerometry-based habitual PA under free-living conditions.

### 5.1.1 Day-to-day variability of habitual physical activity using 24h-accelerometry

The present data revealed a large day-to-day within-person variability of habitual PA based on multiday 24-accelerometry, accounting for around 60% of the total variance of overall activity, whereas between-person variance contributed around 40%. Similar proportions of variance components were found for the time spent in inactivity and in low to very vigorous activity. Thus, differences in PA between days were larger within one person than between persons, which was somewhat surprising. However, it is in accordance with the quite narrow range in the investigated PA parameters (see **Table 6**), indicating that variation of PA across participants was small. In a study by Matthews et al., the between-person variance explained around 60%, whereas for time in inactivity, the within-person variance accounted for the largest component of the total observed variance [241]; the latter is in accordance with results of the present analyses. However, in the study by Matthews et al., uniaxial accelerometry was used during waking only, limiting direct comparability with the present study, where PA was captured via triaxial 24h-accelerometry. As discussed, variability of accelerometry data is supposed to differ between uniaxial accelerometry during waking and triaxial 24h-accelerometry (see section 2.5.1.3). Regarding the day-to-day variability, it has to be considered that in the present study, similar to in most previous studies [75, 241, 255], consecutive days were investigated. Variability may be different for randomly selected days [211].

#### 5.1.1.1 Variability across the days of assessment

Regarding the day of assessment, it was expected that activity is non-habitually high in the first days and decreases over time due to reactivity of wearing the accelerometer (and vice versa for time in inactivity) [31, 58]. However, there was no trend in PA parameters across the days of assessment, and thus, no evidence for assuming behavioral bias. Further, the day of assessment explained only little of the total observed variance of PA. Although there were no systematic differences across the days of assessment, data indicated that time in low activity slightly differed between the days of assessment. Nevertheless, the general finding of no systematic association between the day of assessment and PA is important with regard to epidemiological studies, since reactivity would diminish the informative value of PA data obtained and, thus, would result in attenuated risk estimates for the associations of PA and health [28]. Further, it supports the assumption that using 24h-accelerometry instead of accelerometry during waking only decreases the awareness of being studied and, therefore, the risk of behavioral bias in epidemiological studies (see section 2.5).

#### 5.1.1.2 Variability across the days of the week

Across the days of the week, i.e., Monday to Sunday, the mean daily overall activity, as well as the time spent in inactivity, and in low, moderate, and vigorous activity slightly differed. The highest level of ‘activity’ (overall activity and time in low to vigorous activity) and the lowest level of ‘inactivity’ (time in inactivity) were found on Wednesday and Friday, and Thursday, respectively. These observations are partly in line with findings by Tudor-Locke et al. using uniaxial accelerometry during waking, who found Wednesday, Thursday, and Friday to explain more than 90% of the variability of daily steps and to be the first days entering a regression model that aims to explain variability in PA across the days of the week [314]. Moderate and moderate-to-vigorous activity to differ between days of the week, being highest on Monday and Thursday, was also shown in a study by Hart et al. using an uniaxial ActiGraph model during waking [75]. For moderate and vigorous activity, an association across the days of the week seems reasonable, given that sports and exercise (that mainly belong to these intensity levels [100-103, 315]) are typically structured and planned behaviors (see section 2.1), and, thus, well predictable. Consequently, an association of time in inactivity and in low activity with the day of the week is also reasonable, when assuming that some individuals will do sports as compensation for a sedentary lifestyle and that days of exercise (i.e., time of moderate to vigorous activity) may partly come at the expense of time in inactivity or in low activity. Further, activities that are not randomly performed throughout the week and what persons may have some ‘schedule’ for, like domestic (e.g., cleaning on weekend days), occupational (e.g., office hours), transportation (e.g., taking the bus on working days), or miscellaneous baseline activities (e.g., reading a book on weekend days) mainly fall into the inactivity and low intense activity group [100-103]. All these aspects may have contributed to the present observation that, on a population level, 24h-accelerometry-based overall activity, and time in inactivity, and in low, moderate, and vigorous activity were associated with the day of the week. In contrast, time in very vigorous activity did not differ between the days of the week, which may reflect that this high intensity is not achieved via daily routines, but by an aimed physical training that is supposed to occur seldom and for short periods at the individual and population level, resulting in, on average, little variation across the week [100-102]. This assumption is supported by the findings of a short mean time in very vigorous activity in ActivE and by the low achievability of 10-minutes bouts in VV activity in pretest 2 of the German National Cohort (see **Table 6** and **Table 20**). Nevertheless, generally, there was only little variability of PA parameters between the days of the week, explaining less than 10% of overall PA variance across the entire population. Thus, although PA slightly differed across the week, the day of the week explained only little of the total variance of 24h-accelerometry-based PA. This conclusion is consistent with findings by Matthews et al. and Tudor-Locke et al., who found the day of the week to account for a maximum of 13% of total variance of (waking, uniaxial) accelerometry-based overall activity and time in activity intensities, and for less than 5% of total variance of (waking) pedometer-based steps per day as proxy for overall activity [241, 314].

#### 5.1.1.3 Variability between weekdays and weekend days

Similarly, there were only small differences in the PA parameters between Monday to Friday versus Saturday and Sunday, and the distinction between weekdays and weekend days accounted for less than 19%. Time in moderate activity was shorter on weekend days than on weekdays. One may assume that this finding partly reflects that, on average, most persons will do sports and occupational activity on weekdays and not on weekend days; both activity behaviors mainly are of moderate intensity [100-103]. In contrast, there was no difference between weekdays and weekend days in overall activity or the time in inactivity or in low, vigorous, and very vigorous activity. This was surprising, since previous studies using accelerometry during waking reported PA to substantially differ between weekdays and weekend days and concluded to require at least one weekend day for sound analyses on PA [36, 43, 200, 241, 250-252]. However, this conclusion is not reasonable based on the results of the present study using 24h-accelerometry. Rather, the present data indicates that including both, Saturday and Sunday, or none of both are required to obtain unbiased weekly PA estimates: PA on Saturday was considerably different from Sunday, with overall activity, and time in inactivity and in low and moderate activity on Saturday being comparable to Monday to Friday, while, PA parameters on Sunday were considerably lower (or higher for time in inactivity, respectively). Thus, when combining PA parameters assessed on both weekend days, the mean of Saturday and Sunday may not be different from the mean of all weekdays. Including either Saturday or Sunday would, in contrast, result in an overestimation or underestimation, respectively, of weekend PA amount and intensity (vice versa for time in inactivity). Saturday to intercorrelate with weekdays and Sunday to show lower PA levels than the other days of the week was also found in previous studies using accelerometry during waking or subjective PA measures in adults and adolescents [207, 211, 241, 314]. One hypothesis to explain these apparent differences between both weekend days may be that, on a population level, persons are assumed to use Saturdays to run errands or to do the housekeeping, while Sundays are dedicated to leisure time, resting, and recreation.

Although the distinction between weekdays and weekend days explained the largest proportion of total variance of PA of all variables assessed in this analysis (i.e., day of assessment, days of the week, and weekday versus weekend day), still, around 50% of the total observed variability of PA parameters remained unexplained. This indicates that relevant underlying variables were missed in the models analyzed here. One of these potentially contributing factors may be predisposition, as the genetic background was shown to explain more than 70% of the variability of PA between individuals [96]; in the present study, it was not possible to account for that. Further, although there was no substantial association between the days of assessment, days of the week, or the distinction between weekdays and weekend days and mean PA on the population level, this may not rule out the possibility of any systematic within-person variability on the individual level. Nevertheless, in case such an effect is present, the present data indicates that it was randomly distributed across individuals.

### 5.1.2 Number of days needed to estimate habitual physical activity using 24h-accelerometry

Taking the observed high within-person day-to-day variability into account, the formula derived by Black et al. was used to calculate the number of days needed to validly estimate habitual 24h-accelerometry-based overall activity and time spent in different activity intensities (**Equation 4**) [304, 305]. Accordingly, the present data indicates that around one complete week of 24h-accelerometry is suitable to estimate the average PA with an assumed correlation between observed and true PA of 0.9. This is in line with a previous study on PA variability based on accelerometry during waking, and further is in accordance with common study protocols [70-74, 241]. Setting the correlation between observed and true PA to be 0.9 statistically ensured a high rate of persons to be correctly classified in terms of PA quintiles, whereas the proportion of persons being falsely classified was minimized (see section 3.6.2.2) [304, 305]. Assuming higher or lower confidence levels in classifying persons into groups with different PA levels requires more or fewer days, respectively (see **Table 9**).

The formula by Black et al. was originally derived to determine the number of 24h-dietary recalls needed to estimate the energy intake in children, and is well-established in nutritional epidemiology across all ages [306, 307, 316, 317]. When aiming to estimate the required number of assessment days regarding PA, there are not that many established formulas available. Another previously applied approach, the Spearman-Brown prophecy formula, determines the number of assessment days to obtain PA estimates with a given reliability, i.e., it relies on ICCs [211, 252, 318]. When this approach was applied to the present data, results were not substantially different to results found for Black's formula. However, the applicability of the Spearman-Brown prophecy formula is under debate for calculating the number of PA assessment days due to its dependency on compound symmetry, which may not always be valid for PA assessed across consecutive days of the week [211]. Indeed, the present analyses indicate that PA differs across the days of the week (see section 5.1.1.2). Thus, even though it was developed for dietary assessment and had not yet been applied with regard to PA, it was decided to use the formula by Black et al. for the main analyses in this thesis, since it was considered to not be specific to the nutritional field [304].

A recent study by Wolff-Hughes et al. on the 2003-2006 National Health and Nutrition Examination Survey data examined the number of days and the days of the week needed to estimate the group average of accelerometry-based total PA and time in inactivity and in activity intensities [74]. The authors used simulation studies and 25 alternative analyses protocols, varying in the selection procedure of days, and concluded that a single random day of accelerometry is suitable to estimate the 7-day mean group PA [74]. However, this data is not directly comparable with the present one due to several reasons: Wolff-Hughes et al. examined how to best estimate the *average group PA* using uniaxial accelerometry during waking over one week [74], whereas the present study examined the reliability of triaxial 24h-accelerometry-based PA over two weeks, i.e., to what extent 24h-accelerometry allows a *stable ranking of individuals* into fractions with different PA levels (same classification, when assessment is repeated). Further, the population in Wolff-Hughes et al.'s study encompassed 2,532 adults, and, due to the law of large numbers, the mean obtained from all adults is supposed to be close to the 'true' mean of this population [81, 227]. Thus, the present study fundamentally differs from and extends beyond the observations by Wolff-Hughes et al.

Data for direct comparability of the present data is scarce, since most previous studies on PA variability used uniaxial accelerometry during waking only. One study by Pedersen et al. used triaxial 24h-accelerometry (GT3X+) over four days in Danish adult office workers [214]. However, authors fixed the device to the thigh, assessed working days only, and used a software that combined accelerometry and inclinometer data to derive activity types, like sitting or walking that were used to determine moderate-to-vigorous PA [214]; thus, direct comparison with the previous study is again limited. Nevertheless, Pedersen et al. found six days to be needed for estimating moderate-to-vigorous activity over the total time of assessment, when using the Spearman-Brown prophecy formula [214]. They further reported an intra-individual variability of around 50% to 60% and no significant variability between the (four) days of assessment [214]. These observations support the findings in the present analyses on triaxial 24h-accelerometry.

### 5.1.3 Reliability of habitual physical activity using 24h-accelerometry

When the mean daily PA parameters averaged over an approximately 1-week period were compared between week 1 and 2, the within-person variance made up around 25% of total variance, whereas the between-person variance accounted for the major part, i.e. around 75%. Accordingly, compared to the day-to-day variability (see section 5.1.1), the within-person variance was substantially decreased, when averaging PA over approximately one week. This high between- and low within-person variance then both contributed to the high week-to-week reliability, with ICCs of around 0.75 found for habitual overall activity and time in activity intensities [157, 248, 257]. Using the triaxial GT3X+, averaging PA over one week was further previously shown to significantly reduce the device's technical variability, which also contributes to a high reliability of 24h-accelerometry-based PA over an approximately 1-week period [62]. The finding of a high reliability of accelerometry-based PA in this thesis is in line with findings from two previous studies. Sirard et al. examined the reliability of a uniaxial ActiGraph accelerometer and found ICCs of >0.80, when investigating overall activity (cpm) and daily minutes in light to vigorous activity captured via accelerometry over two weeks, being one to four weeks apart [201]. Using the same device over 21 consecutive days, Hart et al. reported ICCs of around 0.85 to 0.90, when assessing overall PA and time in activity intensities in older adults [75]. Both, Sirard et al. and Hart et al. found slightly higher, but comparable ICCs than observed in the present analyses [75, 201]. However, these two studies assessed PA by uniaxial accelerometry during waking [75, 201] and a higher reliability may, thus, be reasonable (see section 2.5.1.3).

### 5.1.4 Physical activity level in the ActivE study used to assess research question 1

The ActivE population that was used to examine the reliable assessment of habitual PA using 24h-accelerometry spent most of the day in inactivity (almost 20 hours) and low activity (around 130 minutes), whereas less than two hours were spent in moderate to very vigorous activity. Thus, around 82% of the day were spent in inactivity, 9% in low, 7% in moderate, and 1% in vigorous or very vigorous activity, or, compared to active time excluding inactivity, 53%, 40%, and 7.5% in low, moderate, and vigorous or very vigorous activity. As compared to previous studies using accelerometry, the ActivE population may, thus, have been slightly more active, with less time spent in inactivity or low activity, and more time spent in moderate and more intense activities [1, 71, 168, 187, 194, 231, 241, 319]. However, in contrast to previous studies, PA in ActivE was assessed using 24h-accelerometry, and, thus, presumably more comprehensively, including activities around and during reported sleeping, which may have contributed to higher PA estimates (see section 2.5). Additionally, different algorithms were used to determine activity intensities between the previous studies and the present study, further limiting direct comparability [1, 71, 168, 187, 194, 231, 241, 319]. However, it cannot be ruled out that the ActivE population was, on average, slightly more active than the general population or than observed in non-convenience samples. However, the aim of the present study was to examine variability and reliability of habitual PA, and both are not expected to substantially depend on the average group activity level.

### 5.1.5 Contribution of this thesis to the reliable assessment of physical activity using 24h-accelerometry in epidemiology

When aiming to investigate if an exposure, like PA is associated with an outcome, like chronic disease prevalence, either an association is observed, or not. In case of the latter, for a single measurement of PA and without knowing the measurement's reliability (in addition to its reproducibility, see section 2.5.1.3), one cannot rule out that a high within-person fluctuation in the outcome masks existing associations [157, 248, 256]. Thus, the present finding of a high reliability of 24h-accelerometry-based PA has implications for epidemiological studies: On the one hand, for planning new studies, the number of days necessary to validly estimate PA can be derived from data provided. However, it is essential to consider that data presented refers to completely assessed days, i.e., days encompassing 24h of evaluable accelerometry data. Any day needed for study technical reasons, for example, for study center visits, for putting on or off the devices, or for mailing route (from study center to participant or vice versa) must be added to the number of days reported. On the other hand, for data already collected and studies completed, presented correlation coefficients between observed and true PA allow calculation of deattenuated risk estimates for exposure-diseases associations and to reveal, whether the lack of an association is true or due to a high within-person variability of the parameter assessed (see section 2.5.1, **Table 9**) [28]. Both applications of the present results are relevant for deriving reliable and potentially stronger, deattenuated risks estimates in epidemiology aiming to investigate PA as predictor of chronic diseases using 24h-accelerometry.

Thus, the present data indicates that assessing 24h-accelerometry-based PA over an approximately 1-week reduces within-person variability compared to the variability of single days, results in a high reliability of 24h-accelerometry-based PA, and is, thus, a suitable approach to estimate habitual overall activity and time spent in different activity intensities using 24h-accelerometry under free-living conditions.

## 5.2 Detection of accelerometer non-wear time using 24h-accelerometry under free-living conditions (research question 2)

Besides knowledge of the number of needed assessment days, wearing compliance and daily wearing time must be known to enable a valid estimation of habitual PA using 24h-accelerometry. The second aim of this thesis was, therefore, to examine the applicability of algorithms requiring 60 or more consecutive minutes of zero-acceleration readings for NWT detection in 24h-accelerometry in the general adult population. Although most previous studies used a 60-min algorithm, in the present study, up to 90% of diary-based NWT was shorter than 60 minutes. Consequently, the vast majority of reported NWT was not assessable, when using the 60-min algorithm. Applying the 60-min algorithm resulted in a low sensitivity and, especially, low specificity of NWT detection in 24h-accelerometry compared to diary data. Considerable imitations of the algorithm were also evident for the overlap in NWT minutes between 24h-accelerometry and diary, particularly, when analyzing reported NWT of any length. Additionally, false positive NWT detection was high for the 60-min algorithm applied to 24h-accelerometry compared to diary. This holds true over the total time of assessment and for waking and sleeping separately. Therefore, the present data indicates a low suitability of the 60-min algorithm to detect NWT in 24h-accelerometry. NWT algorithms requiring periods of more than 90 to more than 180 minutes of zero-acceleration readings performed better in NWT detection, but, due to their nature, detected only small proportions of reported NWT. Even when applying the most sensitive and specific algorithm, still, up to 80% of reported NWT was missed. None of the tested algorithms allowed detection of as much NWT as possible with high sensitivity, specificity, and large overlap with diary NWT. However, a 120-min algorithm appeared to be a reasonable compromise to detect NWT over the total time of 24h-accelerometry and during waking and sleeping.

After initialization, accelerometers continuously record data over the preset total time of assessment, and the most common approach to detect accelerometer NWT is to use a 60-min algorithm that was derived from uniaxial accelerometry assessed during waking [73, 94]. Considering the advantages and increased application of 24h-accelerometry (see section 2.5), examining to what extent algorithms based on consecutive zero-acceleration readings allow detection of NWT in accelerometry applied over 24h per day is pivotal to obtain unbiased PA estimates (see section 2.5.2.1). Due to the assumption that during sleeping, periods without movement of the center mass are often and typically longer than 60 minutes (see section 2.5.2.4), in the present thesis, a distinct analysis of NWT detection was performed: The 60-min as well as longer NWT algorithms were tested regarding their suitability to detect NWT in 24h-accelerometry over the continuous total time of assessment, and in waking and sleeping phases separately. Overall, as expected, the longer the NWT algorithm was, the fewer NWT periods occurred, while during sleeping, few, but mainly long NWT periods were reported.

### 5.2.1 Waking phases

During waking, only 10 to 15% of all reported NWT were spent in periods longer than 60 minutes. Consequently, a large proportion of all reported NWT is missed, when using the 60-min algorithm during waking, revealing a considerable limitation of this algorithm. This was surprising, given that this algorithm was originally developed based on and is commonly applied in accelerometry during waking [70, 73, 94, 177, 258, 259, 264]. Furthermore, this algorithm had a low sensitivity and, even more pronounced, low specificity to detect NWT in waking phases of 24h-accelerometry data. Additionally, based on a minute-by-minute evaluation, the overlap in NWT, i.e., NWT minutes detected in both, accelerometry and diary was lowest for the 60-min algorithm compared to longer algorithms tested, while the degree of NWT minutes detected in accelerometry, but not in diary was highest, when comparing accelerometry- and diary-based NWT (see **Table 14**). During waking, sensitivity, specificity, and the degree of overlap in NWT minutes were all highest for the 90-min (ActivE) and 120-min (KORA) algorithm. Showing algorithms defining periods longer than 60 minutes to be more suitable for NWT detection during waking is in line with previous studies using ActiGraph accelerometers and a diary as standard reference of NWT detection. Peeters et al. concluded that a 90-min compared to a 60-min algorithm improves NWT detection in accelerometry assessed during waking, and this approach has already been used [71, 266, 320]. Similarly, Choi et al. reported less NWT misclassification, when applying a 90-min instead of a 60-min algorithm, even, when compared to NWT derived from direct observation [267, 268]. Hutto et al. found a 60-min and 90-min NWT algorithm to significantly overestimate the number of NWT periods and to underestimate sedentary time, and suggested a 120-min algorithm [261]. Further, using other than ActiGraph accelerometers during waking, a 120-min algorithm was also recommended [321], while Oliver et al. showed a 180-min algorithm to most validly detect NWT [265]. However, as the latter study focused on a sedentary population (office-based employees during work) [265], findings may not be generalizable and a 180-min algorithm may not be recommended for others than sedentary behavior-related study aims.

