# ASSOCIATION OF FUNCTIONAL AGE WITH PHYSICAL ACTIVITY IN OLDER PEOPLE LIVING AT HOME

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Gerontology and public health master's thesis
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Autumn 2023

# ABSTRACT

Blomqvist, J. 2023. Association of functional age with physical activity in older people living at home. Faculty of Sport and Health Sciences, University of Jyväskylä, a master's thesis on gerontology and public health, 65 pages.

Several individual biomarkers and sets of biomarkers, for example epigenetic clocks, have been developed to measure and gain a deeper understanding of ageing than we can achieve through chronological age. Some biomarkers focus on obtaining information about ageing trough different functional measurement. Physical activity (PA) has been shown to be beneficial for older adults' functional ability in many ways. However, age-related changes in functional capacity can hinder engagement in physical activity and ageing is associated with a decline in PA levels. The aim of this thesis is to investigate the association of a sum variable of functional biological age (fBioAge) with PA in older people living at home.

This cross-sectional study included participants from a population-based study who had worn an accelerometer for at least three whole days and who had participated in measurements of all the elements of sum variable fBioAge: self-reported hearing and vision, maximal isometric hand-grip strength, walking time (3m) and respiratory function (Forced Expiratory Volume in the first second, FEV1) (n=407, 61.7% women). Five functional measurement results were transformed to standard scores and summed up together to create the sum variable fBioAge. Weaker results from the five functional measurements indicate higher functional age. Participants represented age cohorts of 75-, 80- and 85-years. Linear regression analyses were used to investigate the associations of fBioAge with total PA and absolute moderate to vigorous PA (MVPA). Regression models were adjusted for age, sex, lifestyle factors (smoking and alcohol consumption), a number of chronic diseases, Body Mass Index (BMI) and use of assistive devices.

FBioAge ranged between 24.2 and 98.7 with the mean of 49.4 (SD 9.8) in all participants. Women's fBioAge scores were higher on average compared to men (women 50.6 and men 47.4, $p=0.001$). Higher fBioAge was associated with lower amount of total PA (age and sex adjusted standardized coefficient = -0.205, $p<0.001$) and absolute MVPA (-0.183, $p<0.001$). There was no interaction for age and sex in the basic models. Further adjustment for lifestyle factors did not affect the results. The association of fBioAge with total PA (-0.125, $p=0.008$) and absolute MVPA (-0.105, $p=0.027$) remained statistically significant in the fully adjusted models.

FBioAge is associated with objectively measured total PA and absolute MVPA independent of sex and chronological age. However, the association appears to be slightly stronger in men than in women and in the age group of 85 years. It seems that the higher functional age is, the less physically active older people are. Future research is needed to examine the causal relationship between functional age and physical activity in longitudinal study designs with a population that has greater variance in functional ability.

Key words: ageing, biomarker of ageing, functional ability, functional biological age, physical activity

# TIIVISTELMÄ

Blomqvist, J. 2023. Association of functional age with physical activity in older people living at home. Liikuntatieteellinen tiedekunta, Jyväskylän yliopisto, Gerontologian ja kansanterveyden pro gradu -tutkielma, 65 sivua.

Useita biomarkkereita ja niiden yhdistelmiä on kehitetty mittaamaan ikääntymistä, jotta saavutettaisiin syvempi ymmärrys ikääntymisestä ilmiönä kuin mihin kronologisen iän avulla pystytään. Osalla biomarkkereista kerätään tietoa ikääntymisestä erilaisten toiminnallisten mittausten avulla. Fyysisen aktiivisuuden on osoitettu edesauttavan ikääntyneiden toimintakykyä monin tavoin. Ikääntymiseen liittyvät toimintakyvyn muutokset voivat kuitenkin rajoittaa fyysistä aktiivisuutta ja ikääntymisen on havaittu olevan yhteydessä fyysisen aktiivisuuden tason laskuun. Tämän opinnäytetyön tavoitteena on tutkia toiminnallisen biologisen iän summamuuttujan (fBioAge) yhteyttä fyysiseen aktiivisuuteen kotona asuvilla iäkkäillä henkilöillä.

