Physical activity, muscle mass, and physical function in older adults

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Abstract

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Ageing is accompanied by a decline in physical function, including loss of muscle mass and muscle strength, which leads to impaired ability to perform activities of daily living and loss of independence. Physical activity (PA) is currently viewed as a key lifestyle factor with potential to mitigate these age-related deteriorations. Therefore, public health organizations have issued guidelines about amounts and types of physical activity for health benefits, where reductions in daily time spent sedentary in favour of more time in aerobic-type moderate-to-vigorous PA (MVPA) are emphasized. In addition, regular engagement in muscle-strengthening activities (MSA) are recommended to promote maintenance of muscle mass and strength in ageing populations. However, to what extent different amounts and types of PA impact on different indicators of physical function, including muscle mass and strength, remains currently unclear. Therefore, the overall aim of this thesis was to investigate the impact of PA behaviours on muscle mass and physical function in older adults. In study I, it was shown that regular engagement in exercise activities during middle age was associated with a significantly higher muscle mass and a better cardiorespiratory fitness at old age. In study II, replacement of daily sedentary time with PA of at least light intensity was associated with a significantly lower sarcopenia risk in older adults, with greater benefits above the moderate PA intensity. Study III revealed that engagement in MSA at least twice a week was linked to a significantly lower sarcopenia risk in older adults who already perform at least 150 weekly minutes of MVPA. Finally, study IV showed that older adults who accumulate at least 300 weekly minutes of MVPA have a significantly better overall physical function than those who accumulate at least 150 but less than 300 minutes of MVPA per week. Overall, the findings from this thesis highlight the importance of adherence to the aerobic-type MVPA guideline alongside recommended engagement in MSA for mitigating age-related decline in physical function in older adults. Notably, accumulation of MVPA time beyond the minimum recommended amount provides additional functional benefits.

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List of publications

I. Edholm, P.; Veen, J.; Kadi, F.; Nilsson, A. Muscle mass and aerobic capacity in older women: Impact of regular exercise at middle age. *Exp.Gerontol*. 202, 147,111259.

II. Veen, J.; Montiel-Rojas, D.; Kadi, F.; Nilsson, A. Effects of Reallocating Time Spent in Different Physical Activity Intensities on Sarcopenia Risk in Older Adults: An Isotemporal Substitution Analysis. *Biology*. 2022, 11, 111.

III. Veen, J.; Montiel-Rojas, D.; Nilsson, A.; Kadi, F. Engagement in Muscle-Strengthening Activities Lowers Sarcopenia Risk in Older Adults Already Adhering to the Aerobic Physical Activity Guidelines. Int. J. Environ. *Res. Public Health*, 18, 989.

IV. Veen, J.; Edholm, P.; Rodriguez-Zamora, L.; Folkesson, M.; Nilsson, A.; Kadi, F. Adherence to the MVPA guideline beyond the recommended minimum weekly amount: impacts on indicators of physical function in older adults. 2022. In manuscript

Introduction

Improvements in living conditions, nutrition, and medical care [1] have led to life expectancy at birth in Sweden increasing from 33 years for men and 36 years for women in 1751 to 81 and 84 years respectively in 2021 [2]. The increase in life expectancy together with a decreased birth rate has led to population ageing, not only in Sweden but also globally. It is estimated that the global population of adults aged 65 and older will grow to nearly 1.5 billion in 2050, and as a proportion of total population this age group will increase from 6% in 1990 to a projected 16% in 2050 [3]. Although this increase in life expectancy can been seen as a success in itself, the other side of the coin is that population ageing comes with societal challenges, as ageing is naturally accompanied by reduced functional ability, an increase in age-related diseases, and decreased independence [4]. Consequently, population ageing will lead to an increased load on health care systems [3]. Strategies must therefore be developed to delay the age-related functional decline in order to increase the number of healthy years during the life course.

Age-related decline in physical function

Physical function has been defined as the ability to perform basic and instrumental activities of daily living (ADL). It involves the complex integration of multiple physiological systems, and is affected by the presence of disease, injury, and cognitive impairments [5,6]. Older adults progressively experience difficulty in carrying out ADL-related tasks, and are exposed to an increasing risk of hospitalization which continues to increase until independent living becomes impossible. During the life course, the level of physical functioning peaks in early adulthood and then slowly declines [7,8] (Figure 1). The overall age-related decline in physical function, accompanied by an accelerated loss of muscle mass and strength, can ultimately lead to sarcopenia, a condition defined by low muscle strength and mass with poor physical performance [9,10]. Sarcopenia can also be accompanied by an increased adiposity, which has led to the use of the term "sarcopenic obesity" [11]. Finally, sarcopenia can progress into frailty, a geriatric syndrome accompanied by a reduced homeostatic reserve, which increases vulnerability to negative health-related events such as falls and is associated with higher mortality rates [12]. Although muscle mass has traditionally been the primary parameter to define sarcopenia, the current definition by the European Working Group on Sarcopenia in Older People (EWGSOP) highlights both muscle strength and mass, with low physical performance as an indicator of severity [9].

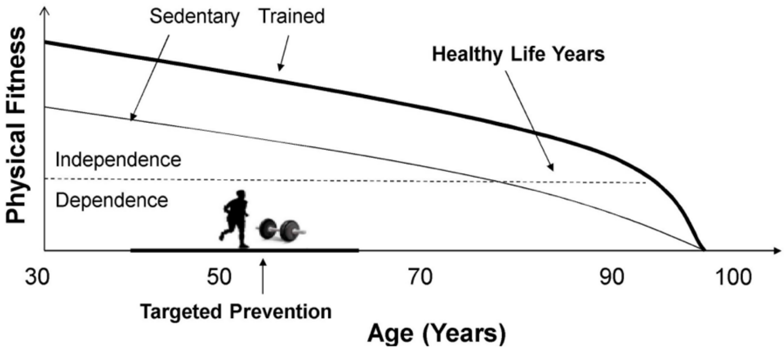


Figure 1. Life course functional trajectories. Figure taken from Strasser and Burtscher. (2018)

Body composition

On average, muscle mass tends to peak before the age of 40[13], and then declines at an average rate of 0.5–1% per year [14]. Around the age of 80 years, about 40% of total lean body mass has been lost [13]. This declining trend is present in both sexes, but the decline is generally faster in men [15]. It is caused by a loss of muscle fibres as well as a reduction in muscle fibre size, primarily in the type II muscle fibres [13]. The loss seems to be unevenly distributed, as some studies report a greater loss in muscle mass in the lower limbs compared to upper limbs [16–18]. Due to denervation, an estimated loss of about 25% in functional motor units can be expected [19], as well as a decreased neural conductivity due to a decrease in alpha motor units [20] and axonal withdrawal [21]. Moreover, during the life course, muscle mass is replaced by adipose tissue [22,23], which can eventually lead to sarcopenic obesity [24].