Thus, although being in accordance with previous studies, even when using the algorithms showing high sensitivity and specificity in the present study, only around 20% of the potential total NWT (i.e., NWT detected by either diary, accelerometry, or both) were identified based on accelerometry during waking (see **Table 16**, **Table 17**). Again, such a small NWT proportion to be detected is surprising, given that the 60-min algorithm was developed for accelerometry used during waking [73, 94].

### 5.2.2 Sleeping phases

Studies investigating NWT occurrence and detection during sleeping are scarce. However, one might expect considerable differences as compared to waking phases, with periods without captured acceleration to be more likely, but actual NWT occurrence to be much lower during sleeping. Indeed, in the present study, a minor proportion of all NWT periods were reported to have been occurred during sleeping, and a majority of NWT during sleeping was longer than all NWT algorithms tested, i.e., longer than 180 minutes. Consequently, sensitivity of NWT detection during sleeping was generally high, with only small differences between the 90-min to 180-min algorithms. In contrast, specificity of the 60-min algorithm was considerably lower compared to the longer algorithms. Thus, the present data indicates that NWT during sleeping is often false positively assigned to actual wearing times based on accelerometry, when using the 60-min algorithm. This was also reflected by the high degree of NWT detected in accelerometry, but not in diary, which was true for both, when applying the NWT algorithms to diary and accelerometry data (see **Table 14**, **Table 15**), as well as when comparing NWT longer than 60 to 180 minutes based on accelerometry with any diary-based NWT (see **Table 16**, **Table 17**). At the same time, overlap in NWT minutes was exceedingly low (5% to 9%) for the 60-min algorithm, further underlining its limited suitability to precisely identify NWT minutes in accelerometry assessed during sleeping. However, even with longer algorithms, less than 50% of all reported NWT were detected in accelerometry during sleeping (see **Table 14** to **Table 17**). Considering the low NWT occurrence during sleeping, limitations in NWT detection found across all algorithms suggest that none of the algorithms tested is unrestrictedly suitable to precisely detect NWT during sleeping. Thus, applying these algorithms to accelerometry data captured during sleeping should be valued cautiously. Simply assuming no NWT during sleeping may provide less biased 24h-accelerometry PA estimates than using any of the NWT algorithms tested.

The specificity of NWT detection during sleeping was slightly higher in KORA than in ActivE. This observation can most probably be explained by the difference in the study protocols that, in case of KORA, required participants to change the accelerometer from the hip during waking to the wrist of the non-dominant hand during sleeping, while in ActivE, participants constantly wore the device on the right hip. Moving the arm or hand while sleeping, is supposed to be more likely than moving the trunk. Thus, the likelihood of false negative NWT detection based on accelerometry may be lower for wrist- (KORA) than for waist-worn (ActivE) accelerometers [267].

### 5.2.3 Total time of assessment

When analyzing the continuous 24h-accelerometry data over the total time of assessment, the 60-min algorithm showed a fair to good sensitivity, but specificities being close to zero. The separate analyses of waking and sleeping phases revealed that the extremely low specificity is due to the extremely high rate of false positive NWT detection during sleeping, with 90% to 95% of the potential total NWT being detected in accelerometry only (see **Table 14** to **Table 17**); proportion during waking was around 22 to 45% only. Nevertheless, even during waking, the 60-min algorithm did not enable a reliable NWT detection. Additionally, similarly to what was found during sleeping, the overlap in NWT minutes identified in both, diary and accelerometry was lowest, whereas the degree of false positive NWT detection based on accelerometry was highest, when analyzing the total time of assessment using the 60-min algorithm. Separated analyses of waking and sleeping phases again showed that limitations of the 60-min algorithm during sleeping substantially contributed to this small overlap in accelerometry and diary NWT over the total time of assessment. Thus, the present data indicates little agreement not only in number, but also in length of accelerometry- and diary-based NWT periods and minutes over the total time of assessment. Accordingly, the 60-min algorithm was found to be less suitable for NWT detection in continuous 24h-accelerometry data due to substantial limitations during included waking as well as sleeping phases, with the latter, as expected, being more pronounced. This conclusion is in line with a previous study by Choi et al. using a uniaxial ActiGraph model to capture PA during a monitored 24h-stay in a calorimetric chamber [268]. These authors found a 60-min algorithm to substantially misclassify wear time as NWT, whereas a 90-min algorithm significantly decreased the rate of NWT misclassification [268].

In this thesis, over the total time of assessment, the 180-min (ActivE) and 120-min (KORA) NWT algorithm showed at the same time a high sensitivity, specificity, and large overlap in NWT minutes between accelerometry and diary. However, this implies that precisely detecting NWT of as short lengths as possible is not feasible based on algorithms defining consecutive zero-acceleration readings as the only NWT criterion. Further, even when the 'best' NWT algorithm in the present analyses was applied, still, 50 to 74% of the potential total NWT was identified in diary, but not in accelerometry (see **Table 16**, **Table 17**). Thus, a considerable proportion of all reported NWT was missed using these algorithms, and, over the continuous total time of 24-accelerometry assessment, NWT detection using any of the algorithms tested in this thesis is limited, either concerning quantity or quality of NWT detection, i.e., regarding the number of detected NWT periods or NWT minutes, or regarding the precision of NWT detection.

### 5.2.4 Non-wear time algorithms and 'gold standard reference' used to assess research question 2

NWT shorter than 60 minutes made up the clear majority of all reported NWT periods during waking and over the total time of assessment. This is in line with findings in a study conducted by Oliver et al. using accelerometry during waking, who found a minority of NWT to be longer than 80 minutes [265]. Thus, these authors also assessed algorithms defining shorter periods as NWT, i.e., 20 and 40 minutes [265]. However, in the present analyses, specificities were close to zero and false positive NWT detection based on accelerometry was very high (and highest compared to the longer algorithms), already when using the 60-min algorithm. Thus, it was expected that for NWT algorithms requiring periods shorter than 60 minutes, performance of NWT detection would have been even weaker than found for the 60-min algorithm. Therefore, NWT algorithms shorter than 60 minutes were not assessed in this thesis.

In addition to false positively assigning true wear times to NWT based on accelerometry (i.e., high rate of NWT detected in accelerometry only), the present data indicates that the largest proportion of reported NWT of any length failed to be detected in 24h-accelerometry over the total time of assessment and during waking (i.e., high rate of NWT detected in diary only) (see **Table 16**, **Table 17**). Without having diary information, the impact of this misclassification of NWT as wear time may only be speculated, since it depends on the behavior performed by the participant while not wearing the accelerometer: If activity was performed during NWT, including these periods (as periods with zero-acceleration) would lead to an underestimation of the activity level. In contrast, removing the accelerometer for baseline activities that are not substantially related to the individual activity level, like grooming, the impact of including these NWT periods on PA estimates is supposed to be small. Indeed, in ActivE, the main reported reasons for taking off the accelerometer were showering and changing clothes. Therefore, inclusion of NWT is expected to not have substantially falsified PA estimates.

When examining the suitability of the different NWT algorithms, the participants' diary was set as 'gold standard reference'. This assumption seems justified, given that the self-reported information on the number and occurrence of NWT periods was expected to be reliable, since it should be easily memorized and reported by participants. However, regarding the length of occurring NWT periods, one may speculate that the information provided by the participant may be less accurate, since participants may tend to estimate or round the beginning and ending of a NWT period, may not look at a clock the minute they take off or put on the accelerometer, or may note time points in retrospect. Therefore, there may be the dilemma that the diary is probably the standard reference for determining the occurrence of NWT events, while the accelerometry data may provide more precise information on the time points and length of NWT periods, once the presence of a NWT is known.

### 5.2.5 Contribution of this thesis to the detection of accelerometer non-wear time using 24h-accelerometry in epidemiology

Generally, one might assume that the likelihood of being a true NWT period is higher the longer the period of zero-acceleration readings is. Since it was further expected that non-moving periods during sleeping may be longer than 60 minutes, the 'performance' of algorithms defining more than 60 to more than 180 minutes as NWT was examined in this thesis. However, a general limitation of any algorithm defining a fixed minimal duration as NWT is that each selected definition will lead to (1) missing all NWT periods shorter than that minimal duration and to (2) misclassifications, i.e., false negative or false positive assignment of NWT to wear time, and vice versa, respectively. Thus, although applying longer NWT algorithms resulted in better NWT detection performances, one must consider that this comes at the expense of detecting less NWT. Therefore, no algorithm tested here was optimal to detect NWT in 24h-accelerometry. However, using the 120-min algorithm seems to be a compromise between sensitivity, specificity, minute-by-minute NWT overlap, as well as detecting as much NWT as possible in 24h-accelerometry. This holds true for the total time of assessment (e.g., without diary information on the week/sleep-rhythm), as well for waking and sleeping assessed separately. Nevertheless, the multifaceted information on shortcomings and advantages of different NWT algorithms provided in this thesis may guide the researchers' choice of the most suitable algorithm for the individual study aim, either regarding a desired certainty, or, when any of the criteria assessed here (i.e., sensitivity, specificity, or overlap) should be given special emphasis to.

## 5.3 Potential determinants of physical activity using multiday 24h-accelerometry under free-living conditions (research question 3)

Results for data quantity from RQ 1 (suitable length of 24h-accelerometry assessment) and for data quality from RQ 2 (suitable NWT definition in 24h-accelerometry) were applied to define the data set for investigating RQ 3, aiming to examine potential determinants of habitual time in overall activity and of active time spent in different activity intensities assessed using 24h-accelerometry under free-living conditions. Among the potential intrapersonal or micro-environmental determinants tested here (see **Table 2**), higher BMI, having a university entrance qualification, not being employed, and, in men only, having a high net household income available were negatively associated with time in overall activity. In contrast, being male, higher age, never consuming alcohol, current and former smoking status, and not reporting the net household income, as well as, in men only, higher waist circumference (residually adjusted for BMI) were associated with the proportion of active time spent in low, moderate, or VV activity, respectively. Further, smoking status was negatively associated with the likelihood of meeting the WHO PA recommendation, while higher waist circumference (residually adjusted for BMI) was negatively associated with the likelihood of being sufficiently active in men, but positively associated in women. All these associations were independent of sex, age, BMI, waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diabetes, dyslipidemia, and study center, respectively. Marital status and pre-existing medical conditions were not associated with habitual PA as assessed in this thesis. Thus, there was evidence for potential biological, behavioral, and economic determinants of 24h-accelerometry-based habitual PA (**Figure 13**).

### 5.3.1 Potential biological determinants

#### 5.3.1.1 Sex

In the present study, sex was associated with the proportion of active time spent in different activity intensities, with men compared to women, on average, spending 2.5% less active time in low and 2.2% more active time in moderate activity. This observation is consistent with a recent study using 24h-accelerometry to assess PA [168].

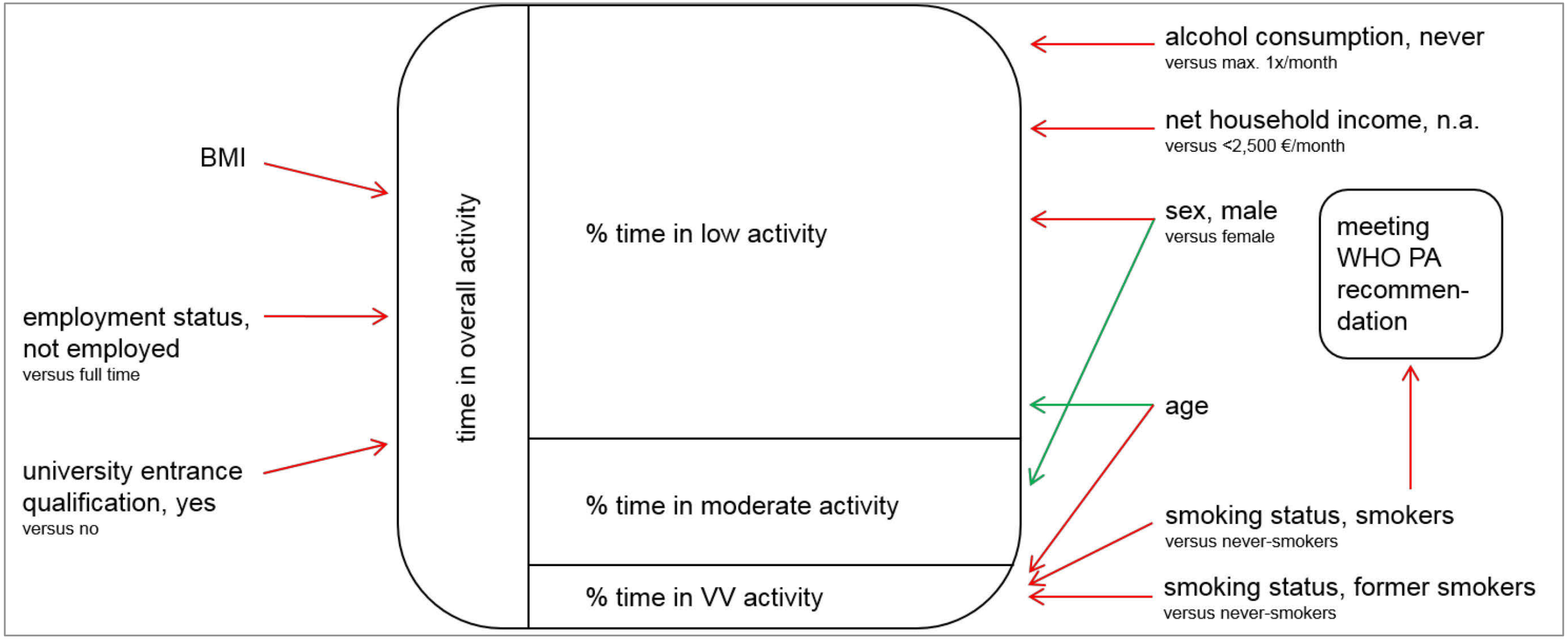


**Figure 13**: Potential determinants of time in overall physical activity, active time spent in different activity intensities, and the likelihood of meeting the World Health Organization physical activity recommendation in the total population pretest 2 of the German National Cohort
Facilitators (green arrows) and barriers (red arrows) of time in overall physical activity (PA, min/d), active time spent in different activity intensities (% time in overall activity), and the likelihood of meeting the World Health Organization (WHO) PA recommendation in the total study population (both sexes) based on linear and logistic regression analyses (for the sake of clarity, sex-specific determinants are not depicted in this figure, see main text for these). Each activity parameter was set as single outcome in a model including sex, age, BMI, waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center. PA data was collected using the triaxial accelerometer GT3X+ and PA parameters were derived from the proprietary ActiLife software (both ActiGraph LLC, Fort Walton Beach, FL, USA). Mean daily proportions (%) of time spent in low (79 to 2,690 triaxial counts per minute, cpm), moderate (2,691 to 6,166 cpm), and vigorous-to-very-vigorous (VV, ≥6,167 cpm) activity were calculated relative to the mean daily time in overall activity, see section 3.4.3 [246]. Meeting the WHO PA recommendation was defined as accumulating at least 150 minutes of moderate or 75 minutes of vigorous activity per week, or an metabolic equivalent of these, see section 3.4.3 [7].

It is further in line with studies on self-reported PA, including a recent survey of the European Commission, showing men to more likely report doing moderate PA, and engaging in moderate activities like sports, exercises, and walking compared to women [24, 59, 100-102, 109]. Similarly, in the National Health and Nutrition Examination Survey, men compared to women more often reported to have been moderately and vigorously active in the past month, and further showed a higher mean activity intensity [322]. Sex differences in engagement in different activity intensities seems reasonable and can partly be explained by a lower fat mass as well as a higher cardiopulmonary and musculoskeletal fitness in men than in women, which, in turn, are preconditions to be capable to perform PA, especially at higher intensities [6, 43, 323]. Furthermore, one may speculate that social factors may partly explain, why women spent less time in moderate activity than men, like social commitments, for example, due to having a child, may limit time to be moderately active, e.g., to do sports [92, 93, 324]. In the present study, a reduction of active time spent in low activity in men by 2.5% equaled a decrease by 8.2 minutes per day (relating to a total of 327.0 minutes spent in low activity in the total population) and a 2.2% increase of active time spent in moderate activity corresponded to a plus of 1.8 minutes per day (regarding 79.4 minutes per day spent in moderate activity). Thus, considering that, for example, meeting the WHO PA recommendation requires 150 minutes of moderate activity accumulated per week, effect sizes observed in this thesis for the impact of sex on the proportion of time spent in different activity intensities were relatively small. Since sex is unmodifiable and *p*-values were close to the significance limit of 0.05, based on the present analyses, women are not considered as ‘population at risk’ for lower PA intensity that should be special attention given to in the context of PA promotion strategies. On the other hand, given that for continuous objective measures of time in light and moderate-to-vigorous activity an association with metabolic markers was previously reported [180], that objectively assessed time in light activity is independently associated with health outcomes [194-197], and given that already a 15-min increase in daily moderate activity may be related to lower mortality risks [45], every even small change in habitual time in low or moderate activity may be epidemiologically relevant.

#### 5.3.1.2 Age

In the present analyses, each 5-years higher age was associated with 0.6% more active time spent in low and 0.2% less active time spent in VV activity. Relative proportion of time in moderate activity tended to be decreased, too. Increasing reported engagement in inactivity and low activity, and decreasing engagement in moderate and vigorous activity intensities with older ages were previously shown in prospective population-based cohorts as well as in cross-sectional studies, including triaxial 24h-accelerometry-based data [6, 96, 109, 168, 322, 325, 326]. Less time spent in moderate and vigorous activity, and increasing levels of sitting time in higher compared to younger ages were also found in a global analysis and in a survey of the European Commission [1, 24]. Additionally, based on U.S. surveillance data, decreasing time in activities that mainly belong to the moderate and vigorous intensity level, like bicycling, running, swimming, or doing sports were shown with increasing age [100-102, 105]. These previous and the present findings are plausible, given the physiologically determined lower cardiorespiratory and musculoskeletal fitness, and, thus, the decline in the ability to perform higher intense activities at older age [6, 43, 96, 327-332]. Additionally, psychosocial aspects may contribute to the finding of more engagement in low activity with older ages, like a decrease in social support for sports with age, or the feeling to be unable or that performing PA of higher intensities is 'unreasonable' [324, 333]. However, the present effect sizes were small, reflecting a plus of 1.8 and a minus of 0.01 minutes per day in active time spent in low and VV activity per 5-years higher age, respectively. Age range in the pretest 2 population encompassed nearly 50 years (youngest versus oldest participant: 21 versus 69 years). This age difference theoretically equaled an increase in active time spent in low activity by around 6% or 18 minutes and a decrease in VV activity by 2% or 0.1 minutes per day. Thus, although the impact is small for a 1-unit increment (i.e., for each five years), when considering larger differences in age between persons, this change in PA intensity may still be relevant for health at a population level, at least for habitual time in low activity as independent risk factor (see section 2.2.1) [194-197]. Age was consistently identified as potential determinant of time in low and VV activity in all regression models (model 1 and model 2) and in the sensitivity analysis (see section 4.3.2.4) performed in this thesis. However, since chronological age is not modifiable, its relevance for individual PA is limited, whereas the elderly population should still be considered as target for PA promotion strategies. In contrast to previous studies on self-reported PA [1, 24, 30, 51, 82, 83, 86, 96, 334, 335], time in overall activity was not related to age in the present analyses; however, the *p*-value of 0.08 suggests that such an association is conceivable. Indeed, in a study by Hansen et al. using a uniaxial ActiGraph accelerometer during waking, age was found to explain the largest proportion of total variation of overall PA [336]. Although direct comparability with the present study using triaxial 24h-accelerometry and a differentially operationalized 'overall activity' measure is limited, one may speculate that age is relevant for habitual time in overall activity in addition to the impact on PA intensity over 24h; however, this needs further clarification.