Tämän poikkileikkaustutkimuksen aineisto koostui väestöpohjaisen tutkimuksen osallistujista, jotka käyttivät kiihtyvyysanturia vähintään kolme päivää ja joilla oli tulos kaikkien summamuuttuja fBioAge:n osatekijöiden mittauksista: itseraportoitu kuulo ja näkö, maksimaalinen puristusvoima, kävelyaika (3 m) ja hengityselimistön toiminta (uloshengityksen sekuntikapasiteetti, FEV1) (n=407, 61.7 % naisia). Toiminnalliset mittaustulokset muutettiin standardipisteiksi, joista muodostettiin summamuuttuja fBioAge. Heikommat tulokset toiminnallisista mittauksista viittaavat korkeampaan toiminnalliseen ikään. Osallistujat edustivat ikäryhmiä 75-, 80- ja 85-vuotiaat. FBioAge:n yhteyttä fyysiseen aktiivisuuden kokonaismäärään sekä keskiraskaan-raskaan fyysisen aktiivisuuden määrään tarkasteltiin lineaarisella regressioanalyysilla. Regressiomallit vakioitiin iällä, sukupuolella, elintapatekijöillä (tupakointi ja alkoholin käyttö), kroonisten sairauksien lukumäärällä, painoindeksillä (BMI) sekä apuvälineiden käytöllä.

FBioAge vaihteli 24.2 ja 98.7 välillä ja oli keskimäärin 49.4 (keskihajonta 9.8). Naisten fBioAge oli keskimäärin korkeampi kuin miesten (naiset 50.6 ja miehet 47.4, p=0.001). Korkeampi fBioAge oli yhteydessä vähäisempään fyysisen aktiivisuuden kokonaismäärään (iällä ja sukupuolella vakioitu standardoitu regressiokerroin = -0.205, p<0.001) ja keskiraskaan-raskaan fyysisen aktiivisuuden määrään (-0.183, p<0.001). Perusmalleissa ei ollut interaktiota iän ja sukupuolen välillä. Vakiointi elintapatekijöillä ei vaikuttanut tuloksiin. FBioAgen yhteys fyysisen aktiivisuuden kokonaismäärään (-0.125, p=0.008) ja keskiraskaan-raskaan fyysisen aktiivisuuden määrään (-0.105, p=0.027) säilytti tilastollisen merkitsevyytensä täysin vakioiduissa malleissa.

FBioAge on yhteydessä objektiivisesti mitattuun fyysisen aktiivisuuden kokonaismäärään sekä keskiraskaan-raskaan fyysisen aktiivisuuden määrään iästä ja sukupuolesta riippumatta. Yhteys näyttäisi olevan hieman vahvempi miehillä kuin naisilla sekä 85-vuotiaiden ikäryhmässä. Vaikuttaisi siltä, että mitä korkeampi toiminnallinen ikä on, sitä vähemmän on fyysistä aktiivisuutta. Tulevaisuudessa tarvitaan pitkittäistutkimuksia toiminnallisen iän ja fyysisen aktiivisuuden yhteyden syy-seuraus-suhteen selvittämiseksi tutkimusjoukossa, jossa on laajempaa vaihtelua toimintakyvyssä.

Asiasanat: ikääntyminen, ikääntymisen biomarkkeri, toimintakyky, toiminnallinen biologinen ikä, fyysinen aktiivisuus

**CONTENTS**

# 1 INTRODUCTION

Ageing is associated with physiological changes which lead to functional decline and structural changes in the body (Chodzko-Zajko et al. 2009). Human ageing is therefore considered to be the sum of several changes, starting with molecular and cellular changes, and ending with visible changes in function (Ferrucci et al. 2018). For decades, the challenge of observing this biologically complex phenomenon only as a chronological timely measurement has been recognised (Kiiskinen et al. 1978).

Defining who is an older person is a challenge and definitions vary in the research field. There is no consensus in literature on when old age begins or who is old (Chodzko-Zajko et al. 2009). There are also no precise guidelines on the minimum age of participants in ageing studies (Chodzko-Zajko et al. 2009). In Finnish legislation, an older person is defined as a person who is entitled to receive an old-age pension (Laki ikääntyneen väestön toimintakyvyn tukemisesta sekä iäkkäiden sosiaali- ja terveyspalveluista 980/2012). The starting date of the old-age pension is determined by the year of birth (Työeläke 2022). When discussing ageing as a phenomenon, the World Health Organization refers to the increasing number of people over 60 years (WHO 2022b). In this thesis, the term older individual is used to refer to people aged 65 years and over and most of the referred studies in this thesis have also focused on people aged 65 years and over. The data analysed in this thesis have been gathered from participants aged 74 to 85 years.