Ageing can also result in a redistribution of fat mass, where more fat is stored around the abdominal area and visceral organs as well as around muscle and bone [25]. This may contribute to the development of metabolic abnormalities [26].

Physical performance

Alongside age-related changes in body composition, several physical performance-related changes take place. One of the most prominent changes is a reduction in maximal oxygen uptake (VO_2max), which is defined as the maximum rate of oxygen consumption and represents an indicator of cardiorespiratory fitness. VO_2max generally starts to decline around the age of 30 years (Figure 2)[27] at an average rate of approximately 0.5–1% per year, and this decline accelerates at old age [28,29]. Since any physical task requires a given level of oxygen consumption, cardiorespiratory fitness is an important predictor of functional ability and ability to perform ADL [30,31]. It is generally assumed that a minimal oxygen consumption of around 18 ml/kg/min for men and 15 ml/kg/min for women is required to maintain an independent life [28,32].

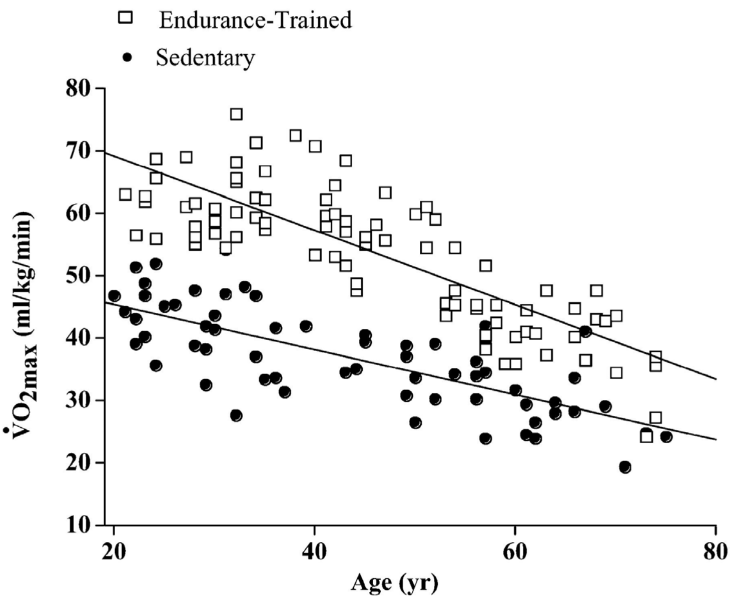


Figure 2. Decline in VO_2 max in endurance-trained and sedentary individuals. Adapted from Pimentel et al. (2003)

A decline in muscle strength is another important age-related change. Muscle strength tends to peak before the age of 40 [14], after which a slow and progressive decline occurs. Although deteriorations in muscle mass and muscle strength occur during ageing, muscle strength is lost at a faster rate than muscle mass [33]. Additionally, previous research has shown that muscle mass itself explains only 13% of the variance in muscle strength, independently of age and gender [34]. This makes the age-related decline in muscle strength a primary concern for disability and functional ability [15]. Larger muscle strength reductions have been observed in the lower body extremities compared to the upper limbs [35]. This may have important clinical implications, as lower limb functional status is important for activities such as rising from a chair, climbing stairs, and other ADL [36].

Several tests are used to assess different dimensions of physical function. One of the most commonly used tests is the handgrip strength test, which is easy to conduct and can predict future health outcomes such as disability, length of hospitalization [9,37], sarcopenia [9], and frailty [38]. To assess lower body performance, the five times sit-to-stand test (5-STS) is frequently used. This test is easy to perform, evaluates lower limb function in terms of strength and balance [39], and can be used to predict disability and falls [40]. Given that sitting and standing are fundamental elements of mobility, the 5-STS is a valuable tool when evaluating functional capacity in older populations [41].

Cardiorespiratory fitness in older adults can be determined using the Åstrand submaximal cycle ergometer test and the six-minute walk test (6MW). These tests are reliable and feasible and are well-adapted for older populations as they do not require maximal effort, which minimizes discomfort and risk of adverse events. The Åstrand submaximal cycle ergometer test makes use of the linear relationship between workload and heart rate to estimate VO_2 max after adjustments for age and sex [42]. The 6MW is another submaximal test that measures the distance walked during six minutes [43] and provides information regarding overall mobility and physical functioning [44].

Determinants of age-related decline in physical function

The rate of decline in physical function may be influenced by several risk factors, such as biological sex, health status, use of medication, living conditions, socioeconomic status, and lifestyle behaviours including physical activity (PA), diet, and smoking [45]. For example, women may be more vulnerable to a decline in functional ability compared to men, as elucidated in studies reporting a higher prevalence of physical limitations in women [46–50]. In terms of lifestyle behaviours, smoking has been negatively associated with muscle strength [51], physical function [52], and cardiorespiratory fitness [53]. Dietary habits represent another lifestyle behaviour which may have an important role in maintenance of physical function. In particular, dietary proteins drive muscle protein synthesis [54], and so there is an emerging interest in the role of protein intake for maintenance of muscle mass and strength in order to prevent sarcopenia. Although a daily protein intake of 0.8 g/kg bodyweight (BW) has long been recommended, recent research indicates that this amount may be inadequate to maintain muscle health in older adults [55]. Indeed, a protein intake above the recommended amount seems to have additional benefits for muscle mass, strength, and physical performance when combined with resistance training [56–59]. A recent cross-sectional study found that meeting a daily protein intake of 1.1 g/kg BW was related to beneficial constructs of physical function in older women [60], which supports other research pointing toward a recommended daily intake above 1.0 g/kg BW [61].

Physical activity for healthy ageing

Physical activity can be defined as any bodily movement produced by skeletal muscles that results in energy expenditure [62]. It can be considered more specifically in terms of intensity, duration, and frequency, which together provide information about PA patterns. According to metabolic equivalent (MET) values, light-intensity PA (LPA) encompasses activities performed at an intensity corresponding to 1.5–3.0 METs such as light gardening and slow walking, whereas moderate to vigorous-intensity PA (MVPA) comprises activities performed at an intensity of ≥3 METs, such as brisk walking and running [63,64]. Accordingly, any waking behaviour characterized by an energy expenditure ≤1.5 METs while in a sitting, reclining, or lying posture has been defined as sedentary behaviour [65].