Reflecting the actual health status, BMI, waist circumference, and pre-existing medical conditions were investigated as potential determinants of 24h-accelerometry-based PA.

#### 5.3.1.3 Body mass index

With each 1-unit higher BMI, persons spent 3.9 minutes less time in overall activity, equaling a 0.9% decrease. An inverse association of BMI and overall activity was indicated previously [51, 86, 109, 337, 338]. Lower levels of overall activity with increasing BMI may partly be explained by the fact that BMI is strongly correlated with body weight, as consequential from the formula used to calculate BMI (see **Equation 2**) [289, 290]; the higher the body weight, the more body mass must be borne and lifted by the person, when moving. Thus, persons with a higher body weight more likely are less overall active in terms of acceleration, even when the activity-related energy expenditure does not compulsorily differ from persons with lower body weight and the same body height (i.e., from persons with lower BMI) [96]. Furthermore, BMI is strongly related to the cardiopulmonary fitness [330], and, accordingly, higher BMI may negatively affect the capacity to be active trough an impaired cardiopulmonary function. In addition to these plausible physiological mechanisms, previous studies have shown that BMI is positively related to the individual discount rate, i.e., the behavioral impatience, indicating if persons prefer an immediate reward above a larger reward at a later time [339, 340]. People with a high discount rate more likely chose a current comfort, while largely disregarding possible future health impairments associated with this behavior [339, 340]. At the same time, the discount rate is negatively related to PA [339, 340]. Accordingly, on the population level, persons with higher BMI may be less overall active, since they more likely prefer the present comfort of inactivity (the reciprocal of time in overall activity for what a negative association with BMI was found) and less likely keep in mind to stay healthy and physically fit in future. Similarly, higher BMI may be associated with other psychological traits, like a decreased self-efficacy, self-confidence, self-esteem, conscientiousness, self-image, neuroticism, impulsivity, straightforwardness, and perceived physical appearance or fitness that all, in turn, can be related to PA [87, 93, 341, 342]. Although the effect size was small for a 1-unit higher BMI, BMI is a modifiable factor and larger differences in BMI may be relevant for time in overall activity. For example, in the study population of pretest 2, the range in BMI encompassed 22.3 kg/m² (highest versus lowest BMI: 17.4 versus 39.7 kg/m²). This theoretically equaled a difference in overall activity of 87.0 minutes or more than 22% per day only because of BMI, which is substantial. Even regarding differences in BMI that are achievable by weight reduction or weight gain (e.g., a 5- or 10-unit decrement), the inverse association of BMI and habitual time in overall activity is considered as epidemiologically relevant.

#### 5.3.1.4 Waist circumference

The BMI is only a rough measure of fat mass and general adiposity, and may not capture the entire spectrum of body mass and fat distribution across all BMI strata [311, 343-346]. Thus, waist circumference was also included in the present regression models to study potential determinants of 24h-accelerometry-based PA. Being residually adjusted for BMI, higher waist circumference was associated with more active time spent in low at the expense of moderate activity. This seems plausible, given that persons with a higher waist circumference have a higher abdominal body weight that is related to energy expenditure and must be borne while moving compared to persons with a lower center mass (but same BMI) (see section 2.3.2.4) [96]. Additionally, Dyrstad et al. showed that waist circumference is negatively associated with cardiorespiratory fitness and with time spent in uniaxial accelerometry-based moderate-to-vigorous activity (ActiGraph), and authors assumed that this may due to an impaired pulmonary function and breathing efficiency, thereby reducing the capability to perform PA at higher intensities [347]. This mechanism could have contributed to the shift from moderate to low habitual activity for higher waist circumference observed in this thesis.

However, in the present analyses, there was a sex difference in the association of higher waist circumference (residually adjusted for BMI) with more active time spent in low and less active time spent in moderate activity, and sex-stratified subgroup analyses revealed that these associations were only true for men, whereas in women, no association was found. This may partly be explained by the fact that, according to results by Dyrstad et al., the negative association of waist circumference and cardiorespiratory fitness is more pronounced in men than in women, and that women with a high waist circumference compared to men with a high waist circumference ten times more likely had a cardiorespiratory fitness that was comparable to the mean fitness in the same-sex group with normal waist circumferences (‘fit fat women’) [347]. In the present analyses, with each increase in waist circumference by 1 cm (residually adjusted for BMI), men spent 0.2% (0.6 minutes) more active time in low and 0.2% (0.1 minutes) less active time in moderate activity per day. Although effect sizes were small for a 1-unit higher waist circumference, waist circumference is modifiable and, as for age and BMI, considering larger differences may result in a relevant impact on PA. Furthermore, one must consider that the increase in active time spent in low at the expense of moderate activity is additional to the results found for BMI. Given that BMI and waist circumference are highly correlated (which was accounted for in the present analyses), having a high BMI as well as large waist circumference is often true at the same time [311]. Thus, with increasing adiposity measures, time in overall activity may decrease (due to a high BMI), with a simultaneous shift from moderate to low activity (due to a high waist circumference), and both effects may be relevant for health [45-57].

Further, following the decreased proportion of active time spent in moderate activity, waist circumference (residually adjusted for BMI) was negatively associated with the OR of meeting the WHO PA recommendation in men, while in women the opposite was true. The latter was surprising, since in women, active time spent in moderate or VV activity (that was used to determine the WHO fulfillment) was not related to waist circumference. However, this may be possible if women with higher versus lower waist circumference (for a given BMI) spent more time in moderate or VV activity in 10-minutes bouts, but not in the proportion of both intensities regarding time in overall activity. Besides physiological aspects, like the concept of ‘fit fat women’ [347], a differential weight-related self-perception between sexes may explain sex differences in the association of waist circumference and the likelihood of being sufficiently active: Compared to their respective counterpart, overweight or obese men were shown to more often misclassify their weight, while overweight or obese women more likely are weight dissatisfied and try to lose weight [348, 349]. Although these results are related to BMI, one may suggest that they are equally valid for waist circumference due to the collinearity of both anthropometric measures [311]. Thus, one may speculate that men with higher versus lower waist circumference for a given BMI less likely (mis)perceive a high own waist circumference as problematic, while women with higher waist circumference presumably more likely aim to adhere to the WHO PA recommendation to decrease abdominal adiposity than men and women, respectively, with the same BMI, but lower waist circumference. OR indicated a 21% decrease in the likelihood of meeting the WHO criteria in men for each 1-cm higher waist circumference (residually adjusted for BMI), while in women, the likelihood was increased by 11%. These changes are substantial, especially, when considering larger differences in waist circumference for a given BMI, and when keeping in mind the association of being sufficiently active with health risk (see sections 2.2.2, 2.2.3). Nevertheless, for the impact of waist circumference on 24h-accelerometry-based habitual PA, strength of the evidence should be considered, since all respective *p*-values were close to the significance limit of 0.05.

#### 5.3.1.5 Pre-existing medical conditions

There is evidence that a better health status as well as fewer physical complaints and comorbidities (cancer, heart disease) are related to higher PA, including accelerometry-based PA assessed 24 per day or during waking [51, 84, 86, 93, 96, 109, 168, 282, 336]. In the study by Hansen et al. using a uniaxial ActiGraph model during waking, better health status was one of the most important factors associated with PA, explaining around 1.5% of the total variance of overall PA [336]. Thus, in the present thesis, it was examined if a diagnosis of diabetes mellitus or dyslipidemia is a potential determinant of 24h-accelerometry-based PA, but none of both pre-existing medical conditions was associated with time in overall activity or active time spent in different activity intensities. One may suggest that being diagnosed with diabetes mellitus or dyslipidemia does not have a long-term effect on PA, since there is often no actual PA-restrictive impairment due to the diagnosis as well as no immediate noticeably improvement in health for the respective person due to being active. Contrary, chronic diseases that impair the cardiopulmonary and physical capacity and functioning and, thus, directly restrict capabilities to be active, like chronic obstructive pulmonary or cardiovascular disease, are probably more relevant for being active [51, 96]. Furthermore, in most previous studies showing a positive association of PA and health, a global measure reflecting the health status (e.g., ‘good’ versus ‘poor’) was investigated [84, 86, 93, 96, 336]. Indeed, people, who are not active, not capable to be active, or feel physically unfit, more likely perceive their health status as ‘poor’, and vice versa [93], making an association of ‘poor health’ and PA plausible. In contrast, the present data suggests that diagnoses of diabetes mellitus and dyslipidemia are not relevant for 24h-accelerometry-assessed habitual PA.

### 5.3.2 Potential behavioral determinants

#### 5.3.2.1 Smoking status

In the present thesis, there was a strong association of smoking status and habitual 24h-accelerometry-based PA, with people reporting to be a current smoker spending more active time in low, and less active time in moderate and VV activity than persons reporting to have never smoked. Generally, a lower engagement in moderate and vigorous activity for current smokers compared to never-smokers seems reasonable: Smoking reduces peak oxygen uptake and systemic oxygen binding in the blood, and impairs cardiopulmonary and musculoskeletal functioning and fitness, as well as energy metabolism, which all result in a decreased energy and oxygen supply, increased perceived effort for higher intensities, decreased capability to perform PA of moderate and VV activity, and, further, promotes fatigue, when being active at higher intensities [96, 98, 350-353]. Furthermore, current smokers are assumed to generally exhibit a more ‘non-healthy’ lifestyle and to be less health-conscious compared to never-smokers, with a lower engagement in sports and exercises [276, 335, 354-358], and, thus, in behaviors of moderate or vigorous activity, as observed in this thesis. Finally, as discussed for BMI, current smokers compared to non-smokers, on average, have a higher discount rate that, in turn, is negatively related to PA [339, 340]. Thus, a shift from higher to low intense activity may also reflect the smokers' choice of current 'comfortable' low over more intense active behaviors. In this thesis, former smokers also spent less active time in VV activity compared to current smokers, indicating that smoking may have a long-term impact on the ability to perform PA at higher intensities.

However, there was an interaction with sex: The association of current smoking with more active time spent in low (5.5% or 18.7 min/d increase) and with less active time spent in moderate activity (4.4% or 3.5 min/d decrease) was only true for female smokers compared to never-smokers; active time spent in VV activity was lower in current smokers in both sexes (1.0% or 0.03 min/d decrease). This observation may partly reflect differences in PA behavior between sexes, with men spending more time in moderate, but less time in low activity than women (see section 5.3.1.1). Additionally, evidence suggests a higher susceptibility to detrimental physiological effects of smoking in women than in men [359-362]. Accordingly, in women, smoking may impair the ability to perform PA of (already) moderate and VV activity, resulting in a shift to low intense activity, while in men, smoking only limits the ability to be VV active, which, due to the small effect in VV activity, does not compulsorily result in an increase in the proportion of active time spent in low activity. Further, smoking is supposed to have a distinct social importance between sexes: For example, compared to men, women started smoking later in history (being, thus, older, when first smoking), start smoking earlier in life nowadays, smoke due to different reasons (stress reduction, weight maintenance; men: social behavior), and metabolize nicotine faster (thus, perceiving withdrawal stronger) [359, 362, 363]. Therefore, regarding findings in the present thesis, one may speculate that female smokers smoke and do endurance PA on a low to moderate intensity level to maintain weight, whereas male smokers smoke for social reasons (that are not activity-related) [364], and smokers of both sexes are less capable to perform VV activity due to limited physiological capacities (see above) [96, 98, 350-353].

Further, in the present analyses, male current as well as former smokers had a lower likelihood of meeting the WHO PA recommendation than never-smokers, while in women this was only true for current smokers. These observations are a plausible consequence of the observed lower proportions of active time spent in moderate (in women) and VV activity (in both sexes), which are the basis for defining fulfillment of the WHO PA recommendation [7]. The OR indicated a reduction in the likelihood of being sufficiently active by 91% and 95% in male current and former smokers, respectively, while likelihood was decreased by 78% in female current smokers. These numbers are remarkable, especially in light of the evidence that meeting the WHO PA recommendation is associated with a substantial decrease in morbidity and premature mortality risk (see sections 2.2.2, 2.2.3) [15, 45, 49, 51, 57]. Thus, the strong impact of smoking on the proportion of time spent in the different activity intensities caused a relevant change in the likelihood of being sufficiently active. Further, given that smoking, activity intensity, and fulfillment of the WHO PA recommendation are independent predictors of the same major chronic diseases, like lung cancer, chronic obstructive pulmonary diseases, and cardiovascular disease (see sections 2.2 to 2.2.3) [8, 45, 49, 51, 362], the present finding that smoking is associated with PA intensity and with being sufficiently active suggests a mutually reinforcing effect of PA and smoking on chronic disease risk. The finding in a previous longitudinal study that being a current smoker versus nonsmoker was associated with a decreased likelihood of being *persistently* active in terms of reported moderate and vigorous activity [325] supports the assumption that smoking has a long-term effect on PA. Thus, smoking is considered as epidemiologically relevant lifestyle factor associated with the proportion of time spent in different activity intensities and the likelihood of meeting the WHO PA recommendation. The importance of smoking on PA is reflected by strength of the evidence in terms of the OR, the significance level (all $p$-values <0.007), and the consistency of findings across regression model 1 and 2 as well as the sensitivity analyses.

#### 5.3.2.2 Alcohol consumption

Further, in this thesis, alcohol consumption was identified as potential determinant of 24h-accelerometry-based PA. Persons, who reported to never drink alcohol, spent 4.3% less active time in low activity compared to persons reporting an alcohol consumption of maximal once a month; at the same time, active time spent in moderate activity tended to be increased. These findings are partly comparable with a previous cluster analyses that showed that persons reporting the lowest alcohol consumption were in the same lifestyle cluster like persons that met the Australian PA recommendation defined via engagement in moderate and vigorous activity [354]. The present and these previous findings may reflect that alcohol abstainers generally exhibit a healthier lifestyle than persons consuming alcohol [354-358], and changing low for moderate activity, thus, seems plausible in these persons. The effect size of 4.3% in the present analyses corresponded to a decrease in low activity by 14.2 minutes per day. This was the largest change in proportion of active time spent in low activity among the potential determinants assessed in this thesis. In light of the evidence showing low intense activity to be an independent health risk factor, this impact may be relevant (see section

2.2.1) [194-197]. Nevertheless, although a change from moderate alcohol consumption to abstention may be manageable for the individual, and although effect sizes were quite high, the strength of the association in terms of the *p*-value was weak. Furthermore, since daily low-to-moderate alcohol consumption may be beneficial for cardiovascular health, promoting a change from moderate alcohol consumption to never drinking alcohol may not be reasonable on a population level [365-367]; of course, promoting to quit heavy alcohol consumption is desirable in every respect.

### 5.3.3 Potential economic determinants

There is a large body of evidence showing that the socioeconomic environment a person is growing up and living in is associated with health and, furthermore, with health-related behavior, like PA [8, 25, 90, 276, 368, 369]. In the present thesis, three potential determinants reflecting the socioeconomic status were investigated [370-372].

#### 5.3.3.1 University entrance qualification

Having versus not having a university entrance qualification was strongly associated with a decrease in time in overall activity by 35.9 minutes per day, equaling a daily 8.6% decrease; this association was evident from both regression models and the sensitivity analysis. At first glance, this is contradictory to evidence showing a positive associations of having a university entrance qualification or of longer educational stay with self-reported overall PA [24, 30, 84, 243, 282, 322, 334, 335, 373]. Indeed, since persons with a higher versus lower socioeconomic status, and, particularly, education typically have a higher (lifetime) income, show a healthier lifestyle, and are more likely 'information seeker' [271, 276, 374, 375], one might have had assumed that persons with versus without a university entrance qualification have a better knowledge, understanding, and awareness of PA benefits, and, thus, intention to exercise, thereby positively influencing PA [30, 87, 93, 376, 377]. However, persons having a university entrance qualification more likely have occupations with low PA demands, like white-collar work (e.g., civil servants, academics), as shown in a recent review [378]. In line with this is the finding, that the socioeconomic status is positively related to occupational sedentary behavior [283]. In turn, low occupational PA was previously shown to be related to lower engagement in leisure-time PA [379], indicating that persons, who are mainly inactive at work, are also mainly inactive after work. Thus, a negative association of having a university entrance qualification with time in overall activity seems plausible and was also shown previously in a longitudinal study [109]. Further, in this thesis applying 24h-accelerometry, overall movement was assessed. Thus, it is still possible that persons with a university entrance qualification do engage in more activity (because of knowledge of PA benefits and having the financial resources to use PA facilities), but, across the day, move less than persons without this qualification that more likely have occupations with higher PA demands (blue-collar work) [380]. On the population level, all these aspects may have contributed to the finding that having versus not having a university entrance qualification was associated with less time in 24h-accelerometry-based overall activity in this thesis.

#### 5.3.3.2 Employment status

Further, unemployed compared to full time employed persons spent 66.2 minutes or 15.9% less time in daily overall activity. This substantial difference was found in regression model 1 and 2 as well as in the sensitivity analyses and was the largest effect in terms of change in PA and significance level (*p*-value) found in the present analyses. Such an association is in accordance with findings from previous reviews as well as from the European Commission on self-reported PA, showing persons not being in paid work to less likely engage in exercise, sports, or other PA [24, 90, 109, 334]. An impact of the employment status on the time in overall activity can partly be explained by the lack of occupational PA that may make up a considerable part of overall PA, especially in manual (blue-collar) occupations [283, 380], as well as the by the lack of transportation PA due to the way to work. In addition to such a directly PA-related impact of unemployment, being employed is associated with more social contacts, whereas not being employed was shown to be related to a higher risk of social deprivation and exclusion, while social isolation and lack of support may, in turn, negatively influence engagement in activity [30, 84, 276], assumingly due to less opportunities and support to be active. Furthermore, not being employed is associated with less individual income, limiting the financial resources, and monetary capacities were shown to be positively related to PA (see section 5.3.3.3). Furthermore, not being employed is associated with poor wellbeing in terms of mental health as well as long illness that both may be related to PA (see section 5.3.1.5) [276]. Finally, persons with a lower socioeconomic status as measured, inter alia, by employment status, tend to show a generally less health-conscious lifestyle, and, furthermore, unemployed persons more likely are less educated, which is also related to a less healthy lifestyle [374, 375] (see section 5.3.3.1). Therefore, less time in overall activity for unemployed versus full time employed persons as observed in this thesis is reasonable and, due to the strength of the impact, unemployed populations are considered as promising targets for PA promotion programs.

#### 5.3.3.3 Net household income

In the present analyses, the net household income was not adjusted for the total number of (financially contributing) household members, since this information was lacking. Because the individually available financial resource decreases with the size of the household for a given household income, the net household income in the present analyses presents a proxy of the truly available individual per-capita financial position. Persons, who did not want to or were not able to give information on the net household income spent 4.2% or 13.9 minutes less active time in low, but 3.5% or 2.8 minutes more active time in moderate activity per day compared to persons reporting a net household income of <2,500 € per month. It seems reasonable to assume that most persons, who do not provide information on their net household income, either have few or much monetary resources available. There is evidence indicating that a high versus low household income is associated with more (self-reported) engagement in PA [30, 334, 335]. Additionally, data from the National Health and Nutrition Examination Surveys suggests that the annual family income is positively associated with self-reported engagement in moderate and vigorous activity [322]. Finally, in a recent study by Shuval et al. using uniaxial (waking) accelerometry data, persons with a higher annual income more likely met the WHO PA recommendation and spent more time in moderate-to-vigorous and less time in light activity [381]. Accordingly, one may assume that the decreased proportion of active time spent in low at the expense of moderate activity observed in the present analyses is related to a group of persons having a high net household income available. This seems plausible, since many opportunities to be active are related to financial resources, such as being a member of a sports club or visiting PA facilities. Additionally, deprivation of neighborhood resources are much more likely in low-income areas that less often provide supportive physical environments for transportation, leisure-time, or recreation PA due to a limited (traffic and crime) safety, aesthetic neighborhood design, and access to open spaces, parks, or recreational facilities, which is supposedly related to PA [84, 88, 93, 271, 283, 334, 382]. Furthermore, like for the other socioeconomic measures, persons with a lower versus higher net household income generally perform a less healthy lifestyle and limited financial recourses to purchase 'healthy decisions' (e.g., regarding diet) may be a simple explanation for this [276, 374, 375]. Finally, low-income families and persons probably more likely face inflexible working environments that may result in time constraints, thereby limiting engagement in PA [92]. Although the direction of association of net household income and PA cannot be proven in this thesis, a positive association seems most likely. In any case, the change in active time spent in low activity was among the largest observed in this study.