Chronological age measures the time since birth and is the most commonly used measure of ageing in ageing studies (Finkel et al. 2017). However, some ageing changes occur earlier in some individuals than others with the same chronological age (Ferrucci et al. 2018) and when examining a large cohort of individuals over 70 years of age, a phenotypically divergent set of individuals is found (Lohman et al. 2021). Compared to chronological age, measuring functional age allows us to examine variations across time, gender, and individuals in relation to individual differences in ageing, and to account for both genetic and environmental factors (Finkel et al. 2017). Functional ageing as a phenomenon has been noticed in the research field at least since the 1970s (e.g. Suominen 1978; Kiiskinen et al. 1977) and several biomarkers have been used to measure ageing in the body (Finkel et al. 2017). However, no single biomarker (e.g., handgrip strength or measurement of respiratory function) has been able to characterise the body's ageing processes in a representative way on its own (Finkel et al. 2017).

Due to the lack of a representative biomarker for ageing processes, researchers have decided to selectively use several biomarkers together to observe the complex processes that occur in the body over time and to observe ageing as a phenomenon (Finkel et al. 2017). Yet there is no standard for such a combination of biomarkers (Finkel et al. 2017). One measure of functional age is the sum variable fBioAge developed by Finkel et al. (2017). The sum variable includes five functional measures of the body: muscle strength (handgrip strength), respiratory function (Forced Expiratory Volume in the first second, FEV1), walking speed and sensory function (vision and hearing) (Finkel et al. 2017).

There is strong evidence that physical activity (PA) improves physical functioning and reduces the risk of age-related physical disability (Office of Disease Prevention and Health Promotion 2018). By exercising and being physically active, people can maintain and improve their quality of life (Liikunta: Käypä hoito -työryhmä 2016). PA can reduce the risk of several serious diseases, depressive symptoms, and disability, plus slow the deterioration of the heart, muscles, metabolism, and respiratory and circulatory systems (Powell et al. 2019; Marzetti et al. 2017; Liikunta: Käypä hoito -työryhmä 2016; Chodzko-Zajko et al. 2009). Moreover, regular PA has been associated with improvements in mental health, psychological, social, and emotional well-being, and cognitive function (Powell et al. 2019; Langhammer, Bergland & Rydwik 2018).

The amount of PA can be assessed in multiple ways. One objective and non-invasive method is an accelerometer, which can not only measure moderate to vigorous intensity PA (MVPA) but also light-intensity PA and sedentary behaviour (Lee & Shiroma 2014). Accelerometer-based movement monitors collect information about acceleration that indicates postural changes and/or activity as well as the time and date when the activity has occurred (Wijndaele et al. 2015). Accelerometers have become gradually easy to access and more affordable and are therefore feasible to use also in large-scale studies (Wijndaele et al. 2015; Lee & Shiroma 2014). The data collected with accelerometers across the globe provide a significant opportunity to understand PA across the intensity spectrum reflecting distribution, determinants, health effects, and burden of disease (Wijndaele et al. 2015).

Although physical activity is beneficial, age-related changes in functional capacity can hinder engagement in physical activity. The purpose of this master's thesis is to investigate the association of functional age with PA in older people living at home. Since new ways of measuring ageing, that are based on biomarkers, have been developed, the topic of this thesis is relevant. In this thesis, the sum variable fBioAge, including self-reported vision and hearing, maximal isometric handgrip strength, walking speed and respiratory function, developed by Finkel et al. (2017), will be used as a marker of functional ageing. Accelerometery data will be utilized as a measure of PA. After the introduction, the phenomenon of aging is examined, drawing form existing literature, followed by a look into physical activity in older people. After this, what is known about the components of fBioage and their relation to PA is examined. Following this, the main purpose of the study, the research questions, and methods are presented, after which the results are examined in-depth. The thesis ends with a discussion of results and potential future research.