PA can also be categorized according to the type of activity. Endurance aerobic-type PA relies primarily on the body's ability to consume oxygen, whereas muscle-strengthening activities (MSA) primarily relies on the ability to generate muscle force, predominantly through anaerobic energy systems. Examples of MSA include resistance training with machines, free weights, or elastic bands; exercises using one's own bodyweight; and holistic exercises such as yoga and qigong [66,67].

Physical activity behaviours

During waking hours, older adults spend the absolute majority of time sedentary and engaged in LPA, and only a small fraction of time engaged in MVPA [68]. In this respect, accumulating excessive amounts of sedentary time has been linked to detrimental effects on physical function [69–71]. In contrast, time spent in MVPA has been associated with better physical function [72–76], higher muscle mass [77–81], greater muscle strength [81–84], and reduced risk of sarcopenia [82,85–88].

However, not all older adults are able to engage in activities in the moderate and vigorous intensity domain. Instead, engagement in LPA is encouraged to promote a physically active lifestyle [89,90]. There is currently an increasing interest in the potential role of time spent in LPA on age-related functional decline. In this respect, there is evidence in favour of the beneficial role of time spent in LPA on indicators of physical function [90–93], frailty risk [94], and sarcopenic obesity [95].

Given that a day has a fixed amount of time, spending more time sedentary will be at the expense of other behaviours [96]. It is therefore of interest to explore the impact on health outcomes of displacing time spent in one activity intensity by another, while holding the remaining time constant. Several studies have taken this approach, finding that the hypothetical reallocation of sedentary time to a corresponding period of MVPA [92,97,98] or LPA [92] was associated with better physical function. Two other studies reported that replacing sedentary time with MVPA was related to a reduced sarcopenia risk and better physical performance, but no such benefit was seen when replacing sedentary time with LPA [82,99].

The vast majority of research in older adults has focused on the importance of current PA behaviours and indicators on physical function, with less focus on the role of PA performed earlier in life. This is unfortunate, as the decline in physical function occurs gradually over decades of time. Importantly, indicators of physical function have been shown to follow from midlife to older age, and to predict disability [100]. For this reason, information about PA habits throughout adulthood may provide new insights into the role of lifelong engagement in PA on outcomes of physical function in older populations. In this respect, there is evidence supporting positive associations between engagement in PA during adulthood and physical function at old age [101–104].

Types of physical activity

Aerobic PA is positively related to longevity and functional ability [32,105–108]. There is compelling evidence showing that VO_2max is trainable in older populations [109,110], which is supported by meta-analyses showing that older adults may improve their VO_2max by up to 30% in response to a structured aerobic training program [109,110]. Aerobic PA may also induce limited increases in muscle mass [111], though not to the extent seen with resistance training [112].

Engagement in MSA such as resistance training with free weights is of particular interest in terms of improving muscle mass [113–117] and muscle strength [114,118–121]. It is recommended to engage in MSA at least twice a week [122,123], although a lower frequency still seems to lead to some improvements in strength and function [124]. Although increases in muscle mass and strength have been indicated in response to high-load resistance training, recent research shows that even light loads can induce improvements in muscle mass and strength, while minimizing the risk of injury [125,126]. This makes MSA safe for older adults when properly performed and supervised [127]. While most studies have indicated that older men increase muscle strength to a larger extent than older women in response to resistance training [128–130], some did not report such differences [130,131].

There is currently an increased interest in MSA, sometimes termed as muscle-strengthening exercises (MSE) [66], as a broader concept encompassing not only resistance training exercises but also other activities that can confer positive effects on muscle strength and mass. Activities such as yoga [132,133] and qigong [134,135] have been shown to improve muscle strength and quality of life in younger and older adults, and should be taken into consideration when investigating the relationship between strengthening activities and muscle mass and physical function.

Physical activity guidelines

The ancient Greek physician Hippocrates famously stated that "eating alone will not keep a man well, he must also take exercise," thereby being the first to issue some sort of professional PA advice to promote health and avert disease [136]. Today, PA guidelines from major public health organizations such as the World Health Organization [89] offer evidence-based PA recommendations for young children, adolescents, adults, and older adults as well as pregnant women and chronic disease populations. These guidelines are issued in connection with a framework known as the WHO global action plan for physical activity 2018–2030, which has the goal of reducing physical inactivity by 15% by 2030 [137].

The recently updated WHO guidelines [89] on physical activity and sedentary behaviour recommend that older adults should perform regular PA and, more specifically, engage in at least 150 weekly minutes of a combination of moderate to vigorous intensities and for additional benefits increase this to 300 weekly minutes and more (Figure 3). Furthermore, older adults should engage in MSA that targets all muscle groups at least twice a week and should also limit their sedentary time. Importantly, the PA guidelines acknowledge that not all older adults are able to perform intense or large amounts of PA and emphasize the need to adjust PA level to the individual's ability and to increase the volume and intensity over time. However, adherence to these guidelines is low [66], with less than 20% of the older adult population in the United States achieving the recommended weekly MVPA time and engagement in MSA [138,139].

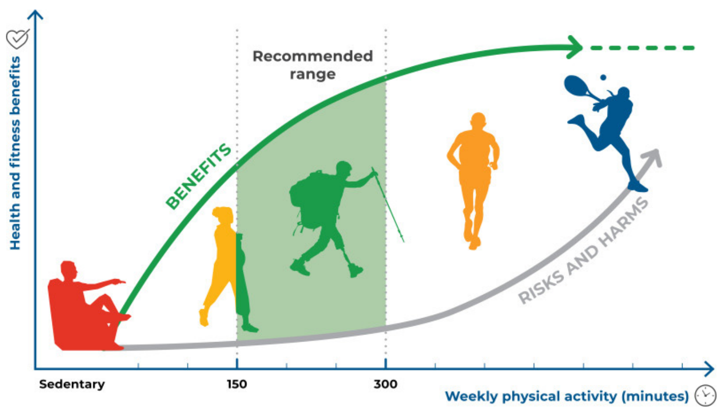


Figure 3. Dose response curve between minutes of MVPA per week and health benefits. Taken from WHO (2020)

Research gaps

Although regular PA may have an important role in age-related changes in indicators of physical function, there are several research gaps that need to be addressed.

First, while PA performed during old age has been shown to improve aerobic fitness and muscle health, less is known about the influence of regular exercise habits during the middle age period on indicators of physical function at old age. This knowledge is particularly important for older women, who typically have lower muscle mass and muscle strength compared to men and are potentially at higher risk of sarcopenia. There is also a lack of data regarding the importance of PA performed during different time periods (e.g. 35–50 vs. 50–65 years) for maintenance of physical function at old age. Therefore, the physical demands of occupation, which may impact on the trajectories of physical function, should be taken into account when investigating the role of PA habits during the middle-aged period on physical function at older age.