There was further an interaction with sex for the association of net household income with time in overall activity, and sex-stratified analyses revealed that men reporting a high net household income (≥4,000 € versus <2,500 € per month) were 48.8 minutes per day less overall active. This corresponded to a decrease by 12.1%, which is considered as relevant change. In women, in contrast, no association was found. These observations are comparable to findings in a study using pedometers during waking, with the individual annual income being negatively associated with total steps in men, but not in women [383]. A negative association of net household income with time in overall activity in men, at first glance, contradicts to the discussion above. However, following the wage gap, indicating the income disparity between men and women, one may assume that men in most households are the main wage earners [384]. Thus, one may suggest that a high net household income is related to a high individual income of men, which, in turn, is often related to high professional positions. These are less often PA demanding, but time-demanding, like manager, group leader positions, or other white collar work [380], and a large occupational time of inactivity and time constraints (whose negative impact on PA exceed the positive impact of financial resources) may decrease time in overall activity compared to men with a lower net household income, as found in this thesis [24, 92]. These assumptions are partly supported by the previous findings that a higher income was associated with more time in occupational and transportation sedentary behavior [283]. Since the impact on activity intensities and overall activity was quite large in the present analyses, persons with a low or high net household income are considered as relevant targets for PA promotion strategies.

### 5.3.4 Potential socio-cultural determinants

#### 5.3.4.1 Marital status

Finally, in this thesis, marital status was investigated as potential socio-cultural determinant of PA. Studies on self-reported PA show contradictory or inconclusive evidence on the impact of the own marital status on the individual PA level in adults [30, 51, 84, 89, 334]. In the present study, no association was found between the marital status and 24h-accelerometry-based PA. This finding can be explained by the fact that the marital status per se does not reflect a specific individual characteristic, but rather encompasses a variety of psychosocial and psychological traits that either act as facilitator or barrier to PA, or do not influence PA [89]. For example, being married may be associated with familiar or household commitments, limiting time for engagement in PA, while, in turn, having an active spouse as companion for PA may act as motivator for

PA [89]. Similar effects are expected in unmarried persons and, thus, on average, the impact of the marital status on PA may be null, as observed in this thesis.

### 5.3.5 Physical activity level in pretest 2 of the German National Cohort used to assess research question 1

In the German National Cohort pretest 2, around 32% of participants fulfilled the WHO PA recommendation, while around two thirds of the population was 'insufficiently' active, which is far more than based on estimates from German surveillance data using subjective PA information [32]. However, as discussed, agreement in PA assessed via subjective methods and accelerometry is limited, and higher prevalences of 'insufficient' PA level based on accelerometry-based were shown previously (see section 2.3.2.4.2). Pretest 2 participants spent 79%, 19%, and 0.7% of active time in low, moderate, or VV activity, and they were, thus, less active than the ActivE population (see section 5.1.3), but still slightly more active in terms of moderate and vigorous activity compared to waking uniaxial accelerometry-based PA levels reported in previous studies [1, 71, 187, 194, 241, 319]. However, triaxial 24h-accelerometry data was analyzed in the present thesis, which may result in more comprehensive and, thus, higher PA estimates than observed for accelerometry used during waking only (see section 2.5). Further, previous studies used other cut points to determine activity intensities than in the present thesis, which further limits direct comparability between studies. Above all, it is not expected that the identification of potential PA determinants is biased due to a possibly slightly higher PA level in the investigated study population.

### 5.3.6 General considerations regarding potential determinants of 24h-accelerometry-based physical activity assessed in research question 3

Generally, evidence from previous studies on potential determinants of accelerometry-based PA is currently scarce, particularly regarding activity intensities and 24h-accelerometry. On the one hand, this limited the comparability of the present with previous data. On the other hand, this underpins the lack of knowledge and the importance of the present analyses on factors influencing 24h-accelerometry-based time in overall activity and in different activity intensities. Sex, age, waist circumference, smoking, and alcohol consumption were not associated with time in overall activity in the present study, although previous studies indicated such associations [1, 24, 30, 51, 82-84, 86, 92, 93, 96, 322, 334, 335, 337, 338, 385-388]. For example, most previous studies showed self-reported total PA to differ between sexes [24, 30, 82-84, 86, 322, 334], which was not evident from the present study. Nevertheless, lack of such a finding in the present study does not question this association in general, but rather suggests that time in overall activity as assessed (movement captured via triaxial 24h-accelerometry) and operationalized (time in low to VV activity) in this thesis does not differ between sexes. Indeed, in a previous study using uniaxial accelerometry during waking, sex was found to explain less than 0.2% of total variability of PA [336] (the study included more than 3,800 participants and the large sample size resulted in an anyway significant association between sex and PA [80, 389]). Accordingly, differences in the assessment and operationalization of PA parameters (see section 2.4) may have contributed to divergent findings on PA influencing factors in the present compared to previous analyses, which has already been shown for objectively versus subjectively assessed PA [243, 282, 283]. Interestingly, in the present thesis, none of the investigated potential determinants was associated with both, time in overall activity and proportion of time spent in different activity intensities. All these aspects underpin the importance of a differentiated analysis of 24h-accelerometry-based habitual time in overall and in differentially intense activity, as performed in this thesis.

In the present analyses, many effect sizes regarding the change in daily PA for a 1-unit increment of the respective potential determinant were small. This may partly be due to the relatively low variance of PA parameters across the entire pretest 2 population, especially, in the proportion of active time spent in the different activity intensities. For example, the 95% CI in time in overall activity encompassed around 20 minutes and less than 2% in proportions of active time spent in the different activity intensities (see **Table 20**). Thus, predictions of differences in PA parameters depending on potential determinants of PA were made based on this small range in the PA outcome, and, compared to that, effect sizes observed in this study are plausible. Further, one must consider that some of the investigated potential determinants are correlated, such as smoking and socioeconomic characteristics; education, employment status, and (net household) income; or age and BMI or waist circumference [276, 311, 374, 375]. Thus, effects of single factors may accumulate, when several potential determinants are applicable to a person. The joint effects may be complementary (effect on overall activity plus effect on activity intensities, see section 5.3.1.4), additive (effects on the same PA measure in the same direction), or contrary (negative plus positive effect). Thus, depending on the individual characteristics, the impact on PA may be important. Further, as discussed for continuous measures, considering larger than 1-unit changes can result in an epidemiologically relevant impact on PA. Finally, given that the most considerable beneficial effect of PA is evident for increasing PA from inactivity to just an above-inactive PA level (see section 2.2, 2.3.2.4) [15, 45, 51, 117, 119, 120, 122, 123, 194-197], already a small impact on PA of potential determinants assessed here may be relevant for the individual.

For the majority of observed associations an underlying, but not assessed variable, either related to the potential determinant and the outcome (unmeasured, residual confounding) or on the pathway from the potential determinant to the outcome (mediator) [26, 30, 80, 81, 227], is assumed to be relevant, as discussed (e.g., cardiopulmonary capacity, lack of time). This is in line with the ecological model suggesting a complex interrelation between several multilayered PA influencing factors and levels [77, 271]. It further supports the call of experts that promoting PA requires multi- and intersectoral engagement [27, 272-274]. Interestingly, in this thesis, most factors found to be related to 24h-accelerometry-based PA were negatively associated with habitual time in overall and differentially intense activity (**Figure 13**). This may indicate that, on the population level, potential barriers to PA have a stronger impact on PA than facilitators, i.e., that decreasing the individual PA level is easier than increasing it.

However, it is important to note that in the present thesis a cross-sectional analysis was conducted. Thus, strictly, causal inferences could not be drawn, but, rather, factors associated with PA were identified (i.e., correlates), enabling to estimate the strength of factors in predicting habitual 24h-accelerometry-based PA and the direction of this association [26, 30, 80, 81, 227]. Similarly, reverse causality cannot be ruled out for modifiable potential determinants, i.e., one cannot always distinguish between the potential determinant and the effect [26, 81, 227]. For example, an inverse association with PA was found for BMI and diabetes or dyslipidemia in both directions, i.e., PA was either the outcome or potential determinant [8-14, 17, 45, 51, 86, 115, 116, 337, 338, 390].

Finally, raw *p*-values were presented and discussed, and some *p*-values were just below the significance level, indicating that the respective findings may also be due to chance. Considering a 5% significance level and four different linear regression models that were analyzed (one for each PA outcome), *p*-values <0,125 are considered to be statistically significant, when taking multiple testing and the most conservative Bonferroni adjustment into account [81, 227]. Accordingly, having a university entrance qualification and not being employed were negatively associated with time in overall activity, while higher age, waist circumference (in men), and current smoking (in women) were associated with the proportion of active time spent in different activity intensities. For meeting the WHO PA recommendation, current smoking remains as factor negatively associated with the likelihood of being sufficiently active. These associations were consistently found in both regression models (model 1 and model 2) assessed in this thesis and were identified as potential PA determinants also in the sensitivity analyses (with exception of waist circumference; see sections 4.3.2.4 and 4.3.3.4), further indicating the relevance of these potential determinants for 24h-accelerometry-based PA.

### 5.3.7 Contribution of this thesis to knowledge on potential determinants of physical activity using 24h-accelerometry in epidemiology

Accordingly, in this thesis, unmodifiable (e.g., age) and modifiable (e.g., smoking status) potential determinants of 24h-accelerometry-based PA were identified. While the presented information on direction (positive versus negative) and strength of associations of modifiable potential determinants with 24h-accelerometry-based PA can help to identify promising targets for PA promotion strategies in terms of individual and public health, unmodifiable potential PA determinants may not be relevant for the individual (which cannot change the respective factor), but still at the population level, since these factors may help to identify populations at risk for lacking PA (e.g., elderly). Further, all potential determinants identified in this thesis may help to guide planning the assessment of predictors in future studies and to include predictors in statistical analyses to draw sound conclusions from analyses with PA as outcome using 24h-accelerometry in epidemiology [26, 30, 80, 81].

## 5.4 Strengths and limitations

### 5.4.1 General strengths and limitations of this thesis

A major strength of the present thesis is the focus on participants assessed under free-living conditions in all studies included, i.e., in ActivE, KORA, and pretest 2 of the German National Cohort. In contrast to most previous studies using accelerometry [31, 70-75], 24h-accelerometry data was available for the present analyses that was assessed over a 1-week to 2-weeks period allowing to capture a comprehensive picture of the individual habitual PA (see section 2.5). All three studies encompassed a broad spectrum of participants' characteristics, including biological, lifestyle, occupational, and health-related factors, which allowed for drawing sound conclusions on the general adult population with similar characteristics. With the ActivE study, voluntary participants that are supposed to have been highly motivated and to have followed the study protocol properly were used to examine the reliable assessment of PA using 24h-accelerometry (RQ 1). Indeed, few NWT were reported in ActivE, thus, best possibly unaffected estimates of habitual PA were presumably retrieved, allowing for drawing meaningful conclusions on variability and reliability of 24h-accelerometry-based habitual PA. Regarding the investigation of NWT detection in 24h-accelerometry (RQ 2), using two independent studies on the general adult population from the North and the South of Germany, as well as from a convenience (ActivE) and a population-based (KORA) sample enabled the evaluation of NWT detection under optimal (ActivE) as well as sub-optimal (KORA) conditions; the latter probably more likely reflects the situation in cohort studies. Since in both, ActivE and KORA, diary data on NWT and the sleep/wake-rhythm was available, differential analyses of the NWT algorithms' performance were possible, i.e., over the total time of 24h-assessment, and for waking and sleeping phases separately. For analyzing potential determinants of multiday 24h-accelerometry-based PA (RQ 3), data from 16 national-wide study centers on the general adult population drawn from population registries was available. The multicentric study design of pretest 2 of the German National Cohort and the use of standard operating procedures to collect data across study centers provided a broad spectrum of individual characteristics from nearly all regions of Germany. This allows for generalizing findings to the general adult German population (external validity). However, generally, previous data for comparability of the present results were scarce regarding all RQs, since previous studies were either based on self-reported PA, used older uniaxial accelerometers or other brands, accelerometry during waking only, were limited to specific population or age groups, did not assess activity intensities, used other cut points to determine activity intensities, or differentially operationalized overall activity. Additionally, the studies used in the context of the present thesis may have some limitations. First, although covering a wide range of characteristics that might be comparable to the spectrum seen in the general German adult population, for example, regarding pre-existing medical conditions, BMI, or the net household income (RQ 3) [391-395], none of the studies originally intended to be fully representative of the German population. For example, in pretest 2, more participants were former smokers, while slightly less participants were current smokers or never-smokers compared to German survey data [396]. This may reflect that, generally, participants in epidemiological studies are supposed to more likely be health-conscious than the general population, and a selection or non-respond bias can, therefore, not be ruled out [26, 80, 397]. Besides being limited to adults, findings from the present analyses may be different in specific populations that show different phenotypes, like extreme obesity, younger or older ages, or narrower age ranges, or chronic diseases (e.g., advanced cardiovascular or respiratory diseases). Since all these conditions may have an impact on the variables of interest in the present thesis, i.e., on variability (RQ 1), on frequency and duration of NWT and (non-) moving periods (RQ 2), on presence and impact of potential PA determinants (RQ 3), as well as on wearing compliance and PA patterns, further studies are warranted to investigate the issues examined in this thesis in other populations.

However, addressing different population groups was beyond the scope of this thesis. Although participants in ActivE, KORA, and pretest 2 were instructed to pursue their normal daily routine, generally, participating in an observational study and, particularly, keeping a diary (ActivE and KORA) may have affected the activity behavior of participants towards a non-habitual manner [31, 58, 59]. Nevertheless, data in ActivE indicated no evidence for reactivity (see section 5.1.1) and one may assume that this holds true for all studies assessed in this thesis. Further, the range in PA parameters was quite small across participants in ActivE (RQ 1) and pretest 2 (RQ 3), but a low variability in PA within populations was also reported in other studies on waking accelerometry [398-401]. For the analyses on a reliable assessment of PA (RQ 1) and on potential determinants of 24h-accelerometry (RQ 3), the ‘Freedson Adult VM3 (2011)’ algorithm was used. Since this algorithm does not allow separating inactivity from low activity, a new cut point was derived for this distinction (see section 3.4.3). Nevertheless, it was not possible to determine sedentary behavior with a validated algorithm in this thesis, although this may be important (see section 2.2.1). Previous studies suggested cut points to distinguish between light activity and sedentary behavior for the GT3X(+) accelerometer, but these were derived from accelerometry used during waking, for uniaxially recorded data only, or for specific populations (inactive office worker), and cut points are not validated [67, 402]. Nevertheless, these studies suggested cut points to determine sedentary behavior of 50 cpm and 150 cpm, which is comparable to the limit derived in the present study; thus, results found for inactivity in RQ 1 (inversely for time in overall activity in RQ 3) in this thesis may be a proxy for sedentary behavior. Finally, investigating different domains or types of PA was not possible in this thesis.

Specific potential limitations regarding the three objectives addressed in this thesis are:

### 5.4.2 Limitations regarding the investigation of the reliable assessment of physical activity using multiday 24h-accelerometry under free-living conditions (research question 1)

For the investigation of a reliable assessment of PA using 24h-accelerometry (RQ 1), the size of the ActivE population was relatively small. However, confidence intervals for ICCs were narrow, indicating the sample size to be sufficient to obtain robust reliability estimates. Further, NWT reported in the diaries was not excluded from accelerometry data, being aware that this may have resulted in overestimation of time in inactivity. Since in this RQ, the absolute time (min/d) spent in activity intensities was used, the above-inactivity intensities were not affected by including NWT periods (see section 2.5.2). However, as the variability found for time in inactivity was in accordance with findings for the other PA measures (i.e., opposite to patterns found for time in activity), the impact of NWT inclusion is supposed to be small. Regarding the observed week-to-week reliability of 24h-accelerometry-based PA, it is important to note that two consecutive weeks were assessed. Reliability of two weeks assessed further apart or randomly selected may be lower. Similarly, focusing on domain-specific PA, like occupational PA may result in a different variability and, thus, reliability of 24h-accelerometry-based PA than observed for general PA in this thesis [214]. Finally, the analyses on reliability did not encompass two entire weeks, because days of assessment had to be excluded due to the study protocol (see section 3.4.1). However, this may only have resulted in an underestimation of reliability, since the calculation of ICCs as measures of the reliability was based on an unbalanced week-to-week comparison and ICCs were still high. Nevertheless, for sensitivity analyses, day 14 (i.e., the sixth day of week 2) was included in all analyses, which allowed a balanced comparison between week 1 and 2 (i.e., six days in each week). Indeed, ICCs for the balanced week-to-week comparison were slightly higher, but, generally, results of all analyses of RQ 1 including day 14 were not substantially different from the main results.

### 5.4.3 Limitations regarding the investigation on detection of accelerometer non-wear time using 24h-accelerometry under free-living conditions (research question 2)

For testing algorithms requiring consecutive zero-acceleration readings for NWT detection in 24h-accelerometry (RQ 2), it should be mentioned that in ActivE and KORA two different ActiGraph models were used, i.e., the GT3X+ in ActivE and the GT3X in KORA. However, there are no fundamental differences in technical characteristics between these two direct following models (see section 3.3.2). Further, PA measures provided by these two devices were shown to highly agree, including counts derived from the vector magnitude that were the basis for examining NWT detection in 24h-accelerometry in the present analyses [219, 301]. Further, in ActivE, accelerometers were hip-worn over the total time of assessment, whereas KORA participants were instructed to wear the accelerometer on the hip during waking and to change the device to the wrist for sleeping. Since a recent validation study using the GT3X accelerometer showed a strong correlation of cpm data between waist- and hip-worn devices [403], while, in turn, data from hip-worn GT3X and GT3X+ also agree [219, 301], differences in wearing protocols between the two studies are expected to not have substantially influenced the findings. This assumption is supported by the similar absolute values and relative differences found between the NWT algorithms in criteria assessed (i.e., sensitivity, specificity, and overlap) between both studies. Accelerometer wear times were defined as absence of any NWT during the period analyzed. Thus, over the total time of assessment, maximal one continuous wearing period was assigned (i.e., continuous wearing period from the first to the last day of assessment), while for waking and sleeping, numbers of potentially continuous wearing periods were much higher due to the interruptions caused by the sleep/wake-rhythm. Since the number of continuous wear times detected by both, diary and accelerometry (i.e., true negative NWT detection) was included as numerator, when calculating the specificity of NWT detection (whereas the true positive detection rate was the numerator for calculating sensitivity), specificities calculated for the total time of assessment cannot directly be compared to the values found for waking and sleeping phases. Finally, participants' diaries were set to be the 'gold standard reference' for the examination of the performance of the different NWT algorithms in 24h-accelerometry, acknowledging the risk of conscious or unconscious misreporting regarding occurrence, time points, or durations of NWT periods, as well as of sleeping and waking times (see section 5.2.3).