# 2 AGEING - FROM CELLULAR TO FUNCTIONAL LEVEL

There are approximately 300 theories about ageing which can be divided into four categories: programmed theories of ageing, stochastic theories of ageing (STA), evolutionary theories of ageing and ecological theories of ageing (Portin 2013). Theories of programmed ageing assume that ageing is genetically programmed in the same way that ontogenesis is from insemination until sexually mature age (Portin 2013). Stochastic theories of ageing assume that ageing is a result of multiple small molecular level errors, mainly in the DNA, that accumulate with time, finally leading to ageing and death (Portin 2013). Theory of disposable soma (Kirkwood 1979), mutation accumulation theory (Gavrilov & Gavrilova 2002) and antagonistic pleiotropy (Gavrilov & Gavrilova 2002) are considered to complement each other in explaining the evolution of ageing (Portin 2013). Lastly the ecological theories of ageing seek to link ageing to the general life cycle of the species and its ecological role in the ecosystem (Portin 2013). Considering ageing from the ecological point of view, old age can be seen as a critical phase in the life course that is deeply influenced by the physical environment (Wahl, Iwarsson & Oswald 2012).

Ageing is associated with physiological changes which can lead to functional decline and structural changes in the body (Chodzko-Zajko et al. 2009). Therefore, human ageing is nowadays considered to be the sum of several changes (Ferrucci et al. 2018). These changes occur in a hierarchy, starting with changes at the molecular and cellular level and ending with physiological and functional changes (Ferrucci et al. 2018). In this chapter common biological and functional ageing changes will be described. Also ageing indicators will be represented, focusing on the functional biological ageing indicator fBioAge, which is under examination in thesis.

## 2.1 Common biological ageing changes

Biological ageing can be defined as a group of processes that originate from a decline in capability and increase in vulnerability of the organ systems through time (Nakamura & Miyao 2008). Biological markers of ageing include a decline in mitochondrial function, shortening of telomeres, loss of cell renewal capacity and intercellular communication, loss of proteostasis, epigenetic changes and a reduction in the body's ability to use nutrients (López-Otín et al. 2013). In addition to the changes mentioned above, disturbances in the microbiome and cellular autophagy, changes in the mechanical properties of cells and extracellular space, inflammation in the body, and dysregulation of RNA looping have been highlighted as new markers of ageing (Schmauck-Medina et al. 2022). These features and the complex interactions between them shape the individual's ageing trajectory and subsequent disease risk (Hägg & Jylhävä 2021).

Biological ageing therefore starts long before any noticeable changes in functional ability and cognition occur (Ferrucci et al. 2018). Biological ageing is consequently considered by Ferrucci et al. (2018) to be the first stage of ageing. The second level is phenotypic ageing, which refers to interrelated changes in body structure or composition, homeostatic control mechanisms, neuronal function, and plasticity (Ferrucci et al. 2018). This kind of changes in physiological systems can be for example decline in cardiac output, pulmonary oxygen transport, control of ventilation, and respiratory muscle function (Roman et al. 2016). Phenotypic changes occur in all ageing individuals over time and may contribute to the clinical conditions that develop in the individual (Ferrucci et al. 2018).

After 20-30 years of age, there is an annual decline of about 1% in cardiorespiratory fitness and in muscle mass after 50 years of age, but both can be slowed down with appropriate physical training (Komulainen & Vuori 2015). However, more significant ageing changes than loss of muscle mass occur in muscle strength and power, which is particularly visible in the deterioration of performances requiring speed (Komulainen & Vuori 2015). Speed of movement is needed, for example, in situations where balance is challenged. In such situations, slowed reaction and force generation speed can lead to loss of balance and falls if the necessary corrective movements cannot be performed with sufficient speed.

## 2.2 Functional ageing changes

Functional ageing refers to age-related decline in physical, cognitive, and social functioning. The decline in function may be so minor that it only appears in circumstances that require significant proportion of individual's maximal capacity or, alternatively, so significant that challenges occur in everyday activities of daily living (Ferrucci et al. 2018). Functional ageing can contribute to an individual's loss of independence (Ferrucci et al. 2018) if they require assistance with activities of daily living and thus become dependent on the help of others. Functional ageing is considered to be the third stage of ageing, where ageing changes are already to some extent affecting a person's daily activities (Ferrucci et al. 2018).

Common diseases and impairments in older people include hearing loss, visual impairment, including cataracts, back and neck pain, osteoarthritis, chronic obstructive pulmonary disease, diabetes, depression, and dementia (WHO 2022b). Muscle mass and strength, balance, mobility, and cognitive functions decline with age (Komulainen & Vuori 2015) and the likelihood of overlapping diseases and functional deficits increases with age (WHO 2022b). Impaired sensory functions can make everyday activities more difficult. Observing the environment and reacting to external stimuli can be challenging if one cannot distinguish signposts on public transport due to impaired vision, or impaired hearing can prevent one from hearing a vehicle coming from behind and, which can in the worst-case scenario lead to dangerous situations. The likelihood of walking difficulties also increases with age and together with balance challenges, these are associated with increased number of falls (Osoba et al. 2019). Due to the fear of falling and the risk of falling, older people are more likely than younger people to use protective gait strategies, with a widened support surface, a longer double stance phase of gait, a shorter sway phase, shorter stride lengths, and slower walking speeds (Pirker & Katzenschlager 2017).