Second, while time spent in PA of moderate to vigorous intensities has been linked to beneficial impacts on indicators of muscle health, uncertainties remain about PA performed at lighter intensities. The majority of previous reports have studied the health impacts of separate dimensions of PA behaviours, without considering that daily time spent at one PA intensity inevitably displaces time spent at another.

Third, PA guidelines currently stipulate that older adults should engage in MSA at least twice per week in order to maintain physical function. However, the potential benefits of MSA on indicators of muscle health beyond those obtained by meeting the guideline of 150 weekly minutes of MVPA remains unclear. When investigating this question, it is important to account for adherence to protein intake guideline, as this is an important factor related to muscle growth and sarcopenia risk.

Finally, current PA guidelines stipulate that older adults should engage in at least 150 weekly minutes of a combination of moderate to vigorous PA intensities, and that additional benefits may be achieved by increasing weekly time in MVPA to at least 300 minutes. It remains to be clarified whether ≥300 weekly minutes of MVPA in older adults has a greater benefit for indicators of physical function compared to at least 150 but less than 300 weekly minutes of MVPA.

Aims

The overall aim of this thesis was to investigate the impact of PA behaviours on muscle mass and physical function in older adults.

Study I
To explore the impact of regular exercise habits in middle age on skeletal muscle mass and function in old age, while taking into account the physical demand of former occupation and objectively assessed present PA level.

Study II
To determine the impact of reallocating time at different PA intensities on indicators of muscle mass and function in older adults, while taking into account physical activity type (MSA) and adherence to guidelines for protein intake.

Study III
To determine whether engagement in MSA is linked to sarcopenia risk in older adults who meet the PA guidelines of 150 min of MVPA per week.

Study IV
To explore differences in physical function indicators between older adults accumulating ≥150 to <300 min/week and those accumulating >300 min/week of MVPA while taking into account adherence to MSA and protein intake guidelines.

Methods

Study design and participants

The studies included in the present thesis are based on a cross-sectional design. Study I included a sample of 112 community-dwelling older women aged 65–70 recruited during 2011. Studies II–IV were based on a sample of 252 community-dwelling older men and women aged 65–70 recruited during 2018. Participants in all studies were recruited through local advertisement. Exclusion criteria were overt diseases including cardiovascular disease, diabetes, psychiatric disorders, and disabilities that limit mobility.

Body composition

All measurements of body composition took place in the morning after an overnight fast. Body height and weight were measured using standard procedures. Waist circumference was measured to the nearest 0.1 cm at the midpoint between the iliac crest and lower costal margin, using a measurement tape. Skeletal muscle mass index (SMI) was assessed using bioelectrical impedance analysis (Study I: Tanita BC-420MA, Tanita Corporation, Japan; Studies II–IV: Tanita MC-780, Tanita Amsterdam, Netherlands). Skeletal muscle mass (SMM) was calculated using the equation of Janssen et al. [140], and thereafter divided by BW to obtain the SMI in kg/BW: SMI (kg) = [height2/BIA resistance x 0.401) + (gender x 3.825) + (age x -0.071)] + 5.102, where height is in cm, BIA resistance is in ohms, gender = 0 for women, and age is in years.

Physical activity and sedentary behaviour

Objective assessment of PA was performed using an ActiGraph GT3x accelerometer (ActiGraph, Pensacola, FL), worn on the right hip for a week. A minimum of four days and at least 10 hours of wearing time per day were required to be included in the analysis. Non-wear time was defined as a minimum of 60 min of continuous zero counts. Accelerometer cut-off points for different intensities of PA were: sedentary time (SED) <100 counts per min (CPM), LPA >100–2019 CPM, MVPA >2019 CPM [63].

Engagement in exercise-related activities between 35 and 65 years of age was assessed with the Historical Adulthood Physical Activity Questionnaire (HAPAQ). Former occupations were classified as either sedentary, where participants spent most of the time sitting, or manual, where participants spent most of the time standing and which required moderate to vigorous physical efforts. To be classified into the sedentary occupation category, participants should have spent at least 20 years in sedentary occupations between the ages of 35 and 65.

Engagement in MSA was assessed on basis of the EPAQ2 questionnaire [141]. Duration and frequency of MSA performed during the last 12 months were reported, including strength exercises, rubber band resistance exercises, yoga-type activities, and sit-ups. Based on reported frequencies, participants were classified as engaging in MSA twice a week or not.

Performance tests

Maximal isometric strength

Maximal isometric strength was measured with a force sensor (K. Toya 333A, Toya-Korea, Seoul, South Korea) during arm flexion and knee extension tests using standardized procedures [142]. The dominant arm and leg were used for all assessments.

Handgrip strength

Handgrip strength was assessed with a Jamar handheld dynamometer (Paterson Medical, Warrenville, IL, USA) using standard procedures. The test was performed with the dominant hand, and participants were encouraged to squeeze as hard as possible. The highest value of three attempts was reported.

Squat jump test

Lower limb power was assessed by a standardized squat jump test using a force platform (Kistler 9281 B; Kistler Nordic AB, Jonsered, Sweden). Maximum ground reaction force was recorded from the concentric phase of the jump. Three squat jumps were performed, separated by recovery periods of 1.5 minutes. Participants were instructed to place their hands on their thighs and start the jump from a squat at an angle of 90 degrees between the upper and lower legs.

Cardiorespiratory fitness

The Åstrand submaximal exercise test was performed on a cycle ergometer (model 874 E; Monark, Varberg, Sweden). Participants cycled for 6 minutes at 50 revolutions per minute with a constant workload (75–125 watts, depending on the participant's current fitness level), and heart rate was measured throughout the test. Predicted maximal oxygen uptake (VO_2max, $mlO_2 \cdot min^{-1} \cdot kg^{-1}$) was derived based on the average heart rate during the last 2 minutes of the test [42].

The 6MW was used to assess functional walking capacity, and lower body musculoskeletal and cardiorespiratory fitness [143]. Participants were instructed to walk as far as possible along a 50-meter corridor for a period of 6 minutes. No running was allowed.

The five times sit-to-stand test (5-STS)

The 5-STS was used to assess lower extremity strength and the ability to repeatedly transfer from a seated to a standing position and vice versa. Participants were instructed to stand fully upright from a chair and then sit down again. This sequence was repeated five times and performed as fast as possible [39].