### 5.4.4 Limitations regarding the investigation of potential determinants of physical activity using multiday 24h-accelerometry under free-living conditions (research question 3)

Although, in this thesis, around one week of 24h-accelerometry was found to reliably estimate PA, for the analyses of potential determinants of 24-accelerometry-based PA (RQ 3) a data set was required to include at least five valid days. This decision was made, since, in RQ 1, an acceptable confidence of r≥0.85 was observed for all PA parameters, when five or more 24h-accelerometry days were available per participant (see **Table 9** and section 3.4.3). Acknowledging that this is not strictly in line with the conclusion for RQ 1, this compromise was made due to the partly poor compliance of pretest 2 participants to the wearing protocol (see section 3.4.3), while aiming to obtain a sufficiently large sample size. Requiring seven days per participant, as concluded for RQ 1, would have had resulted in 63 suitable participants (see section 4.3.1), which was considered as far too small sample for drawing sound conclusions on potential determinants of 24h-accelerometry-based PA. Further, with exception of on-site assessed anthropometric measurements, factors investigated as potential PA determinants were self-reported by participants, and information could not be verified. Thus, the possibility of reporting or social desirability bias should be considered [404]. However, especially those factors assumingly being prone to bias, like alcohol consumption, smoking status, or socioeconomic characteristics showed highly significant results, indicating that such bias may not have been a major issue. Additionally, although a variety of factors potentially related to PA was included as predictors in the regression models, and the study center was adjusted for to account for the multicentric study design, residual confounding cannot be ruled out [26, 80, 81, 227]. Strictly speaking, ‘dyslipidemia’ was not assessed, since in pretest 2, subcomponents of dyslipidemia that all must be fulfilled for being diagnosed with dyslipidemia were assessed as one question (‘or’-linked) (see **Supplementary Table 1**, **Supplementary Table 2**) [289]. Further, the item on ‘dyslipidemia’ did not ask for decreased high-density lipoproteins that are part of the medical diagnoses ‘dyslipidemia’ [289]. Prevalence of ‘dyslipidemia’ may, therefore, have been underestimated in the present analyses compared to results seen in the general adult German population [391]. There was no diary information on NWT available and wearing compliance is, thus, uncertain. However, by applying the most suitable NWT algorithm derived from RQ 2, and by requiring a minimum of 5 valid days to ensure validity with a satisfactory confidence as derived from RQ 1, attempts were made to ensure validity of accelerometry data as best as possible. Since there was also no data on the sleep/wake-rhythm of participants, and since NWT during sleeping is limited (RQ 2), waking was assumed to be from 6 a.m. to 10 p.m., and no NWT longer than 120 consecutive minutes (RQ 2, see section 5.1.5) was allowed in this period. This assumed waking phase, however, will not hold true for all persons. For example, if a person got out of bed after 6 a.m., non-moving phases during sleeping between 6 a.m. and getting up may have been false positively defined as NWT. Further, as shown in this thesis, NWT detection is generally suboptimal in 24h-accelerometry, even during waking. Thus, false positive NWT identification may have caused unnecessary exclusion of participants, potentially resulting in a too strictly selected study population. Nevertheless, this may only have prevented finding existing associations and may not have resulted in false positively identifying potential determinants of PA. Allowing for up to 120 minutes of NWT was a quite liberal approach, but was chosen following the findings regarding NWT detection in 24h-accelerometry (RQ 2); further, this amount of time was previously indicated to be tolerable for NWT per day [58]. However, sensitivity analyses were performed by using a more conservatively defined sample (60-min NWT algorithm). Results were quite similar to the main results, with factors strongly related to PA in the main analyses being still identified as potential determinants. Furthermore, some participants were excluded from analyses due to missing data, either in the interview or in accelerometry. Nevertheless, there were no substantial differences in characteristics between included and excluded participants (see section 4.3.1), and, thus, the possibility of a selection bias is supposed to be neglectable. Determination, whether participants fulfilled the WHO PA recommendation, or not, was made based on time in at least moderate or vigorous activity in at least 10-minutes bouts (see section 3.5). However, by setting these two limit values (activity intensity and time), some participants may have been missed, for example, if a person spent 9 minutes in moderate activity, followed by 1 minute of low activity, followed by 2 minutes in vigorous activity. Although, in total, 11 minutes were spent in moderate-to-vigorous activity, these two activity periods did not account for the fulfillment of the WHO PA recommendation due to the 1-minute break. Finally, variability of PA parameters was quite low, which may have limited the likelihood of finding an association with potential determinants. In contrast, there was variability in potential determinants, and this broad spectrum in characteristics in the study population allowed to investigate potential determinants of 24h-accelerometry-based PA under free-living conditions.

## 5.5 Conclusion

Reliably assessing and unbiasedly estimating 'mean' PA is a precondition for identifying potential determinants of the habitual time in overall activity and in different activity intensities. In turn, a precise and detailed PA assessment and knowing PA influencing factors is a key requirement for understanding and drawing robust conclusions on the association of PA and health risk in epidemiology using 24h-accelerometry.

The present thesis showed a high within-person day-to-day variability of overall activity and of time spent in low to very vigorous activity as assessed using multiday 24h-accelerometry in the general adult population. This variability, however, was neither substantially explained by the day of assessment nor by the day of the week or by the distinction between weekdays and weekend days. Around one week of evaluable 24h-accelerometry data was found to be suitable for reliably estimating mean habitual overall activity and time in the different activity intensities. Data provided may help researchers planning the assessment length of 24h-accelerometry in new epidemiological studies and, further, allows calculation of deattenuated risk estimates from existing multiday 24h-accelerometry data assessed under free-living conditions.

In addition to knowing the required number of assessment days before data collection, examining wearing compliance, i.e., accelerometer NWT is pivotal to obtain unbiased PA estimates from collected 24h-accelerometry data. The present data suggests that an algorithm requiring 60 or more consecutive minutes of zero-acceleration readings is less appropriate to detect NWT periods and minutes in 24h-accelerometry due to a high rate of false positive NWT detection during waking and, especially, during sleeping. Since during sleeping, all tested algorithms performed weakly, while, at the same time, occurrence of NWT was generally low, NWT detection during sleeping should be valued cautiously. Additionally, all algorithms assessed missed a substantial proportion of reported NWT, since more than 85% of all NWT were shorter than 60 minutes over the total time of assessment. Further, a substantial proportion of NWT was false positively identified in 24h-accelerometry by all tested algorithms. Making a compromise between the accuracy of NWT detection and detecting as much NWT as possible, using a 120-min algorithm appears to be acceptable for NWT detection in multiday 24h-accelerometry assessed under free-living conditions.

Applying the findings from RQ 1 (number of days) and RQ 2 (NWT detection), there was evidence that higher BMI, having a university entrance qualification, and not being employed are negatively associated with time in overall activity, while for proportions of time spent in low to VV activity sex, age, smoking status, alcohol consumption, and net household income were potential determinants. Potential sex-specific determinants of active time spent in low and moderate activity were waist circumference in men and smoking status in women. Thus, the present thesis suggests that, following the ecological model explaining health behavior choices, the identified biological, behavioral, and economic factors should be considered, when planning or evaluating epidemiological studies on habitual PA using multiday 24h-accelerometry under free-living conditions.

# 6 Outlook

In the present thesis, assessing sedentary behavior with a validated algorithm using triaxial accelerometry data was not possible, although it is an independent health risk factor and, thus, epidemiologically relevant (see section 2.2.1, 2.3.2.4.1). Thus, developing and validating an algorithm to enable determination of sedentary behavior in triaxial (24h-) accelerometry data is warranted. Then, analyses regarding RQ 1 and RQ 3 performed in this thesis should be repeated, since knowing variability, reliability, and potential determinants of sedentary behavior is essential for understanding its association with health risk in epidemiology using 24h-accelerometry.

Regarding RQ 1, due to possible seasonal as well as month-to-month variability of PA [31, 207-214], investigating variability, number of days needed, and reliability of non-consecutive weeks, being randomly selected over the course of the year and including different seasons, is desirable to enable statements on the estimation of long-term, i.e., habitual, average overall activity by a single measurement in epidemiological studies.

In terms of RQ 2, instead of processed data, using raw accelerometry data for NWT detection may provide more detailed information that presumably allows detection of slightest movements. Alternatively, other approaches for NWT detection based on processed data should be explored. While using cumulative distribution functions, as proposed for another wrist-worn accelerometer brand than used in this thesis, may only be a population-specific approach to define the suitable length of NWT definition [270], deriving algorithms that define NWT based on additional criteria than only requiring consecutive zero-acceleration readings may be a promising approach. For example, detecting a short strong acceleration before and after a potential NWT may indicate a higher probability of a recorded removing and putting on of the accelerometer, supporting the assumption of a true NWT period. Further, without having diary information, challenges may arise from the need to detect wearing days (e.g., when the device is not put on in the study center, but mailed to participants) or waking phases. Previous studies using the GT3X+ in older adults or another accelerometer brand showed that this may be possible based on automated algorithms applied to accelerometer data [405, 406], but further studies should address this issue in the general population.

Regarding RQ 3, to fully understand the impact of identified potential determinants of 24h-accelerometry-based PA, the association of the respective factors with health outcomes should be investigated. Further, in the present analyses only information on individual characteristics belonging to the intrapersonal and micro-environmental home or household level was available to be studied as potential PA determinants (see **Table 2** and section 3.6.4). Since several factors belonging to other levels of influence (see **Table 2**) are purportedly related to PA, like psychological (e.g., goal orientation), physical (e.g., proximity to green areas), or political (e.g., land use policies) factors [78, 82-84, 86-92, 275, 276], further prospective studies on determinants of 24h-accelerometry-based PA are warranted to gain inside into the interplay of factors influencing 24h-PA. Additionally, genetic, hormonal, or metabolic markers should be considered as endogenous factors, since these may affect the physiological capacity or psychological traits, like fatigue, listlessness, neuroticism, or openness, thereby potentially influencing PA [87, 407, 408]. Evaluating (longitudinal) data from the main phase of the German National Cohort may provide an opportunity for such more comprehensive analyses on determinants of 24h-accelerometry-based PA [76, 167, 292].

To account for limitations in assessing PA by only accelerometry, using complementary methods that may make up for the limitations of only one measurement should be further addressed, like a combined assessment of self-reported and objective PA or using multiphasic devices that capture several physiological markers including acceleration, heart rate, skin temperature, or sweating [31, 36, 40, 43, 173]. Such multisensing assessment approaches are supposed to overcome shortcomings of each single technique, since the sources of measurement errors are independent from each other [31, 36, 40, 43]. For example, when using a combination of accelerometer plus heart rate monitor, capturing the increase in heart rate might compensate for the limited ability of accelerometers to capture non-static exertion (see section 2.3.2.4.2), while the possibility of elevated heart rates due to non-PA-related factors (see section 2.3.2.2) can be accounted for, when movement is detected via an accelerometer [36, 40, 43]. Similarly, a combined approach may help to differentiate times of non-wear from times of inactivity; detecting a heart rate ensures that the device was worn during periods of zero-acceleration readings [43]. Although devices combining an accelerometer and heart rate monitor are relatively new, first validation studies show promising results as compared to established methods [36, 40, 43]. However, multisensing methods are quite expensive and, thus, not affordable in the context of large-scale epidemiological studies, and they further require technical expertise for processing and evaluating the complexity of data assessed [40, 43].

In the present thesis, bouted triaxial 24h-accelerometry data, i.e., accelerometry data aggregated over 1 second to 60 seconds (see section 3.5), was analyzed. Although this already exceeds many of the previous studies that mostly rely on self-reported PA, uniaxial accelerometry, accelerometry applied during waking only, or longer accelerometry data bouts, still, it did not take full advantage of the comprehensive accelerometry data (see section 2.4.2). Thus, the use of raw (or high-frequency) data requires further analyses regarding its possible contribution to fully benefit from the extensive PA data provided by accelerometry. Although previous studies indicate sophisticated techniques, such as machine learning techniques as suitable approaches for using raw data and for PA pattern recognition [173, 232, 238-240, 409] that may overcome limitations of accelerometry in detecting the individual PA behavior (see section 2.3.2.4.2), studies using such techniques based on triaxial (24h-) accelerometry data assessed under free-living conditions are scarce [230, 410, 411]. Investigating different PA patterns in terms of type or domain that may be epidemiological relevant should be targeted in future by using these methods [12, 49, 50, 52, 122, 161, 162].

Given the increased application of triaxial accelerometry in epidemiology, and given the evidence, showing activity intensities to have a distinct and independent effect on health risk (see sections 2.2.1 and 2.3.2.4.3), more research is warranted on the valid determination of activity intensities from triaxial accelerometer data. Further, considering the development of accelerometry-based PA guidelines should be put forward, since the health impact of accelerometry-based PA is supposed to differ from subjectively reported PA [31, 33, 191, 192], limiting the applicability of, for example, the WHO PA recommendation on accelerometry. Above all, consensus on data collection, processing, operationalization, and analyses, or, at least, proper reporting on this information is needed to allow comparability and data harmonization between studies [31, 166, 200].

Finally, following the concept of time-use epidemiology, future studies should not only assess PA as isolated lifestyle behavior, but should rather take into account times of sleeping and inactivity, since together with PA, these basic behaviors make up the total 24h of a day, being mutually exclusive [412]. Thus, above all, given its advantages for comprehensively assessing PA with high feasibility and acceptance under free-living conditions (see section 2.5) and assuming validated algorithms for data processing, promoting the application of 24h-accelerometry over multiple days in epidemiology to assess habitual movement-related behavior 24h per day is strongly recommended.

# 7 Funding


## 7.1 Detection of accelerometer non-wear time using 24h-accelerometry under free-living conditions (research question 2)

The KORA study was initiated and financed by the Helmholtz Zentrum München – German Research Center for Environmental Health, which is funded by the German Federal Ministry of Education and Research (BMBF) and by the State of Bavaria. This work was further supported by the Comprehensive Pneumology Center Munich (CPC M) as member of the German Center for Lung Research.

## 7.2 Determinants of physical activity using multiday 24h-accelerometry under free-living conditions (research question 3)

This project was conducted in the context of the Pretest studies of the German National Cohort. These were funded by the participating institutes of the Helmholtz Association and by grants by the Federal Ministry of Education and Research to the participating universities and Institutes of the Leibniz Association. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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# Appendix

## Supplementary Tables

**Supplementary Table 1**: List of questions from the personal computer-assisted interview during pretest 2 of the German National Cohort, German version

| Variablenlabel | Wert | Label |
|---|---|---|
| **Geschlecht** | 1 | m |
| | 2 | w |
| **Alter** | Jahre | |
| **Haben Sie jemals Zigaretten, Zigarren, Zigarillos, Pfeife oder andere Tabakprodukte geraucht?** | 1 | Ich habe nie geraucht |
| | 2 | Ja, ich rauche bis heute |
| | 3 | Ja, ich habe früher geraucht |
| | 999 | Weiß nicht |
| | 888 | Möchte nicht antworten |
| **Wie oft nehmen Sie ein alkoholisches Getränk, also z. B. ein Glas Wein, Bier, Mixgetränk, Schnaps oder Likör zu sich?** | 1 | Nie |
| | 2 | 1 Mal im Monat oder seltener |
| | 3 | 2 bis 4 Mal im Monat |
| | 4 | 2 bis 3 Mal pro Woche |
| | 5 | 4 Mal pro Woche oder öfters |
| | 999 | Weiß nicht |
| | 888 | Möchte nicht antworten |
| **Welchen höchsten allgemeinbildenden Schulabschluss haben Sie?** Sagen Sie es mir bitte anhand dieser Liste. | 1 | Schüler/-in, besuche eine allgemeinbildende Vollzeitschule |
| | 2 | Von der Schule abgegangen ohne Hauptschulabschluss (Volksschulabschluss) |
| | 3 | Hauptschulabschluss (Volksschulabschluss) |
| | 4 | Realschulabschluss (Mittlere Reife) |
| | 5 | Polytechnische Oberschule der DDR mit Abschluss der 8. oder 9. Klasse |
| | 6 | Polytechnische Oberschule der DDR mit Abschluss der 10. Klasse |
| | 7 | Fachhochschulreife, Abschluss einer Fachoberschule |
| | 8 | Allgemeine oder fachgebundene Hochschulreife/Abitur |
| | 9 | Abitur über zweiten Bildungsweg nachgeholt |
| | 10 | Einen anderen Schulabschluss |
| | 999 | Weiß nicht |
| | 888 | Keine Angabe |

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***Supplementary Table 1 continued from previous page***

| Variablenlabel | Wert | Label |
|---|---|---|
| **Sind Sie zurzeit erwerbstätig? Sagen Sie es mir bitte anhand dieser Liste.** Unter Erwerbstätigkeit wird jede bezahlte bzw. mit einem Einkommen verbundene Tätigkeit verstanden, egal welchen zeitlichen Umfang sie hat. | 1 | Vollzeit erwerbstätig |
| | 2 | Teilzeit erwerbstätig |
| | 3 | Altersteilzeit |
| | 4 | Geringfügig erwerbstätig, 400 Euro- oder Mini-Job |
| | 5 | "Ein-Euro-Job" (bei Bezug von Arbeitslosengeld II) |
| | 6 | Gelegentlich oder unregelmäßig beschäftigt |
| | 7 | In einer beruflichen Ausbildung / Lehre |
| | 8 | In Umschulung |
| | 9 | Bundesfreiwilligendienst / Freiwilliges Soziales / Ökologisches Jahr |
| | 10 | Mutterschafts-, Erziehungsurlaub, Elternzeit oder sonstige Beurlaubung |
| | 11 | Nicht erwerbstätig |
| | 999 | Weiß nicht |
| | 888 | Keine Angabe |
| **Ich lege Ihnen jetzt eine Liste vor. Bitte sagen Sie mir anhand dieser Liste, wie hoch ungefähr das monatliche Nettoeinkommen Ihres Haushaltes insgesamt ist.** Das heißt, das Einkommen, das alle Haushaltsmitglieder zusammen haben. Gemeint ist dabei die Summe, die sich aus Lohn, Gehalt, Einkommen aus selbständiger Tätigkeit, Rente oder Pension ergibt. Rechnen Sie bitte auch alle Einkünfte aus öffentlichen Verpachtung, Vermögen, Wohngeld, Kindergeld und sonstige Einkünfte Beihilfen, Einkommen aus Vermietung, hinzu. Ziehen Sie dann Steuern und Betriebsausgaben und Sozialversicherungsbeiträge ab. Bitten nennen Sie mir die Zahl, die vor dem ungefähren monatlichen Nettoeinkommen Ihres Haushaltes steht. Sagen Sie es mir bitte anhand dieser Liste. | 1 | Unter 500 € |
| | 2 | 500 € bis unter 750 € |
| | 3 | 750 € bis 1,000 € |
| | 4 | 1,000 € bis 1,250 € |
| | 5 | 1,250 € bis 1,500 € |
| | 6 | 1,500 € bis 1,750 € |
| | 7 | 1,750 € bis 2,000 € |
| | 8 | 2,000 € bis 2,250 € |
| | 9 | 2,250 € bis 2,500 € |
| | 10 | 2,500 € bis 3,000 € |
| | 11 | 3,000 € bis 3,500 € |
| | 12 | 3,500 € bis 4,000 € |
| | 13 | 4,000 € bis 4,500 € |
| | 14 | 4,500 € bis 5,000 € |
| | 15 | 5,000 € bis 6,000 € |
| | 16 | 6,000 € bis 8,000 € |
| | 17 | 8,000 € oder mehr |
| | 999 | Weiß nicht |
| | 888 | Keine Antwort |