### 2.3 Age indicators

Chronological age, i.e., calendar age, measures the time since birth and thus cannot vary between time, sex, or individuals (Finkel et al. 2017). However, some ageing changes occur earlier than others with the same chronological age (Ferrucci et al. 2018). Indeed, Lohman et al. (2021) pointed out that when examining a large cohort of individuals over 70 years of age, a phenotypically divergent set is found, even if all individuals in the sample are chronologically the same age. Finkel et al. (2017) draw on previous research literature to note that biological ageing, health, and longevity differ between sexes. The study of Chodzko-Zajko et al. (2009) also came to the conclusion that ageing varies widely across individuals and they presumed that genetic and lifestyle factors would contribute to these substantial differences between individuals.

There are different measures of biological age (biomarkers of ageing) that describe the ageing of the body in isolation from the chronological age of the person, i.e., the calendar age. The American Federation of Aging Research has proposed criteria for a good biomarker of ageing. A good ageing biomarker should predict the progression of ageing independently and more accurately than chronological age, measure the phenotype underlying ageing, be practical, reproducible, and safe in terms of measurement method and functional in both experimental animals and humans (The

American Federation of Aging Research 2016). Biomarkers used to assess biological ageing include epigenetic clocks such as DNA methylation-based Horvath clock, DNAmPhenoAge and DNAmGrimAge, telomere length, proteomic and metabolomic measurements (Lu et al. 2019; Levine et al. 2018; Jylhävä et al. 2017).

Lohan et al. (2021) note that finding the single "best" biomarker is a challenge and stress the importance of the purpose of the study in selecting a biomarker. No single biomarker has been shown to be representative of the body's ageing processes on its own and researchers often selectively use multiple biomarkers together to better observe these complex processes that change over time (Finkel et al. 2017). However, there is yet no standard for such a combination of biomarkers (Finkel et al. 2017). Jylhävä et al. (2017) have called for the need to find a validated set of markers that predict healthy life span rather than mortality and overall life span.

Anstey et al. (1996) have reviewed the measurement of human functional age. In these studies, measures of functional age have included sensorimotor function, cognition, psychosocial, behavioural, anthropometric, biomedical, physiological, and dental measures. One measure of functional (biological) age is the sum variable fBioAge, which consists of five different functional measures including muscle strength, respiratory function, walking speed, and sensory (vision and hearing) measures (Finkel et al. 2017). Sternäng et al. (2019), on the other hand, have used a four-variable version of fBioAge that excludes gait speed measurement. Both Sternäng et al. (2019) and Finkel et al. (2017) justify their choice of functional measures with Anstey et al.'s (1996) review of functional age measures.

The sum variable fBioAge developed by Finkel et al. (2017) measures sensory function (hearing and vision) based on self-assessment. The maximal hand grip strength measurement was performed with a hand-held dynamometer and maximal result in kilograms was retained (Finkel et al. 2017). For the measurement of walking speed, time to walk three meters and return was recorded with a stopwatch and FEV1 (Forced Expiratory Volume) obtained from spirometer measurements was used to measure respiratory function (Finkel et al. 2017). The sum variable fBioAge was created by transforming the five functional variables to standard scores (z-scores) and then summing those up and further converting summed z-scores to t-scores (Finkel et al. 2017). Both z- and t-scores are standard scores, which represent standard deviations from the mean (Meier et al. 2014). Weaker results from the five functional measurements indicate higher functional age. The advantage of the functional age measure fBioAge compared to chronological age is that fBioAge allows for variations between time, gender, and individuals, and takes into account both genetic and environmental factors (Finkel et al. 2017).