Physical performance score

A physical performance score was created based on handgrip strength, 5-STS performance, squat jump performance, and 6MW. The four variables were averaged and merged into a sex-specific composite score, with a higher score indicating a better physical performance.

Sarcopenia risk score

In accordance with the recent operational definition by the EWGSOP, a sarcopenia risk score (SRS) was created based on handgrip strength, SMI, and the 5-STS. Sex-specific standardized values of each variable were averaged and merged into one composite score, with a higher score indicating a higher sarcopenia risk.

Covariates

Adherence to a daily protein intake of 1.1 g/kg BW was assessed using a validated food-frequency questionnaire [144] with 9 fixed response alternatives: never, occasionally, 1–3 times/month, 1 time/week, 2–3 times/week, 4–6 times/week, 1 time/day, 2–3 times/day, and ≥4 times/day. Tobacco use was assessed by asking the participants about their current and past tobacco use. Medication use was also assessed by self-report.

Ethical considerations

Prior to inclusion, participants received written information about the aim of the project, procedures, benefits, and potential risks and discomfort before they provided their written consent. They were informed that participation was voluntary and that they could discontinue their participation at any moment. Their safety, wellbeing, health, integrity, human dignity, and confidentiality were secured throughout all steps of the project. All tests were conducted by trained personal with adequate experience and competence. Participants received instructions on how to perform the physical tests. The selected physical tests are known to carry only a minimal amount of risk and/or discomfort. All data were anonymized and stored in accordance with the personal data act. All procedures were conducted according to the principles set by the declaration of Helsinki, and all studies were approved by the regional ethics committee of Uppsala, Sweden (refs: 2011/033 and 2017/511).

Statistical analyses

Statistical analyses were conducted with the SPSS statistical software package (SPSS, Chicago, IL, USA). All data are reported as means ± standard deviation (SD) unless otherwise stated. Assumptions related to parametric tests used in the studies, including normality, linearity, homoscedasticity, and multicollinearity between independent variables, were checked and variables were transformed when necessary to fit a normal distribution. The level of significance was set at $p < 0.05$. Sample sizes used for each study allowed small to moderate effect sizes to be detected with a power of ≥80% with alpha set to 0.05.

In Study I, participants were classified into two groups based on whether or not they reported a weekly average of at least 600 MET minutes of leisure-time PA during middle age (active vs. not active). They were also categorized into whether they had a sedentary occupation or not during middle age. Factorial analysis of variance (ANOVA) was conducted to investigate the impact of participation in regular exercise (yes vs. no) and having a sedentary occupation (yes vs. no) during middle age on functional outcomes and SMI. The models were further adjusted by present physical activity level. Analyses were conducted across the whole middle-age period (35–65 years), followed by separate analyses of the early (35–50 years) and late (50–65 years) periods.

In Study II, simple linear regression was employed to assess the association between time spent at different PA intensities (in periods of 10 minutes) and SRS and related subcomponents. An isotemporal substitution analysis was used to investigate the effect on indicators of muscle health of hypothetical changes in time spent at different PA intensities while holding total wear time constant. All models were adjusted by waist circumference and adherence to the recommendation on protein intake (1.1 g/kg BW). Models were further adjusted by type of PA (MSA, yes/no).

In Study III, factorial ANOVA was used to assess differences in sex-specific SRS and its components between those reporting MSA at least twice a week (adherence) or not (no adherence). The models were adjusted by age, sex, use of prescribed medication (yes/no), tobacco use (never, past use, current use), waist circumference, and adherence to the recommendation on protein intake (1.1 g/kg BW).

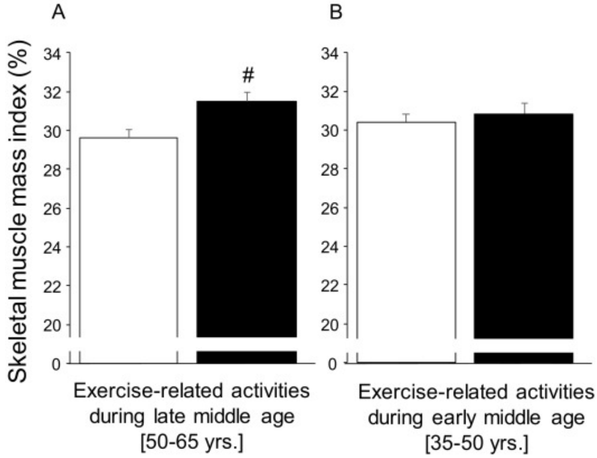
In Study IV, factorial ANOVA was used to assess differences in physical function between participants reporting ≥150 - <300 min/week and those reporting ≥300 min/week of MVPA. All models were adjusted by sex, MSA, protein intake, and waist circumference.

Main results and discussion

Study I: Regular exercise habits in middle age and skeletal mass and cardiorespiratory fitness in old age

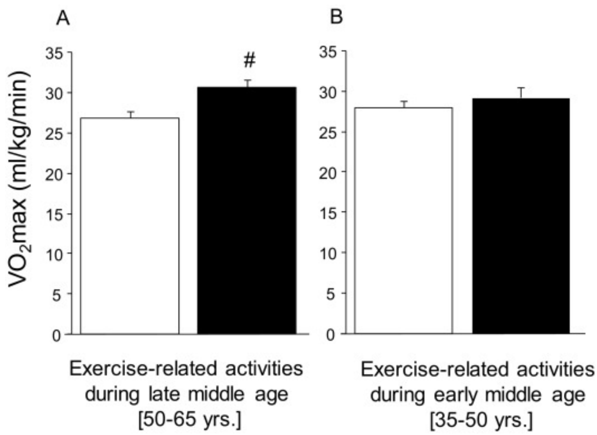
The older women (67.5±1.7 years old; 164.5 ± 5.7 cm; 68.3 ± 11.5 kg) included in Study I had a SMI of 30.4 ± 3.9% and a VO_2max of 28.4 ± 7.4 ml $O_2 \cdot min^{-1} \cdot kg^{-}1$. A total of 47% reported an average amount of at least 600 MET minutes (median: 487; IQR: 772) during middle age. Older women who regularly engaged in exercise-related activities (≥ 600 MET minutes per week) during late middle age (35–65 years)] had a significantly higher SMI (p <0.01; Figure 4A) and better cardiorespiratory fitness (p <0.01; Figure 5A) at old age, compared to their less-active peers (< 600 MET minutes per week). This finding remained significant after adjustment for type of occupation and the current amount of performed PA. The beneficial impacts of exercise habits during middle age were driven by engagement in regular exercise during the late middle age period (50–65 years), whereas no corresponding impacts were evident for the early middle age period (35–50 years).