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***Supplementary Table 1 continued from previous page***

| Variablenlabel | Wert | Label |
|---|---|---|
| **Welchen Familienstand haben Sie?** Beachten Sie bitte: "Verheiratet", "Geschieden" und "Verwitwet" beziehen sich auch auf eine eingetragene gleichgeschlechtliche Lebenspartnerschaft. "Getrenntlebend" heißt sich voneinander getrennt zu haben und nicht nur räumlich getrenntlebend. | 1 | Verheiratet, mit Ehepartner/-in zusammenlebend |
| | 2 | Verheiratet, vom Ehepartner/-in getrenntlebend |
| | 3 | Ledig |
| | 4 | Geschieden |
| | 5 | Verwitwet |
| | 999 | Weiß nicht |
| | 888 | Keine Angabe |
| **Wurde bei Ihnen jemals von einem Arzt eine Zuckerkrankheit, auch Diabetes mellitus genannt, diagnostiziert?** | | *Männer:* |
| | 1 | Ja |
| | 2 | Nein |
| | 999 | Weiß nicht |
| | 888 | Keine Angabe |
| | | *Frauen:* |
| | 1 | Ja, die Erstdiagnose erfolgte im Rahmen einer Schwangerschaft, nach der Schwangerschaft war aber kein Diabetes mehr feststellbar |
| | 2 | Ja, die Erstdiagnose erfolgte im Rahmen einer Schwangerschaft, nach der Schwangerschaft war der Diabetes weiterhin feststellbar |
| | 3 | Ja, die Erstdiagnose erfolgte nicht im Rahmen einer Schwangerschaft |
| | 4 | Nein |
| | 999 | Weiß nicht |
| | 888 | Keine Angabe |
| **Wurden bei Ihnen jemals von einem Arzt erhöhte Blutfette bzw. Cholesterin und/oder Triglyzeride diagnostiziert?** | 1 | Ja |
| | 2 | Nein |
| | 999 | Weiß nicht |
| | 888 | Keine Angabe |

f, female; m, male

**Supplementary Table 2**: English translation of the list of questions from the personal computer-assisted interview during pretest 2 of the German National Cohort

| variable label | value | label |
|---|---|---|
| **sex** | 1 | m |
| | 2 | f |
| **age** | years | |
| **Have you ever smoked cigarettes, cigars, cigarillos, pipes, or other tobacco products?** | 1 | I have never smoked |
| | 2 | yes, I currently smoke |
| | 3 | yes, I smoked in the past |
| | 999 | don't know |
| | 888 | do not want to answer |
| **How often do you consume an alcoholic drink, e.g., a glass of wine, beer, mixed drinks, schnapps, or liquor?** | 1 | never |
| | 2 | max. 1x/month |
| | 3 | 2 - 4x/month |
| | 4 | 2 - 3x/week |
| | 5 | 4x/week or more frequently |
| | 999 | don't know |
| | 888 | do not want to answer |
| **What is your highest school-leaving qualification?** Please answer according to this list. | 1 | school student, I am visiting a full-time school with general educational value |
| | 2 | leave school without having completed junior high school |
| | 3 | completed junior high school |
| | 4 | secondary school certificate |
| | 5 | polytechnic secondary school (8 and 9 grades completed) (German Democratic Republic) |
| | 6 | polytechnic secondary school (10 grades completed) (German Democratic Republic) |
| | 7 | advanced technical college certificate ('Fachhochschulreife', 'Anschluss eider Fachoberschule') |
| | 8 | university entrance qualification or subject-related entrance qualification/abitur |
| | 9 | abitur through second chance education |
| | 10 | other |
| | 999 | don't know |
| | 888 | not specified |

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***Supplementary Table 2 continued from previous page***

| variable label | value | label |
|---|---|---|
| **Are you currently employed? Please answer according to this list.**<br><br>'Employment' comprises any payed or income-related occupation regardless of its duration | 1 | full time employed |
| | 2 | part time employed |
| | 3 | partial retirement |
| | 4 | marginally employed, 400-Euro-job, or 'mini-job' |
| | 5 | "one-Euro-job' (while receiving unemployment benefit') |
| | 6 | occasionally or sporadically employed |
| | 7 | in vocational training/apprenticeship |
| | 8 | in retraining |
| | 9 | voluntary civil service/social year/ecological year |
| | 10 | maternity leave, childcare leave, parental leave, or other leave of absence |
| | 11 | not employed |
| | 999 | don't know |
| | 888 | not specified |
| **I am going to show you a list. Please tell me according to this list, what is your approximate net monthly household income in total?**<br>That is the income that all household members have together. Here, the sum of wage, salary, income from self-employed work, retirement pay, and pension is meant. Please consider all income from public subsidies, leasing, renting, capital, housing allowance, child benefit, an all other income. Then, subtract taxes, business expenses, and social security contributions. Please tell me the number standing ahead of your approximate net monthly household income. Please tell me according to this list. | 1 | < 500 € |
| | 2 | 500 € to 750 € |
| | 3 | 750 € to 1,000 € |
| | 4 | 1,000 € to 1,250 € |
| | 5 | 1,250 € to 1,500 € |
| | 6 | 1,500 € to 1,750 € |
| | 7 | 1,750 € to 2,000 € |
| | 8 | 2,000 € to 2,250 € |
| | 9 | 2,250 € to 2,500 € |
| | 10 | 2,500 € to 3,000 € |
| | 11 | 3,000 € to 3,500 € |
| | 12 | 3,500 € to 4,000 € |
| | 13 | 4,000 € to 4,500 € |
| | 14 | 4,500 € to 5,000 € |
| | 15 | 5,000 € to 6,000 € |
| | 16 | 6,000 € to 8,000 € |
| | 17 | 8,000 € or more |
| | 999 | don't know |
| | 888 | not specified |
| **What is your marital status?**<br>Please note: 'Married', 'divorced', and 'widowed' also relate to registered same-sex partnerships. 'Living apart from spouse' means to have separated from each other and not only to live spatially apart. | 1 | married, living together with spouse |
| | 2 | married, living apart from spouse |
| | 3 | unmarried |
| | 4 | divorced |
| | 5 | widowed |
| | 999 | don't know |
| | 888 | not specified |

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***Supplementary Table 2 continued from previous page***

| variable label | value | label |
|---|---|---|
| **Have you ever by a physician been diagnosed with diabetes mellitus?** | | *men:* |
| | 1 | yes |
| | 2 | no |
| | 999 | don't know |
| | 888 | not specified |
| | | *women:* |
| | 1 | yes, initially diagnosed during pregnancy; after pregnancy, no diabetes mellitus determinable anymore |
| | 2 | yes, initially diagnosed during pregnancy; after pregnancy, diabetes mellitus still determinable anymore |
| | 3 | yes, not initially diagnosed during pregnancy |
| | 4 | no |
| | 999 | don't know |
| | 888 | not specified |
| **Have you ever by a physician been diagnosed with elevated blood lipid levels, hypercholesterolemia, and/or hypertriglyceridemia?** | 1 | yes |
| | 2 | no |
| | 999 | don't know |
| | 888 | not specified |

f, female; m, male

**Supplementary Table 3**: Physical activity within- and between-person variance and number of days to assess habitual physical activity using the Spearman-Brown prophecy formula, total (N=50)

| PA parameter[a] | within-person variance | between-person variance | | number of days |
|---|---|---|---|---|
| | $s_w^2$ | $s_b^2$ | $ICC_s$ | N[b] |
| overall activity, cpm | 0.09593 | 0.06317 | 0.40 | 7 |
| time in inactivity, min/d | 0.00273 | 0.00225 | 0.45 | 5 |
| time in low activity, min/d | 0.06727 | 0.05627 | 0.46 | 5 |
| time in moderate activity, min/d | 0.09604 | 0.05033 | 0.34 | 8 |
| time in vigorous activity, min/d | 0.28890 | 0.21890 | 0.43 | 6 |
| time in very vigorous activity, min/d | 0.57190 | 0.34590 | 0.36 | 7 |

cpm, counts per minute; $ICC_s$, single-day reliability ($s_b^2/(s_b^2+s_w^2)$); min/d, minutes per day; N, number of days to assess physical activity based on a desired reliability $ICC_t$ [211]; PA, physical activity; $s_b^2$, between-person variance over 11 days of physical activity; $s_w^2$, within-person variance over 11 days of physical activity

[a]all analyses were performed using log-transformed data

[b]N is calculated based on a desired reliability of $ICC_t$=0.8 and is rounded up to the nearest full number of days

**Supplementary Table 4**: Physical activity within- and between-person variance and number of days to assess habitual physical activity, sensitivity analyses using 12 days per participant, total (N=50)

| | | | % of total variance | | |
|---|---|---|---|---|---|
| **PA parameter[a]** | **within-person variance** | **between-person variance** | **within-person variance** | **between-person variance** | **number of days** |
| | **$s_w^2$** | **$s_b^2$** | **$s_w^2$** | **$s_b^2$** | **$D^b$** |
| overall activity, cpm | 0.09679 | 0.06273 | 60.7 | 39.3 | **7** |
| time in inactivity, min/d | 0.00269 | 0.00221 | 54.8 | 45.2 | **6** |
| time in low activity, min/d | 0.06541 | 0.05703 | 53.4 | 46.6 | **5** |
| time in moderate activity, min/d | 0.09905 | 0.04941 | 66.7 | 33.3 | **9** |
| time in vigorous activity, min/d | 0.28250 | 0.21320 | 57.0 | 43.0 | **6** |
| time in very vigorous activity, min/d | 0.56600 | 0.32400 | 63.6 | 36.4 | **8** |

cpm, counts per minute; D, number of days to assess physical activity based on a given r (with r as assumed correlation between observed and true mean of physical activity parameter) [304]; min/d, minutes per day; PA, physical activity; $s_b^2$, between-person variance over 12 days of physical activity; $s_w^2$, within-person variance over 12 days of physical activity

[a]all analyses were performed using log-transformed data

[b]D is calculated based on an assumed correlation between observed and true mean physical activity of r=0.9 and is rounded up to the nearest full number of days

**Supplementary Table 5**: Explanation of variance of habitual physical activity, sensitivity analyses using 12 days per participant, total (N=48)

| PA parameter[a] | sex | subject | week (1 vs. 2) | day of the week (Mon-Sun) | weekday vs. weekend day | residual |
|---|---|---|---|---|---|---|
| | % of total variance | | | | | |
| overall activity, cpm | 0.0 | 39.7 | - | 0.7 | - | 59.6 |
| | 0.0 | 37.5 | 0.0 | - | 11.7 | 50.8 |
| time in inactivity, min/d | 2.2 | 44.6 | - | 1.3 | - | 52.0 |
| | 2.1 | 42.5 | 0.0 | - | 10.6 | 44.8 |
| time in low activity, min/d | 7.7 | 42.4 | - | 7.7 | - | 42.3 |
| | 7.3 | 39.9 | 0.0 | - | 15.3 | 37.5 |
| time in moderate activity, min/d | 0.0 | 33.5 | - | 2.0 | - | 64.5 |
| | 0.0 | 30.7 | 0.0 | - | 16.7 | 52.6 |
| time in vigorous activity, min/d | 0.0 | 43.4 | - | 0.8 | - | 55.8 |
| | 0.0 | 42.2 | 0.0 | - | 6.5 | 51.3 |
| time in very vigorous activity, min/d | 0.0 | 36.7 | - | 1.1 | - | 62.2 |
| | 0.0 | 36.1 | 0.4 | - | 2.3 | 61.2 |

cpm, counts per minute; min/d, minutes per day; vs., versus
[a]all analyses were performed using log-transformed data

**Supplementary Table 6**: Correlations between observed and true physical activity based on a given number of days of assessment, sensitivity analyses using 12 days per participant, total (N=50)

| **PA parameter**[a] | **within-person variance** | **between-person variance** | | **$r_D$** | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **$s_w^2$** | **$s_b^2$** | **$s_w^2/s_b^2$** | **$D_r$=1** | **$D_r$=2** | **$D_r$=3** | **$D_r$=4** | **$D_r$=5** | **$D_r$=6** | **$D_r$=7** | **$D_r$=8** | **$D_r$=9** | **$D_r$=10** | **$D_r$=11** | **$D_r$=12** |
| overall activity, cpm | 0.09679 | 0.06273 | 1.54 | 0.63 | 0.75 | 0.81 | 0.85 | 0.87 | 0.89 | 0.91 | 0.92 | 0.92 | 0.93 | 0.94 | 0.94 |
| time in inactivity, min/d | 0.00269 | 0.00221 | 1.21 | 0.67 | 0.79 | 0.84 | 0.88 | 0.90 | 0.91 | 0.92 | 0.93 | 0.94 | 0.94 | 0.95 | 0.95 |
| time in low activity, min/d | 0.06541 | 0.05703 | 1.15 | 0.68 | 0.80 | 0.85 | 0.88 | 0.90 | 0.92 | 0.93 | 0.94 | 0.94 | 0.95 | 0.95 | 0.96 |
| time in moderate activity, min/d | 0.09905 | 0.04941 | 2.00 | 0.58 | 0.71 | 0.77 | 0.82 | 0.84 | 0.87 | 0.88 | 0.89 | 0.90 | 0.91 | 0.92 | 0.93 |
| time in vigorous activity, min/d | 0.28250 | 0.21320 | 1.33 | 0.66 | 0.78 | 0.83 | 0.87 | 0.89 | 0.91 | 0.92 | 0.93 | 0.93 | 0.94 | 0.94 | 0.95 |
| time in very vigorous activity, min/d | 0.56600 | 0.32400 | 1.75 | 0.60 | 0.73 | 0.79 | 0.83 | 0.86 | 0.88 | 0.89 | 0.91 | 0.92 | 0.92 | 0.93 | 0.93 |

cpm, counts per minute; $D_r$, number of days of physical activity assessment; min/d, minutes per day; PA, physical activity; $r_D$, correlation between observed and true mean of physical activity parameter based on a given $D_r$, adapted from [304]; $s_b^2$, between-person variance over 12 days of physical activity; $s_w^2$, within-person variance over 12 days of physical activity
[a]all analyses were performed using log-transformed data

**Supplementary Table 7**: Within- and between-person variance and week-to-week reliability of habitual physical activity, sensitivity analyses using 12 days per participant, total (N=48)

| | | | % of total variance | | | |
|---|---|---|---|---|---|---|
| **PA parameter**[a] | **week 1** | **week 2** | **within-person variance** | **between-person variance** | **ICC week 1 vs. 2** | |
| | **GM** | **GM** | **$s_w^2$** | **$s_b^2$** | **ICC** | **95% CI** |
| overall activity, cpm | 438.0 | 415.6 | 24.0 | 76.0 | 0.77 | (0.62, 0.86) |
| time in inactivity, min/d | 1,186.0 | 1,194.4 | 23.4 | 76.6 | 0.78 | (0.65, 0.87) |
| time in low activity, min/d | 127.2 | 123.9 | 22.2 | 77.8 | 0.80 | (0.68, 0.88) |
| time in moderate activity, min/d | 96.2 | 91.6 | 32.5 | 67.5 | 0.69 | (0.51, 0.81) |
| time in vigorous activity, min/d | 14.0 | 13.4 | 18.7 | 81.3 | 0.82 | (0.70, 0.89) |
| time in very vigorous activity, min/d | 3.7 | 3.3 | 33.5 | 66.5 | 0.68 | (0.49, 0.80) |

cpm, counts per minute; ICC, intraclass correlation coefficient; GM, geometric mean; min/d, minutes per day; PA, physical activity; $s_b^2$, between-person variance of physical activity between week 1 and week 2; $s_w^2$, within-person variance of physical activity between week 1 and 2; vs., versus; 95% CI, 95% confidence interval
[a]all analyses were performed using log-transformed data

**Supplementary Table 8**: Characteristics of included and excluded participants for research question 3, pretest German National Cohort, 2012

| | **included participants** (N=262) | | **excluded participants** (N=85) | | **test for participant differences**[a] |
|---|---|---|---|---|---|
| | **n** | **%** | **n** | **%** | **p** |
| sex | | | | | 0.46 |
| men | 120 | 45.8 | 35 | 41.2 | |
| women | 142 | 54.2 | 50 | 58.8 | |
| smoking status | | | | | 0.54 |
| never-smokers | 108 | 41.2 | 30 | 38.9 | |
| smokers | 59 | 22.5 | 22 | 28.6 | |
| former smokers | 95 | 36.3 | 25 | 32.5 | |
| alcohol consumption | | | | | 0.39 |
| never | 8 | 3.1 | 1 | 1.5 | |
| max. 1x/month | 59 | 22.5 | 17 | 24.7 | |
| 2 - 4x/month | 79 | 30.2 | 22 | 31.9 | |
| 2 - 3x/week | 66 | 25.2 | 22 | 31.9 | |
| ≥4x/week | 50 | 19.1 | 7 | 10.1 | |
| school education | | | | | 0.65 |
| university entrance qualification | 126 | 48.1 | 38 | 45.2 | |
| no university entrance qualification | 136 | 51.9 | 46 | 54.8 | |
| occupation | | | | | 0.07 |
| full time | 143 | 54.6 | 33 | 40.2 | |
| part time | 65 | 24.8 | 25 | 30.5 | |
| not employed | 54 | 20.6 | 24 | 29.3 | |
| net household income per month | | | | | 0.05 |
| <2,500 € | 89 | 34.0 | 37 | 44.1 | |
| 2,500-3,999 € | 97 | 37.0 | 34 | 40.5 | |
| ≥4,000 € | 61 | 23.3 | 8 | 9.5 | |
| n. a. | 15 | 5.7 | 5 | 6.0 | |
| marital status | | | | | 0.17 |
| not married | 98 | 37.4 | 38 | 45.8 | |
| married | 164 | 62.6 | 45 | 54.2 | |
| diabetes mellitus[b] | 18 | 6.9 | 4 | 4.7 | 0.48 |
| dyslipidemia[b] | 74 | 28.2 | 21 | 24.7 | 0.51 |
| | **mean** | **SD** | **mean** | **SD** | |
| age, years | 51.0 | 10.9 | 49.3 | 13.4 | 0.31 |
| height, cm | 170.9 | 9.4 | 170.1 | 9.3 | 0.48 |
| weight, kg | 76.8 | 14.4 | 75.1 | 14.0 | 0.34 |
| BMI, kg/m² | 26.2 | 4.0 | 25.9 | 4.1 | 0.53 |
| waist circumference, cm | 90.1 | 13.0 | 88.5 | 12.5 | 0.33 |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; n, number; n. a., not available; SD, standard deviation
[a]continuous variables, normally distributed: t-test; continuous variables, not normally distributed: Mann-Whitney U test; discrete variables: Chi-Square test/Fisher's exact test
[b]data for 249 out of the total 262 participants available

**Supplementary Table 9**: Multivariable association of potential physical activity determinants and log-transformed proportion of active time in vigorous-to-very-vigorous physical activity intensity, model 2[1], total (N=249)

| **potential determinant** | **time in VV activity**, % of time in overall activity | | | |
|---|---|---|---|---|
| | **β** | **95% CI** | **p[a]** | |
| sex (men vs. women) | 0.5 | (0.0, 0.9) | **0.04** | |
| age (5 years) | -0.2 | (-0.3, -0.1) | **<.0001** | |
| BMI, kg/m² | 0.0 | (-0.1, 0.0) | 0.25 | |
| waist circumference, cm[b] | 0.0 | (-0.1, 0.0) | **0.03** | |
| smoking status | | | | |
| never-smokers | 0 | (reference) | | |
| smokers | -0.9 | (-1.3, -0.5) | **<.0001** | **<.0001** |
| former smokers | -0.2 | (-0.5, 0.2) | 0.32 | |
| alcohol consumption | | | | |
| never | 0.5 | (-0.2, 1.2) | 0.18 | |
| max. 1x/month | 0 | (reference) | | |
| 2 - 4x/month | 0.0 | (-0.5, 0.4) | 0.87 | 0.55 |
| 2 - 3x/week | 0.1 | (-0.4, 0.6) | 0.75 | |
| ≥4x/week | 0.2 | (-0.4, 0.7) | 0.54 | |
| university entrance qualification (yes vs. no) | 0.3 | (0.0, 0.6) | 0.07 | |
| occupation | | | | |
| full time | 0 | (reference) | | |
| part time | 0.1 | (-0.3, 0.4) | 0.93 | 0.94 |
| not employed | 0.0 | (-0.5, 0.5) | 0.97 | |
| net household income per month | | | | |
| <2,500 € | 0 | (reference) | | |
| 2,500-3,999 € | 0.0 | (-0.4, 0.3) | 0.93 | 0.65 |
| ≥4,000 € | -0.1 | (-0.6, 0.3) | 0.48 | |
| n. a. | 0.3 | (-0.3, 1.0) | 0.35 | |
| marital status (married, no vs. yes) | -0.3 | (-0.6, 0.1) | 0.14 | |
| diabetes mellitus (yes vs. no) | 0.2 | (-0.3, 0.7) | 0.43 | |
| dyslipidemia (yes vs. no) | 0.1 | (-0.2, 0.5) | 0.51 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; n. a., not available; vs., versus; VV, vigorous to very vigorous; 95% CI, 95% confidence interval
[1]Results were derived from a multivariable linear regression analysis with the potential determinants included as independent and proportion of time spent in overall activity spent in vigorous-to-very-vigorous activity included as dependent variable. β-coefficients can be interpreted as change in minutes in overall activity per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, smokers spent 0.9 % less active time in vigorous-to-very-vigorous compared to never-smokers. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
**bold**: *p*-value <0.05