FBioAge has not yet been widely used in the research field, however Finkel et al. (2017) have stated according to previous analyses that fBioAge seems to meet many criteria of a good indicator of ageing. According to Finkel et al. (2017) fBioAge changes at a rate that reflects the rate of ageing and captures individual differences in genetic and environmental factors, reflects physiological age, and the relationship with illness and ADL (Activities of Daily Living) indicates that fBioAge is crucial to the maintenance of health. Moreover, fBioAge successfully differentiates short- and long-term survival and demonstrates a significant change over a short period of time (Finkel et al. 2017).

# 3 PHYSICAL ACTIVITY IN OLDER PEOPLE

According to the World Health Organisation (WHO), PA is defined as bodily movement produced by skeletal muscles that uses energy. PA is therefore a term that refers to all movement, including leisure time movement, movement from one place to another and possibly movement within the workplace (WHO 2022a). Older adults can gain multiple health benefits from being physically active. There are however some potential risk factors and conditions that set limits to attending certain types of activities especially in the older population. The Finnish UKK Institute has created its own PA recommendations for people over 65 (UKK-instituutti 2019) and similarly, the US Physical Activity Recommendation has a section for people aged 65 and over (Office of Disease Prevention and Health Promotion 2018).

Use of the terms exercise, training and PA and their definitions vary in the research field. In this thesis exercise, exercise training, flexibility training, training, and endurance training in different intensities (light, moderate and vigorous) are all considered to be different forms of PA, similarly as WHO's (2022a) definition of PA refers to all movement. The terms of different forms of PA will only be used if considered essential for maintaining an accurate content of the original source. Other terms used in this thesis that are linked to PA are functioning, mobility, and functional or mobility limitations. Functioning refers to people's physical, cognitive, social, and psychological capacity to cope with everyday activities (THL 2023b). Physical functioning appears as an ability to be physically active and move one's body (THL 2023b). Mobility and muscle strength are dimensions of physical functioning that are known to decline with aging (THL 2023b; UKK-instituutti 2022). Mobility and functional limitations can narrow one's ability to be physically active and perform daily activities (UKK-instituutti 2022; von Bonsdorff & Rantanen 2011).

## 3.1 Health effects and risks of physical activity in older people

There is strong evidence that PA improves physical functioning and reduces the risk of age-related physical disability (Office of Disease Prevention and Health Promotion 2018). There is also evidence that the benefits of PA on physical functioning are greater in older adults with physical functioning challenges compared to their healthy counterparts (Office of Disease Prevention and Health Promotion 2018). Aerobic, muscle-strengthening, and varied PA would appear to have the strongest association with physical functioning in the older population (Office of Disease Prevention and Health Promotion 2018).

Long-term regular PA has been found to reduce the risk of falls (de Souto Barreto et al. 2019; Marzetti et al. 2017) and fall-related injuries (Powell et al. 2019). Risk factors for falls are generally divided into internal and external factors, as well as behavioural factors (Havulinna et al. 2017; Ambrose et al. 2013). Internal risk factors are related to the person herself, the most important of which are advanced age (over 75 years), female sex, impaired health, and reduced functional and mobile capacity (Havulinna et al. 2017). External risk factors for falling are associated with the housing- and living environment, and their safety (Havulinna et al. 2017). Those are for example bad lighting, inappropriate footwear, or assistive devices and slippery surfaces (Ambrose et al. 2013). The older a person is, the more often internal risk factors are causing the falls (Havulinna et al. 2017).

The risk of falling increases with age and with the number of existing risk factors (Ambrose et al. 2013). Long-term PA (one year and over) has been shown to have a modest but significant association with reducing the risk of falls and injurious falls in older adults (de Souto Barreto et al. 2019). Diverse PA has claimed to be essential in preventing falls and fall related injuries in older people living at home (Havulinna et al. 2017). PA should include exercises that improve balance and increase muscle strength (Havulinna et al. 2017). The most optimal effect on reducing the risk of falls appears to be with moderate intensity, multicomponent training twice or three times a week, approximately 50 minutes per session (de Souto Barreto et al. 2019). Furthermore, individually planned and implemented changes to housing and living environment play an important part of the prevention of falls in older people at high risk of falling (Havulinna et al. 2017). Multifactorial assessment of known fall risk factors and management of the identified risk factors has been highlighted when creating strategies for reducing the risk of falls (Ambrose et al. 2013). According to a meta-analysis by de Souto Barreto et al. (2019), exercising more frequently than three times per week would appear to increase the risk of adverse effects of exercise, including possible falls. They speculated that this could be due to the older target population, who may be inherently more vulnerable, and therefore the dose-response relationship may differ from the rest of the adult population. The type of PA and the environment were the activity takes place should be considered from the perspective of safety.