Fig. 4A and 4B



Figures 4A and 4B. Skeletal muscle mass index (SMI) (mean ± standard error, SE) in older women reporting weekly regular exercise (≥600 MET minutes) (■) or not (□) at age intervals 50–65 years (A) and 35–50 years (B). All data are adjusted for occupation type and present PA level. # *p* <0.01.

Fig. 5A and 5B



Figures 5A and 5B. Cardiorespiratory fitness (VO_2max) (mean ± standard error, SE) in older women reporting weekly regular exercise (≥600 MET minutes) (■) or not (□) at age intervals 50–65 years (B) and 35–50 years (A). All data are adjusted for occupation type and present PA level. #*p* <0.01.

Our findings highlight the importance of regular engagement in exercise during the late middle age years, specifically for the maintenance of muscle mass at old age. It is possible that engagement in exercise-related activities during middle age will also promote muscle hypertrophy. Engagement in regular exercise during middle age was also beneficial for maintenance of cardiorespiratory fitness, which in turn may have important implications in terms of maintained ability to perform ADL in old age. While engagement in regular exercise in the late middle age period was related to better muscle health in old age, the lack of corresponding effects from the early middle age period may be due to the substantial time gap between the reported behaviour and the hypothesized effect. Nevertheless, promotion of engagement in regular exercise during the full adulthood period should still be encouraged, as there are reports indicating that adoption of regular exercise habits in early adulthood may be maintained into old age [145].

Study II: Reallocation of time spent at different PA intensities and indicators of muscle mass and function in older adults

Study II included 235 older men and women aged 67±2 years. The women were 165.5 ± 6.5 cm tall and weighed 64.8 ± 10.2 kg, and the men were 178.6 ± 6.5 cm tall and weighed 80.8 ± 10.7kg. Overall, 45% were currently on medication, 8% currently used tobacco, and 55% reported past tobacco use. Data on PA behaviours and components of sarcopenia risk are presented in Table 1.

Table 1. General characteristics of the study population.

	Men	**Women**
n	88	147
Physical Activity		
SED, min	516 ± 72	492 ± 68*
LPA, min	274 ± 70	296 ± 66*
MVPA, min	40 ± 21	43 ± 25
Sarcopenia risk		
SMI, % BW	34.5 ± 3.2	26.5 ± 3.5*
HG, kg	44.0 ± 7.1	27.7 ± 5.3*
5-STS, s	10.2 ± 2.0	10.4 ± 2.5

Data are presented as mean ± SD unless otherwise indicated. Min, minute; BW, bodyweight; kg, kilogram; s, seconds; SED, sedentary time; LPA, light physical activity; MVPA; moderate to vigorous physical activity; SMI, skeletal muscle index; HG, handgrip strength; 5-STS, five times sit-to-stand test. * p <0.05 vs. women.

Replacing a period of 10 minutes of sedentary time with a corresponding period of LPA was related to a significantly reduced sarcopenia risk (p <0.05), and this result remained significant (p <0.05) when adjusted for MSA, protein intake, and central obesity (Table 2).

Table 2. Effect (β coefficient, 95% CI) of isotemporal relocation of time spent at different PA intensities on SRS and subcomponents.

		SRS	SMI	5-STS	HG
Replace 10 min **SED** with	**LPA**	−0.020 [−0.033 to −0.006] *	0.023 [0.006 to 0.040] *	-	-
	MVPA	−0.086 [−0.120 to −0.051] *	0.075 [0.031 to 0.118] *	0.072 [0.017 to 0.127] *	0.111 [0.060 to 0.162] *
Replace 10 min **LPA** with	**MPVA**	−0.066 [−0.101 to −0.032] *	0.051 [0.008 to 0.094] *	-	0.093 [0.043 to 0.144] *

CI: confidence interval; SED: sedentary time; LPA: light physical activity; MVPA: moderate to vigorous physical activity; SMI: skeletal muscle mass index; HG: Handgrip strength; 5-STS: five times sit-to-stand test. Adjusted for accelerometer wear time, waist circumference, and adherence to protein intake guidelines + activity type (MSA). *p <0.05.

Our findings are consistent with a previous report showing that replacing sedentary time with LPA was associated with a significantly better 5-STS performance [99]. They also support the contention that PA performed at intensities below the moderate to vigorous intensity domain may be related to reduced risk of sarcopenic obesity, metabolic abnormalities, and all-cause mortality [95,146–148]. It should however be noted that greater benefits in terms of SRS were evident when sedentary time was reallocated to MVPA, suggesting that older adults can further reduce sarcopenia risk by engaging in PA above the MVPA threshold. This is in line with the results of [82], who found a reduced likelihood of sarcopenia when LPA was replaced by MVPA, and places emphasis on the guidelines that support engagement in the moderate-to-vigorous activity intensity domain [89]. The impact on SRS of reallocating time at different PA intensities was not affected by adherence to MSA guidelines, which indicates that reducing sedentary time may be beneficial for muscle health in older adults irrespective of the type of PA performed.

Study III: Engagement in MSA and sarcopenia risk in older men and women

Study III included 193 older men (n=71, age 67 ± 2 years) and women (n=122, age 67 ± 2 years) who performed at least 150 min of MVPA per week. Overall, 24% of the men and 30% of the women engaged in MSA at least twice a week. Adherence to the MSA guideline was related to a significantly ($p < 0.05$) lower SRS (Figure 6), a higher SMI (Figure 7a), and a better 5-STS performance (Figure 7b) even after adjustment for adherence to the protein intake guideline. Reporting engagement in MSA at least once a week had a beneficial impact on 5-STS performance only.