**Supplementary Table 10**: Multivariable association of potential physical activity determinants and time overall activity, model 2[1], sensitivity analyses, total (N=201)

| potential determinant | time in overall activity, min/d | | | |
|---|---|---|---|---|
| | β | 95% CI | p[a] | |
| sex (men vs. women) | -23.5 | (-56.0, 9.0) | 0.16 | |
| age (5 years) | 1.7 | (-6.0, 9.5) | 0.66 | |
| BMI, kg/m² | -1.5 | (-5.1, 2.2) | 0.43 | |
| waist circumference, cm[b] | -0.9 | (-2.9, 1.1) | 0.38 | |
| smoking status | | | | |
| never-smokers | 0 | (reference) | | |
| smokers | 18.2 | (-15.1, 51.4) | 0.28 | 0.08 |
| former smokers | -18.3 | (-43.0, 6.4) | 0.15 | |
| alcohol consumption | | | | |
| never | 70.7 | (7.3, 134.0) | **0.03** | |
| max. 1x/month | 0 | (reference) | | |
| 2 - 4x/month | 18.0 | (-14.7, 50.6) | 0.28 | 0.07 |
| 2 - 3x/week | 26.6 | (-10.8, 64.0) | 0.16 | |
| ≥4x/week | 47.5 | (10.8, 84.1) | **0.01** | |
| university entrance qualification (yes vs. no) | -34.3 | (-59.7, -8.9) | **0.008** | |
| employment status | | | | |
| full time | 0 | (reference) | | |
| part time | -1.0 | (-29.0, 27.0) | 0.81 | 0.10 |
| not employed | -39.3 | (-77.1, -1.4) | **0.04** | |
| net household income per month | | | | |
| <2,500 € | 0 | (reference) | | |
| 2,500-3,999 € | 3.4 | (-24.8, 31.5) | 0.81 | 0.92 |
| ≥4,000 € | -3.8 | (-42.7, 35.0) | 0.85 | |
| n. a. | 12.6 | (-30.5, 55.8) | 0.56 | |
| marital status (married, no vs. yes) | -13.0 | (-41.5, 15.5) | 0.37 | |
| diabetes mellitus (yes vs. no) | 30.8 | (-22.5, 84.0) | 0.26 | |
| dyslipidemia (yes vs. no) | 4.5 | (-24.8, 33.8) | 0.76 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; min/d, minutes per day; n. a., not available; vs., versus; 95% CI, 95% confidence interval
[1]Results were derived from a multivariable linear regression analysis with the potential determinants included as independent and time in overall activity as dependent variable. β-coefficients can be interpreted included as change in minutes in overall activity per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, persons not being employed spent 39.3 minutes per day more time in overall activity. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
**bold**: *p*-value <0.05

**Supplementary Table 11**: Multivariable association of potential physical activity determinants and proportion of active time in different activity intensities, model 2[1], sensitivity analyses, total (N=201)

| potential determinant | time in low activity, % of time in overall activity | | | | time in moderate activity, % of time in overall activity | | | | time in VV activity, % of time in overall activity | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **β** | **95% CI** | **p[a]** | | **β** | **95% CI** | **p[a]** | | **β** | **95% CI** | **p[a]** | |
| sex (men vs. women) | -1.6 | (-4.2, 1.1) | 0.24 | | 1.6 | (-0.8, 4.0) | 0.20 | | 0.0 | (-0.8, 0.9) | 0.95 | |
| age (5 years) | 0.6 | (0.2, 1.1) | **0.008** | | -0.4 | (-0.8, 0.0) | 0.08 | | -0.2 | (-0.4, -0.1) | **0.003** | |
| BMI, kg/m² | -0.3 | (-0.5, 0.0) | **0.04** | | 0.3 | (0.1, 0.6) | **0.005** | | -0.1 | (-0.2, 0.0) | 0.19 | |
| waist circumference, cm[b] | 0.1 | (0.0, 0.3) | 0.16 | | -0.1 | (-0.2, 0.0) | 0.16 | | 0.0 | (-0.1, 0.0) | 0.69 | |
| smoking status | | | | | | | | | | | | |
| never-smokers | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| smokers | 3.9 | (1.8, 6.0) | **0.0003** | **<.0001** | -2.9 | (-4.9, -1.0) | **0.003** | **0.002** | -1.0 | (-1.5, -0.5) | **0.0004** | **0.002** |
| former smokers | 0.2 | (-1.4, 1.8) | 0.81 | | 0.3 | (-1.1, 1.8) | 0.66 | | -0.5 | (-1.0, 0.0) | **0.05** | |
| alcohol consumption | | | | | | | | | | | | |
| never | -4.9 | (-10.1, 0.3) | 0.06 | | 4.0 | (-1.0, 9.0) | 0.12 | | 0.9 | (-0.2, 2.0) | 0.12 | |
| max. 1x/month | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| 2 - 4x/month | 1.4 | (-1.0, 3.9) | 0.25 | 0.06 | -1.1 | (-3.2, 1.0) | 0.30 | 0.11 | -0.3 | (-1.2, 0.6) | 0.51 | 0.23 |
| 2 - 3x/week | 0.2 | (-2.2, 2.6) | 0.87 | | -0.2 | (-2.2, 1.8) | 0.86 | | 0.0 | (-1.1, 1.1) | 0.97 | |
| ≥4x/week | -0.7 | (-3.6, 2.2) | 0.62 | | 1.0 | (-1.5, 3.5) | 0.44 | | -0.3 | (-1.3, 0.8) | 0.61 | |
| university entrance qualification (yes vs. no) | -0.4 | (-2.0, 1.2) | 0.60 | | 0.4 | (-1.0, 1.7) | 0.59 | | 0.1 | (-0.5, 0.6) | 0.84 | |
| employment status | | | | | | | | | | | | |
| full time | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| part time | -0.5 | (-2.3, 1.4) | 0.83 | 0.40 | 0.8 | (-0.9, 2.5) | 0.80 | 0.31 | -0.3 | (-0.9, 0.3) | 0.93 | 0.64 |
| not employed | -1.7 | (-4.2, 0.8) | 0.18 | | 1.7 | (-0.6, 4.0) | 0.14 | | 0.0 | (-0.7, 0.8) | 0.95 | |
| net household income per month | | | | | | | | | | | | |
| <2,500 € | 0 | (reference) | | | 0 | (reference) | | | 0 | (reference) | | |
| 2,500-3,999 € | -0.2 | (-2.2, 1.8) | 0.83 | 0.17 | 0.2 | (-1.6, 2.1) | 0.80 | 0.29 | 0.0 | (-0.6, 0.5) | 0.93 | 0.72 |
| ≥4,000 € | -0.5 | (-3.0, 1.9) | 0.67 | | 0.4 | (-1.7, 2.5) | 0.73 | | 0.2 | (-0.7, 1.0) | 0.73 | |
| n. a. | -3.9 | (-7.4, -0.3) | **0.03** | | 3.4 | (-0.1, 6.9) | **0.06** | | 0.5 | (-0.6, 1.6) | 0.34 | |
| marital status (married, no vs. yes) | -0.2 | (-2.1, 1.6) | 0.80 | | 0.8 | (-0.8, 2.4) | 0.34 | | -0.5 | (-1.1, 0.1) | 0.08 | |
| diabetes mellitus (yes vs. no) | -1.0 | (-3.2, 1.2) | 0.36 | | 0.6 | (-1.5, 2.7) | 0.57 | | 0.4 | (-0.3, 1.1) | 0.24 | |
| dyslipidemia (yes vs. no) | 0.6 | (-1.2, 2.5) | 0.49 | | -0.6 | (-2.3, 1.0) | 0.45 | | 0.0 | (-0.5, 0.4) | 0.96 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; n. a., not available; vs., versus; VV, vigorous to very vigorous; 95% CI, 95% confidence interval
[1]Results were derived from three different multivariable linear regression analyses with the potential determinants included as independent and proportion of active time spent in the three different activity intensities included as single dependent variables. β-coefficients can be interpreted as relative change (%) in the proportion of time in overall activity spent in the different activity intensities per day, referring to a 1-unit increment for continuous variables or to the respective reference category for categorical variables; for example, with each 5-years higher age, persons spent 0.6% more active time in low activity. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.
[a]*p*-values presented are raw values
[b]residually adjusted for body mass index
**bold**: *p*-value <0.05 (bold p=0.05 for former smokers and time in VV activity: *p*-value not rounded=0.048)

**Supplementary Table 12**: Univariable association of potential physical activity determinants and fulfillment of the physical activity recommendation of the World Health Organization, model 1[1], total (N=262)

| potential determinant | meeting WHO recommendation[a] (yes vs. no) | | | |
|---|---|---|---|---|
| | OR | 95% CI | p[b] | |
| sex (men vs. women) | 0.59 | (0.34, 1.00) | **0.05** | |
| age (5 years) | 0.98 | (0.87, 1.11) | 0.78 | |
| BMI, kg/m² | 0.94 | (0.87, 1.00) | 0.06 | |
| waist circumference, cm[c] | 0.98 | (0.94, 1.01) | 0.18 | |
| smoking status | | | | |
| never-smokers | 1 | (reference) | | |
| smokers | 0.26 | (0.12, 0.59) | **0.001** | **0.005** |
| former smokers | 0.71 | (0.40, 1.25) | 0.23 | |
| alcohol consumption | | | | |
| never | 0.76 | (0.14, 4.13) | 0.75 | |
| max. 1x/month | 1 | (reference) | | |
| 2 - 4x/month | 1.18 | (0.57, 2.44) | 0.65 | 0.91 |
| 2 - 3x/week | 1.22 | (0.58, 2.58) | 0.61 | |
| ≥4x/week | 0.89 | (0.39, 2.03) | 0.77 | |
| university entrance qualification (yes vs. no) | 1.38 | (0.82, 2.33) | 0.22 | |
| occupation | | | | |
| full time | 1 | (reference) | | |
| part time | 1.11 | (0.60, 2.08) | 0.73 | 0.94 |
| not employed | 1.00 | (0.51, 1.96) | 1.00 | |
| net household income per month | | | | |
| <2,500 € | 1 | (reference) | | |
| 2,500-3,999 € | 1.08 | (0.58, 2.01) | 0.81 | 0.36 |
| ≥4,000 € | 0.96 | (0.47, 1.96) | 0.91 | |
| n. a. | 2.62 | (0.86, 7.96) | 0.09 | |
| marital status (married, no vs. yes) | 0.66 | (0.39, 1.13) | 0.13 | |
| diabetes mellitus (yes vs. no)[d] | 0.59 | (0.19, 1.84) | 0.36 | |
| dyslipidemia (yes vs. no)[d] | 0.85 | (0.47, 1.54) | 0.60 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel
BMI, body mass index; n. a., not available; OR, odds ratio; vs., versus; WHO, World Health Organization; 95% CI, 95% confidence interval
[1]Results were derived from a univariable logistic regression analysis with the potential determinants included as independent and fulfillment of the World Health Organization (WHO) physical activity (PA) recommendation included as dependent variable [7]. β-coefficients can be interpreted as change in the likelihood (odds ratio, OR) of meeting the WHO PA recommendation, referring to a 1-unit increment for continuous variables or the respective reference category for categorical variables; for example, the likelihood of meeting the WHO PA recommendation was decreased by 74% in smokers compared to never-smokers.
[a]meeting World Health Organization physical activity recommendation: ≥150 minutes of moderate activity/week, or ≥75 minutes of vigorous activity/week, or an equivalent of these [7]
[b]*p*-values presented are raw values
[c]residually adjusted for body mass index
[d]data for 249 out of the total 262 participants available
**bold**: *p*-value <0.05 (bold p=0.05 for sex: *p*-value not rounded=0.048)

**Supplementary Table 13**: Multivariable association of potential physical activity determinants and fulfillment of the physical activity recommendation of the World Health Organization, model 2[1], sensitivity analyses, total (N=201)

| potential determinant | meeting WHO recommendation[a] (yes vs. no) | | | |
|---|---|---|---|---|
| | **OR** | **95% CI** | **p[b]** | |
| sex (men vs. women) | 0.76 | (0.24, 2.36) | 0.63 | |
| age (5 years) | 1.11 | (0.88, 1.40) | 0.39 | |
| BMI, kg/m² | 0.92 | (0.82, 1.04) | 0.18 | |
| waist circumference, cm[c] | 0.98 | (0.91, 1.06) | 0.66 | |
| smoking status | | | | |
| never-smokers | 1 | (reference) | | |
| smokers | 0.21 | (0.07, 0.65) | **0.007** | **0.02** |
| former smokers | 0.61 | (0.28, 1.33) | 0.21 | |
| alcohol consumption | | | | |
| never | 0.40 | (0.02, 9.40) | 0.57 | |
| max. 1x/month | 1 | (reference) | | |
| 2 - 4x/month | 1.10 | (0.39, 3.08) | 0.86 | 0.95 |
| 2 - 3x/week | 1.01 | (0.35, 2.96) | 0.98 | |
| ≥4x/week | 1.33 | (0.38, 4.66) | 0.65 | |
| university entrance qualification (yes vs. no) | 1.18 | (0.55, 2.52) | 0.68 | |
| occupation | | | | |
| full time | 1 | (reference) | | |
| part time | 0.87 | (0.33, 2.30) | 0.78 | 0.96 |
| not employed | 1.00 | (0.29, 3.39) | 0.99 | |
| net household income per month | | | | |
| <2500 € | 1 | (reference) | | |
| 2500-3,999 € | 0.71 | (0.28, 1.83) | 0.48 | 0.84 |
| ≥4000 € | 0.80 | (0.27, 2.42) | 0.70 | |
| n. a. | 1.26 | (0.28, 5.63) | 0.76 | |
| marital status (married, no vs. yes) | 1.86 | (0.75, 4.57) | 0.18 | |
| diabetes mellitus (yes vs. no) | 1.54 | (0.37, 6.43) | 0.55 | |
| dyslipidemia (yes vs. no) | 0.83 | (0.34, 2.04) | 0.69 | |

information was derived from self-reports during a personal interview, anthropometric measures were taken by trained personnel

BMI, body mass index; n. a., not available; OR, odds ratio; vs., versus; WHO, World Health Organization; 95% CI, 95% confidence interval

[1]Results were derived from a multivariable logistic regression analysis with the potential determinants included as independent and fulfillment of the World Health Organization (WHO) physical activity (PA) recommendation included as dependent variable [7]. β-coefficients can be interpreted as change in the likelihood (odds ratio, OR) of meeting the WHO PA recommendation, referring to a 1-unit increment for continuous variables or the respective reference category for categorical variables; for example, the likelihood of meeting the WHO PA recommendation was decreased by 79% in smokers compared to never-smokers. Model includes sex, age, body mass index (BMI), waist circumference (residually adjusted for BMI), smoking status, alcohol consumption, university entrance qualification, employment status, net household income, marital status, diagnosed diabetes, diagnosed dyslipidemia, and study center.

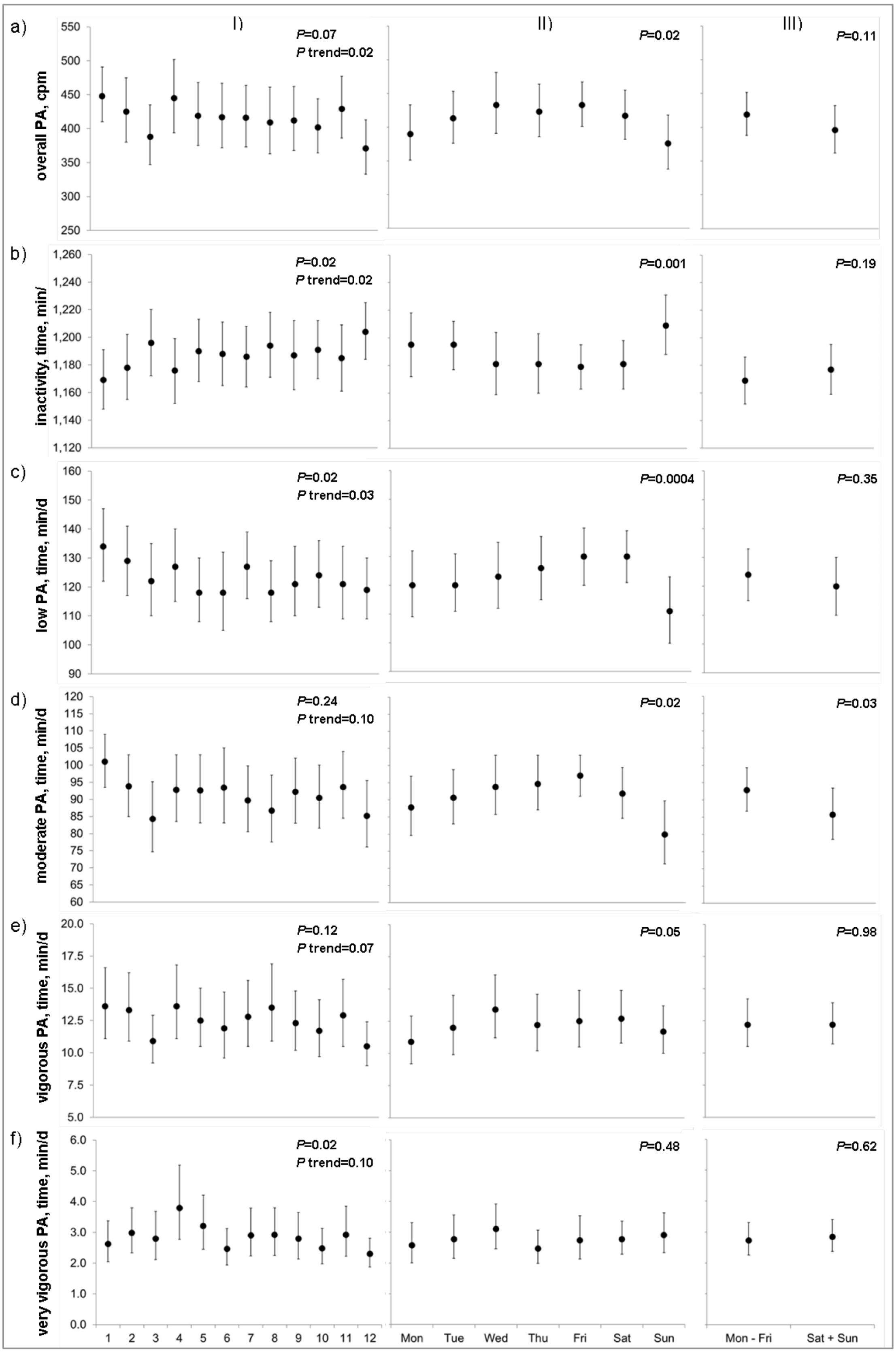
[a]meeting World Health Organization physical activity recommendation: ≥150 minutes of moderate activity/week, or ≥75 minutes of vigorous activity/week, or an equivalent of these [7]