Fig. 6

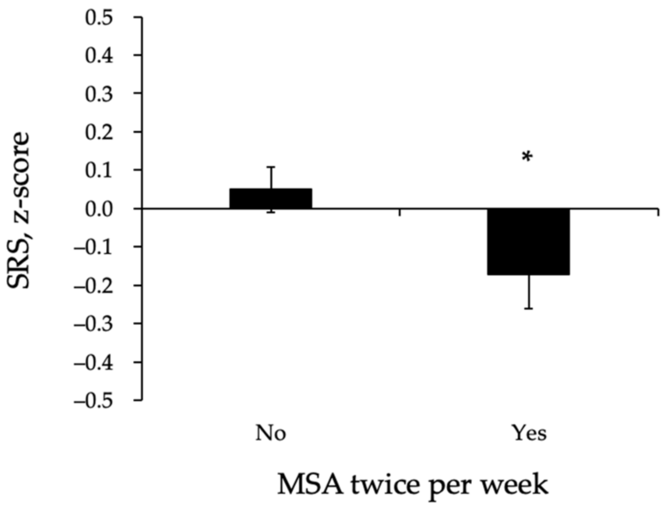
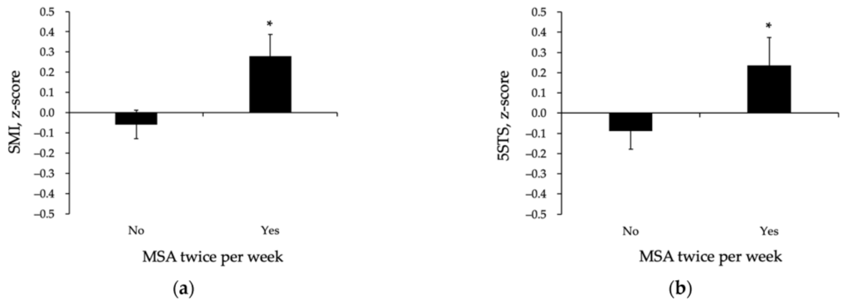


Figure 6. Sarcopenia risk score in older adults who reported muscle-strengthening activities (MSA) twice a week (yes) and those who did not (no). Means ± SEM adjusted for age, gender, waist circumference, and protein intake. * p <0.05.

Fig. 7A and 7B



Figures 7A and 7B. (a) Skeletal muscle mass index and (b) five times sit-to-stand test (5STS) in older adults who reported muscle-strengthening activities (MSA) twice a week (yes) and those who did not (no). Means ± SEM adjusted for age, gender, waist circumference, and protein intake. * p <0.05.

Our findings indicate the beneficial role of engagement in MSA for muscle health, and provide further support to studies showing that muscle strengthening exercises such as resistance training with the use of weights, elastic bands, or bodyweight [127] and yoga-type exercises [132] can have positive effects on muscle mass and muscle strength. The results of our study add to existing knowledge by emphasizing that adhering to both the recommendation of 150 weekly minutes MVPA and the recommendation of MSA twice a week is related to better muscle health than adhering to the aerobic PA guideline alone. It has been suggested that engagement in MSA once a week can lead to improvements in muscle mass and strength [149,150]; this is supported by our finding of a beneficial impact of MSA performed once a week on 5-STS performance, which represents an important indicator of physical function. However, adherence to MSA twice a week should be promoted for prevention of sarcopenia.

Study IV: Accumulated time in MVPA and indicators of physical function in older men and women

Among the physically active older men and women who participated in Study III, 52% accumulated ≥150 to <300 weekly minutes of MVPA (31.6± 6.3 min) and 48% accumulated ≥300 weekly minutes of MVPA

(63.8± 19 min). Indicators of physical function in physically active (≥150 to <300 weekly minutes) and in highly physically active (≥300 weekly minutes) are shown in Table 3.

Table 3. Indicators of physical function in groups stratified by weekly time spent in MVPA.

	Physically active	**Highly physically active**
6 MW(m)	631 ± 63	655 ± 62*
HG (kg/BW)	0.48 ± 0.1	0.50 ± 0.10
5-STS (s)	10.3 ± 2.0	10.0 ± 2.3
Squat jump (N/kg)	9.4 ± 2.3	9.8 ± 2.2

Data are presented as mean ± SD unless otherwise indicated. m, meter; HG kg/BW, handgrip strength in kg divided by bodyweight in kg; s, seconds; N/kg, Newton per kg bodyweight; 6MW, six-minute walking test; 5-STS, five times sit-to-stand test. *$p < 0.05$ vs. ≥300min/week.

The physical performance score, combining all indicators of physical function, was significantly higher in those accumulating ≥300 min/week compared to those with less MVPA time. This result remained significant ($p < 0.05$) when adjusted for sex, MSA, protein intake, and waist circumference (Figure 8). Further analyses of the separate PPS components showed that those accumulating ≥300 min/week had a significantly better 6MWT performance ($p<0.05$) compared to the less active group (Table 3), which remained evident after adjustment for MSA, sex, WC and protein intake. In contrast, no significant differences in indicators of muscle strength and function were observed between the two groups (Table 3).

Fig. 8

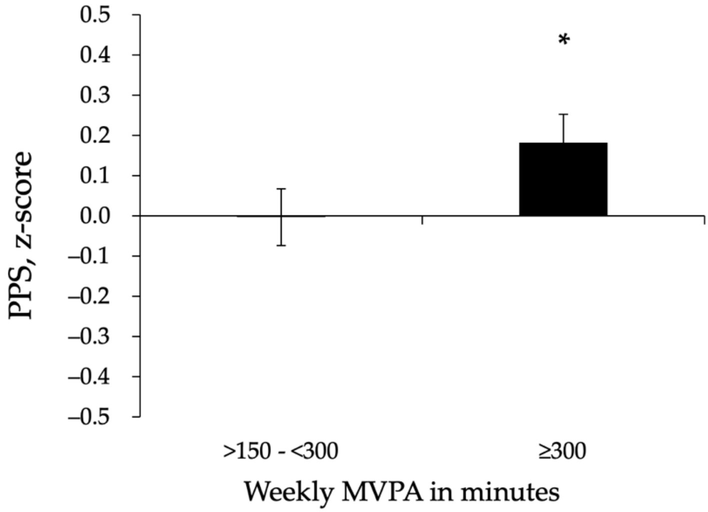


Figure 8. Physical performance score (PPS) in older adults reporting ≥300 of MVPA per week and those reporting ≥150 - <300. Means ± SEM adjusted for sex, muscle strengthening activities, waist circumference, and protein intake. * $p < 0.05$.

These results are in agreement with the recent prospective data showing that adults reporting at least twice the recommended minimum amount of MVPA had a significantly lower mortality risk compared to the less active group [151]. The highly physically active group in this study showed a greater walking performance compared to their less active peers. This may hold implications with regards to the ability to perform activities of daily living, reduction of the burden of physically disability and its health-care related cost. In contrast, no corresponding benefits were observed for any indicators of muscle strength and function. It may be that most activities performed within the MVPA domain are predominantly of aerobic type, which unlikely elicits significant improvements in forearm muscle flexors. By further taking advantage of using a force-platform alongside the 5-STS to determine lower limb strength and function, the lack of beneficial impact of accumulating twice the minimum recommended MVPA amount on lower limb strength was strengthened.