[b]*p*-values presented are raw values

[c]residually adjusted for BMI

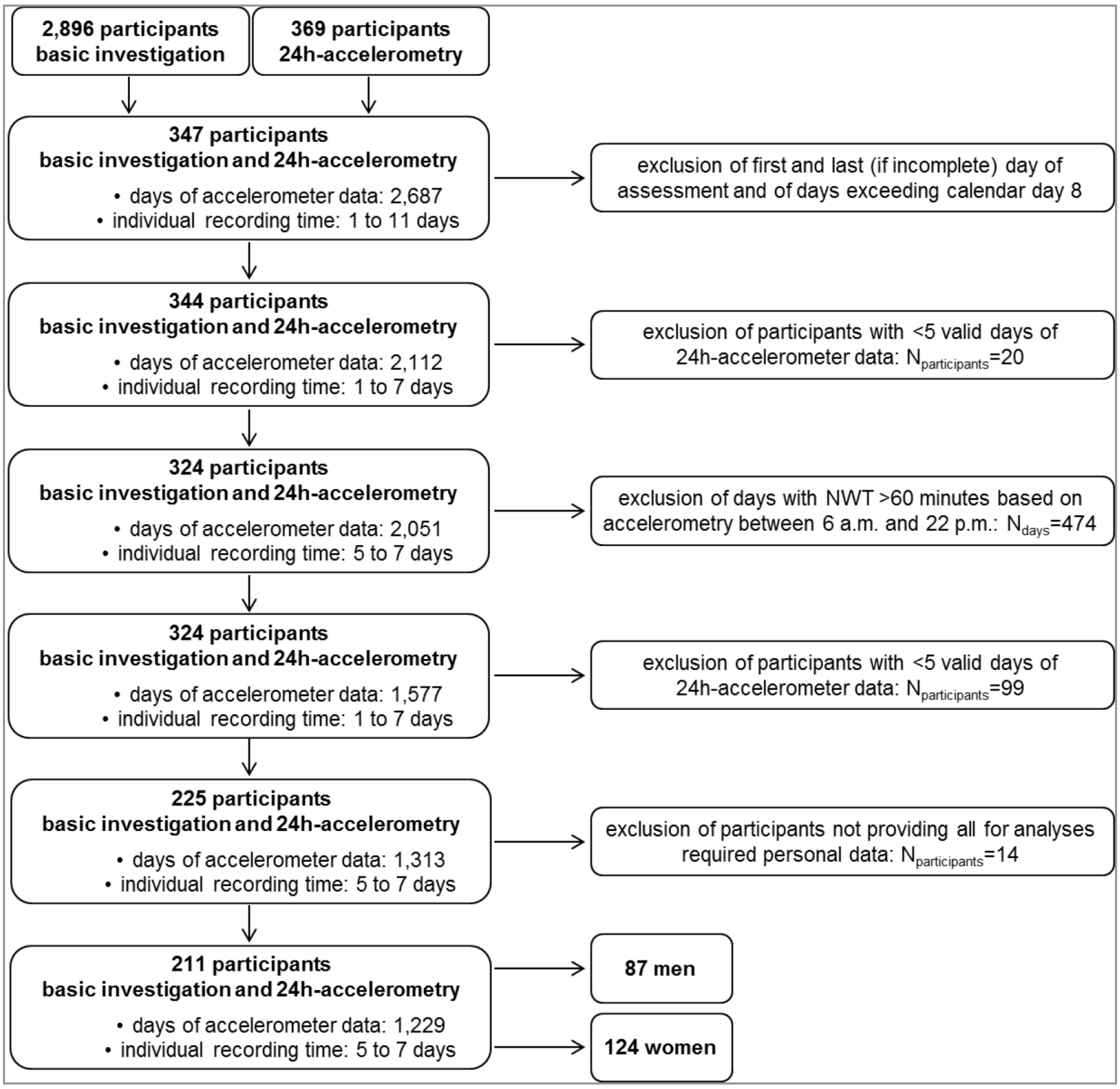
**bold**: *p*-value <0.05

## Supplementary Figures



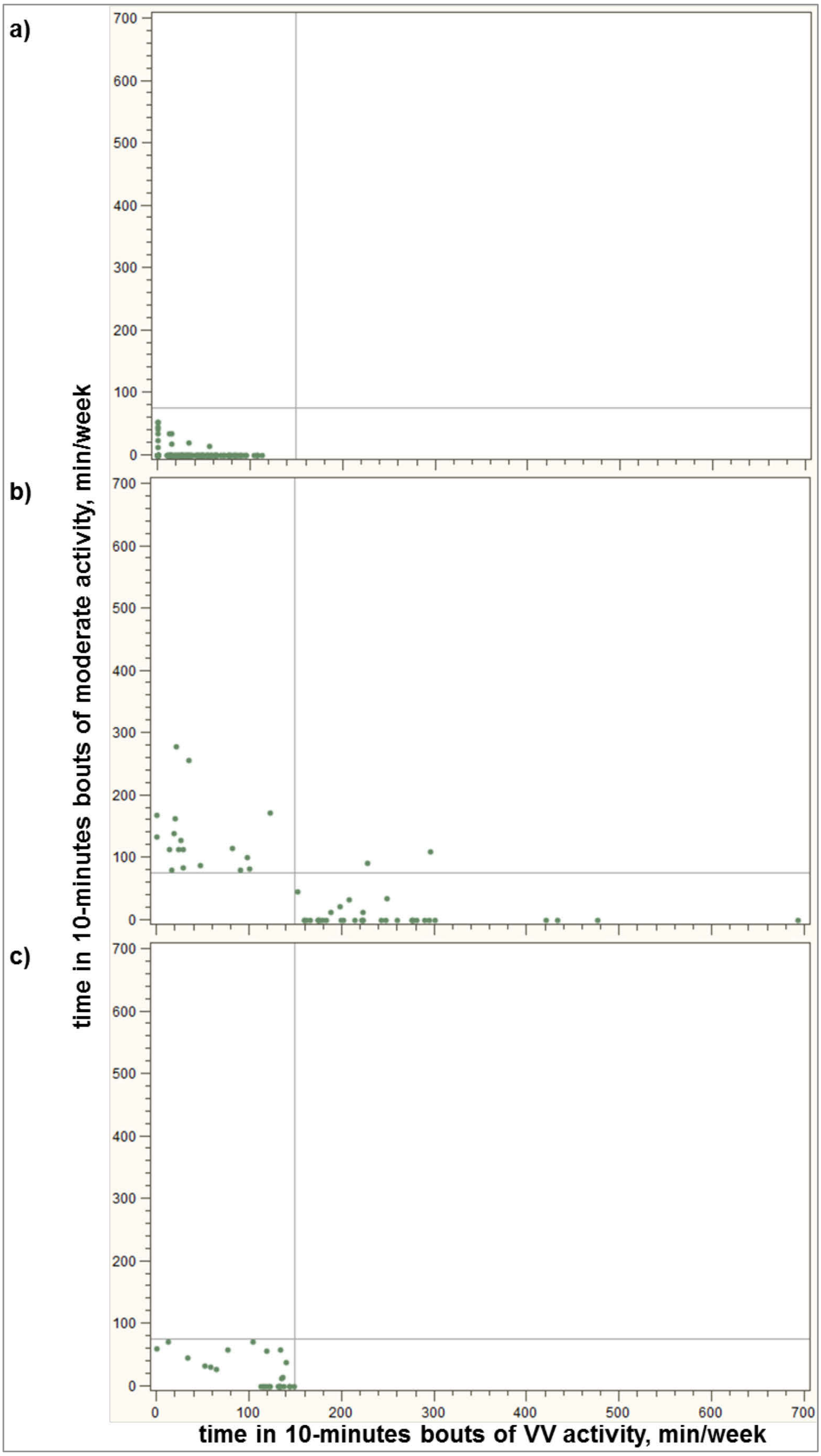

**Supplementary Figure 1**: Physical activity across the days of assessment, the days of the week, or between weekend days and weekdays, sensitivity analyses using 12 days per participant, total (N=50)

Results of linear mixed-effects models with adjustment for sex (panel I) or week and sex (Panels II and III). Dots indicate geometric least square means and error bars 95% confidence intervals for overall physical activity (PA, triaxial counts per minute, cpm, panel a), time in minutes per day in inactivity (panel b), and in low (panel c), moderate (panel d), vigorous (panel e), or very vigorous activity (panel f). *P*-values presented refer to the main fixed effects, i.e., day of assessment (panel I; overall *p*-value and *p*-value for trend analyses), day of the week (panel II), or weekdays versus weekend days (panel III). Results for analyses depicted in panel II and III are based on 48 participants. Note that for the sake of graphic representability, in panel a) to panel e) the lower end of the y-axes is hidden and y-axes, thus, do not begin with 0.



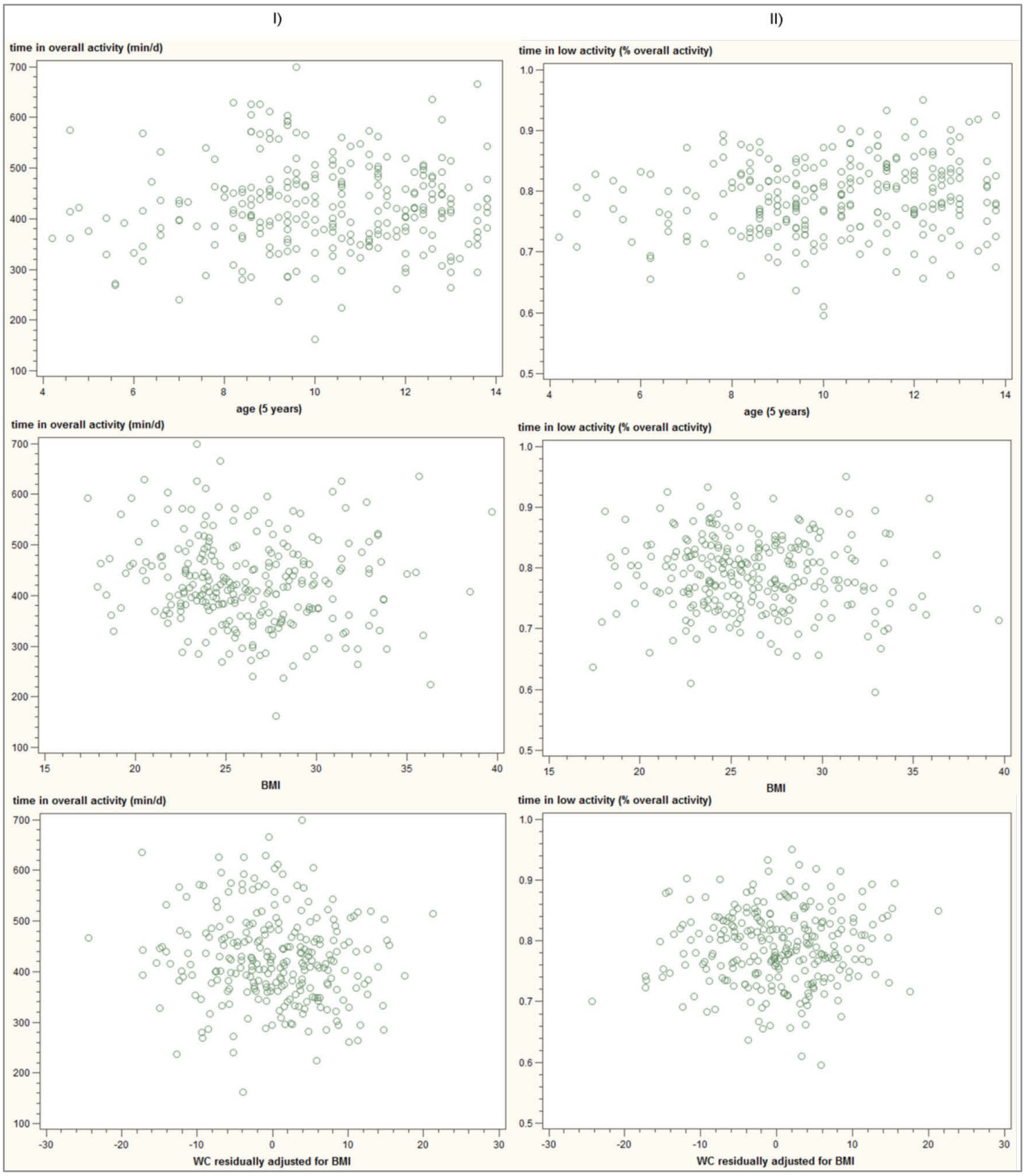

**Supplementary Figure 2**: Data selection for the sensitivity analyses of potential determinants of physical activity using 24h-accelerometry data in pretest 2 of the German National Cohort (research question 3)

In pretest 2 of the German National Cohort, initially, 2,869 participants provided data on basic characteristics, 369 on 24h-accelerometry, and 347 on both. After exclusion of invalid days (i.e., days with automatically detected accelerometer non-wear time (NWT) >60 minutes between 6 a.m. and 10 p.m. using ActiLife, versions 6.12.1 to 6.13.2; ActiGraph LLC, Fort Walton Beach, FL, USA), invalid data sets (i.e., data sets with <5 valid days available), or incomplete data sets a total of 211 German National Cohort pretest participants fulfilled all inclusion criteria and were included in the sensitivity analyses of potential determinants of 24h-accelerometry-based physical activity.

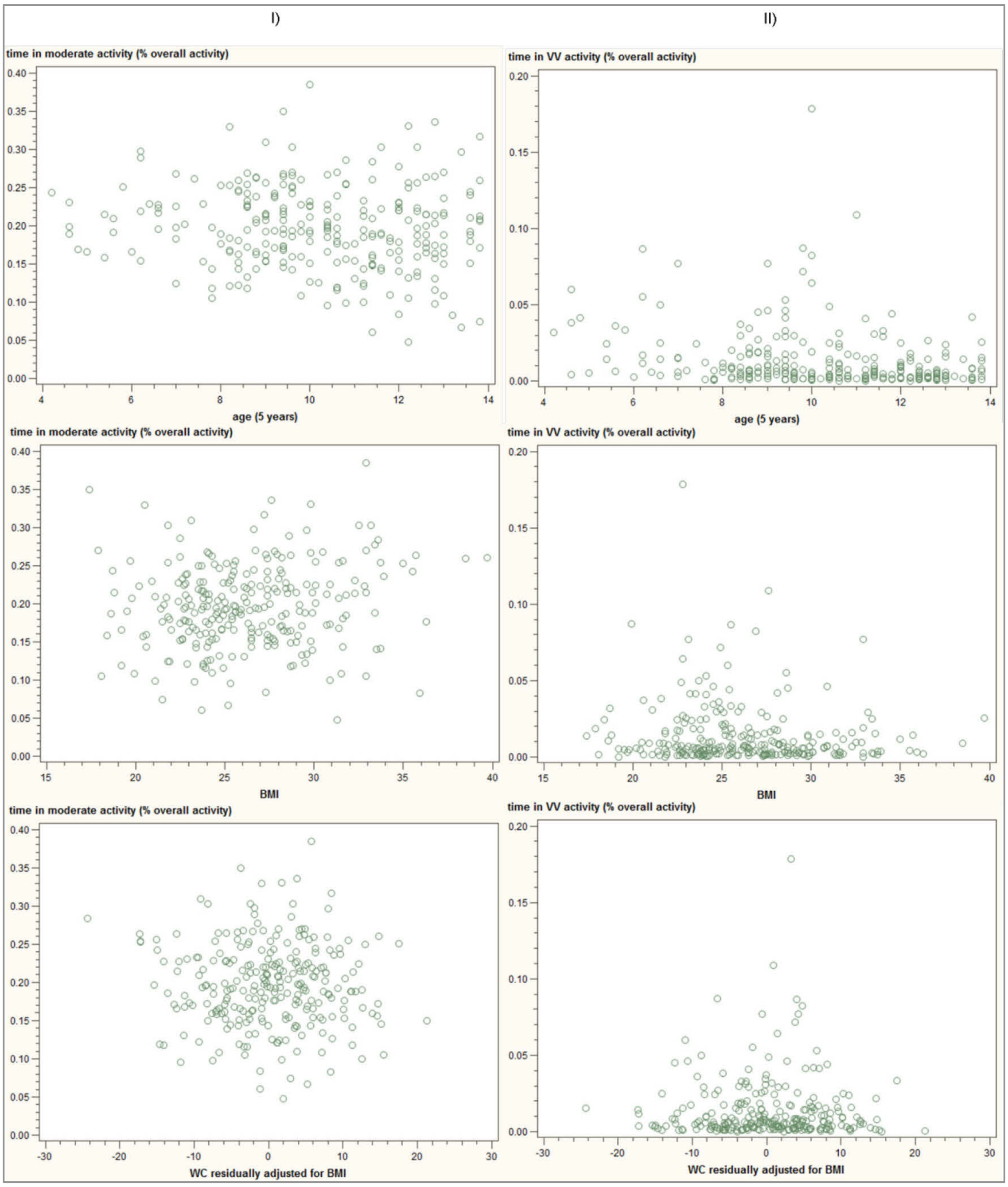



**Supplementary Figure 3**: Time in 10-minutes bouts of moderate and vigorous-to-very-vigorous physical activity per week depending on the fulfillment of the physical activity recommendation of the World Health Organization in pretest 2 of the German National Cohort (N=262)

Each dot indicates a participant’s physical activity data as assessed using the triaxial accelerometer ActiGraph GT3X+ (ActiGraph LLC, Pensacola, FL, USA) for time in 10-minutes bouts in moderate (2,691-6,166 counts per minutes, cpm) or vigorous-to-very-vigorous activity (≥6,167 cpm), [246]. Solid lines indicate the time in 10-minutes bouts of moderate (≥150 minutes/week) and vigorous-to-very-vigorous (VV, ≥75 min/week) activity defined as threshold to meet the World Health Organization PA recommendation [7]. Out of the total of 262 participants, 178 were not sufficiently active based on the recommendation (panel a), 58 participants met the recommendation based on the time in 10-minutes bouts of moderate and/or VV activity per week (panel b, see also 3.5 in the main document), and 28 participants fulfilled the recommendation by reaching a metabolic equivalent of the latter [7] calculated as weekly minutes in 10-minutes bouts multiplied by 4 or 8 metabolic equivalents of task for moderate or VV activity, respectively (see also **Equation 3** in the main document) [1].




**Supplementary Figure 4**: Scatter plots on the relationship between time in overall activity (min/d) and time in low activity (% of overall activity min/d) with age, body mass index, and waist circumference in pretest 2 of the German National Cohort (N=262)
Each dot represents one participant and the association between time in overall activity (min/d) (≥79 counts per minute, cpm; panel I) or relative time in low activity (79-2,690 cpm, % of overall activity min/d; panel II) (see 3.4.3, [246]) with age, body mass index (BMI), and waist circumference (WC, residually adjusted for BMI). Physical activity data were assessed using the triaxial accelerometer ActiGraph GT3X+ (ActiGraph LLC, Pensacola, FL, USA).




**Supplementary Figure 5**: Scatter plots showing the relationship between time in moderate (% of overall activity min/d) and in vigorous-to-very-vigorous activity (% of overall activity min/d) with age, body mass index, and waist circumference in pretest 2 of the German National Cohort (N=262)

Each dot represents one participant and the association between relative time in moderate (2,691-6,166 counts per minute, cpm; panel I) or in vigorous-to-very-vigorous (VV) activity (≥6,167 cpm, % of overall activity min/d; panel II) [246] with age, body mass index (BMI), and waist circumference (WC, residually adjusted for BMI). Physical activity data were assessed using the triaxial accelerometer ActiGraph GT3X+ (ActiGraph LLC, Pensacola, FL, USA).

# Danksagung

Die vorliegende Dissertation ist am Max-Delbrück-Centrum für Molekulare Medizin in der Helmholtz-Gemeinschaft (MDC) in der Arbeitsgruppe Molekulare Epidemiologie unter der Leitung und Betreuung von Prof. Dr. Tobias Pischon entstanden.

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