Methodological considerations and limitations

All four studies assessed PA via accelerometery, which is a valid and non-invasive method for assessment of physical activity behaviours in free living settings [152–154]. One limitation of this method is that non-ambulatory activities may not be accurately captured [155]. However, our use of self-report by the validated EPAQ2 [141] allowed MSA to be captured. Leisure time exercise habits during middle age were measured using the validated HAPAQ questionnaire [156]. It should be noted that all self-report tools collecting retrospective data are prone to recall bias, leading to cruder measures of PA [157,158]. However, limiting the data collection to engagement in regular leisure time sport activities, and excluding everyday activities such as walking, likely reduces the measurement error due to recall bias.

Assessment of muscle mass can be conducted using different methods, including computed tomography, magnetic resonance imaging, dual-energy x-ray absorptiometry, and bioelectrical impedance analysis (BIA). Despite being less accurate than other methods, BIA is considered an accurate tool for assessment of functioning muscle mass [140]. It is easy to use, requires no technical expertise, does not involve exposure to radiation, and is less expensive than other tools [159]. For these reasons, BIA is widely used for assessment of muscle mass in older adults in clinical settings and epidemiological research [160], as recommended by the European Working Group on Sarcopenia in Older People [9]. The measurement validity is further improved when standardized procedures are followed (overnight fast, no strenuous activities or alcohol intake prior to the measurement) [160] and population-specific equations are used [140].

Assessment of physical function was performed using a battery of physical performance tests adapted to cause minimal discomfort and risk of injuries in older adults. While indirect calorimetry generally generates more accurate estimations of VO_2max in adults, submaximal estimations of cardiorespiratory fitness are more adapted to the older population, as maximal exertion is not required [42,161].

All four studies were based on a cross-sectional design. As the data were drawn from a population at a single point at time, causal relationships cannot be derived [162]. Additionally, it is important to emphasize that the older adults included in the thesis (narrow age range, absence of overt disease) are not representative of a broader population of older adults with variation in ethnicity, age, sociodemographic background, physical activity level, and health status. Finally, although several covariates were considered in the present work, confounding influences from other non-measured factors cannot be ruled out.

Conclusions

The present thesis aimed to investigate the role of PA behaviours on muscle mass and physical function in older adults. The main conclusions are:

1. Regular engagement in exercise activities during middle age is associated with higher muscle mass and better cardiorespiratory fitness at old age.

2. Displacement of daily sedentary time with PA of at least light intensity is associated with a lower sarcopenia risk in older adults, with additional benefits above the moderate PA intensity threshold.

3. Engagement in MSA at least twice a week is linked to lower sarcopenia risk, larger muscle mass, and better physical performance in older adults who already perform at least 150 weekly minutes of MVPA.

4. Older adults accumulating at least 300 weekly minutes of MVPA have a better walking performance compared to those adhering to the minimum weekly amount of MVPA.

Practical implications

Although ageing is inevitable, the present thesis shows that an active lifestyle is an important element in slowing the rate of decline in muscle mass, muscle strength, cardiorespiratory fitness, and physical function among older adults.

One salient finding was the importance of engagement in regular exercise activities during middle age for physical function in old age. This implies that optimization of muscle mass and physical function in old age requires preventive efforts targeting the middle-aged population as well as those who have already reached old age.

This thesis also highlights the benefits of engaging in LPA for indicators of muscle health in older adults. Emphasis should therefore be placed on breaking prolonged sedentary behaviours for more active pursuits, in order to preserve adequate muscle mass and function in old age. This is particularly important for older adults whose participation in activities of higher intensities is limited. Notwithstanding this, in order to benefit from additional effects on physical function, accumulation of time spent in MVPA should be endorsed, which supports current PA guidelines. Older adults able to accumulate twice the currently recommended minimum amount of weekly time in MVPA (≥300 instead of >150 min/week) could receive additional benefits in terms of improved physical function.

Finally, the present findings highlight the need to promote adherence to the MSA part of current PA guidelines for older adults, in addition to adherence to >150 min/week of aerobic-type PA.

Perspectives for future research

The findings in this thesis highlight the importance of both past and current physical activity levels to maintain physical performance and reduce sarcopenia risk in older adults. For future research, the following aspects should be considered.

1. There is a need to generate data based on randomized controlled trials investigating the effect of reallocating time spent at different physical activity intensities on indicators of muscle health in older adults.

2. Longitudinal designs aiming to capture age-related trajectories of changes in muscle mass and physical function and the impact of physical activity behaviours would clarify the direction of relationships between these factors.

3. There is a need to better understand the dose response relationship between PA and physical function in order to determine the optimal dose of PA for preservation of muscle health in older adults.

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Svensk sammanfattning

Åldrandet är kopplat till en gradvis nedsatt fysisk funktion, inbegripet förlust av muskelmassa och muskelstyrka, vilket leder till försämrad förmåga att utföra dagliga aktiviteter. Fysisk aktivitet anses vara en viktig livsstilsfaktor med potential att bromsa åldersrelaterad nedgång i fysisk funktion. Riktlinjer om mängd och typ av fysisk aktivitet för hälsoeffekter fokuserar på minskad tid i stillasittande till förmån för ökad tid i fysisk aktivitet av aerob karaktär med minst måttlig intensitet. Dessutom rekommenderas regelbunden styrketräning för att främja bibehållen muskelmassa och muskelstyrka hos äldre. I vilken utsträckning olika mängd och typ av fysisk aktivitet kan påverka olika dimensioner av fysisk funktion är för närvarande oklart. Det övergripande syftet med denna avhandling var att undersöka betydelsen av fysisk aktivitet på muskelmassa och fysisk funktion hos äldre. Studie I påvisade att regelbundna motionsvanor under sen medelålder (50-65 år) var kopplat till en signifikant större muskelmassa och en bättre aerob kondition vid 65-70 år. Studie II visade att om man ersätter en period av stillasittande med fysisk aktivitet av lättare intensitet så är det kopplat till en signifikant lägre risk för sarkopeni hos äldre. Studie III visade att styrketräning minst två gånger i veckan var kopplat till en signifikant lägre risk för sarkopeni hos äldre som redan uppnår minst 150 minuter av fysisk aktivitet per vecka. Slutligen, studie IV visade att äldre som är fysisk aktiva minst 300 minuter/vecka har en signifikant bättre fysisk funktion jämfört med de som är fysisk aktiva mellan 150 och 300 minuter per vecka. Sammantaget belyser avhandlingen vikten av regelbunden fysisk aktivitet i enlighet med nuvarande rekommendationer för att bromsa åldersrelaterad nedgång i fysisk funktion hos äldre.

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