PA plays an important role in ageing by reducing the risk of several serious diseases, depressive symptoms, and disabilities (Powell et al. 2019; Marzetti et al. 2017; Liikunta: Käypä hoito -työryhmä 2016; Chodzko-Zajko et al. 2009). PA has been shown to be associated with lower risk of cancer (bladder, breast, colon, endometrium, oesophagus, kidney, stomach, and lung), diabetes, ischaemic heart disease and ischaemic stroke (Powell et al. 2019; Marzetti et al. 2017; Kyu et al. 2012). Moreover, PA currently appears to be the most effective treatment for sarcopenia (Marzetti et al. 2017). Regular PA enhances physical functioning in older people despite of frailty or existing chronic disease (Powell et al. 2019) and PA can maintain and improve the quality of life and contribute to metabolism (Liikunta: Käypä hoito -työryhmä 2016). Balance, fitness of muscles, joints, and respiratory and circulatory systems can also be maintained and improved by being physically active (Liikunta: Käypä hoito -työryhmä 2016). In addition, regular PA has been associated with improvements in mental health, psychological, social, and emotional well-being, and cognitive function (Powell et al. 2019; Langhammer, Bergland & Rydwik 2018). Meeting new people and socializing can be experienced as more attractive than the PA participated (Boulton, Horne & Todd 2018). On the other hand, some might feel that meeting a group of strangers is a barrier for participating in PA and therefore it is important to pay attention to creating a friendly and welcoming atmosphere for all who are engaging in the activity (Boulton, Horne & Todd 2018). Social aspect of PA has been noted to be especially important for older people who live alone or feel lonely (Boulton, Horne & Todd 2018).

There are some conditions that are contraindications for endurance training and weightlifting exercises. These are unstable coronary artery disease, untreated heart failure, uncontrolled arrhythmias, severe pulmonary hypertonia, severe aortic stenosis, acute myocarditis, pericarditis and endocarditis, acute infection, untreated hypertonia, and aortic dissection (Laukkanen 2015). Heavy muscle strength training (80-100% of one repetition maximum) is also prohibited in patients with active proliferative retinopathy or exacerbated non-proliferative diabetic retinopathy (Laukkanen 2015). In addition, certain type of medication use, and diminished balancing ability pose challenges in engaging PA and can be risk factors for falls (Havulinna et al. 2017; Hartikainen et al. 2007). The risk of adverse effects of exercise can be minimised by careful planning and activity selection (Bangspo et al. 2019). In older people with poor functional capacity, PA should be carried out in small groups in order to take into account the individual needs of every person and to ensure the safety of the training (Havulinna et al. 2017). If necessary, healthcare professionals can be consulted, for example if a person repeatedly experiences chest pain, arrhythmias, dizziness, or other symptoms during PA (Bangspo et al. 2019).

### 3.2 Physical activity recommendations for over 65-year-olds

The PA recommendations created by the UKK Institute summarise the amount of PA required per week for health effects and provide examples of possible forms of PA. A separate PA recommendation for people aged 65 and over differs from the PA recommendation for adults aged 18-64 years in that more emphasis is placed on muscle strength and balance, which are considered to have a particular impact on, for example, coping with everyday life and preventing falls (UKK-instituutti 2019).

The UKK Institute recommends that people over 65 years of age should engage in at least 150 minutes of moderate intensity exercise per week that increases heart rate, or alternatively, at least 75 minutes of vigorous intensity exercise per week. In contrast to former recommendations, the recommended amounts of exercise can be compiled of short bouts of exercise, even a few minutes at a time (UKK-instituutti 2019). According to the results of the FinTerveys2017 survey, about half of the population aged 50-59-years reaches the recommended amount of PA for endurance exercise, and both endurance exercise and leisure-time PA was found to decrease with age, especially in women. Among people aged 80 and over, only less than a quarter of men and just over a tenth of women reached the recommended amount of endurance exercise (Koponen et al. 2018).

In addition to the benefits of PA, the harms of physical inactivity, including sedentary lifestyle and low amount of MVPA, have also been identified. Prolonged periods of continuous sitting and sedentary behaviour have been found to have adverse health effects, including increasing risk of type II diabetes, arterial disease, obesity, and premature death (UKK-instituutti 2019). Indeed, physical inactivity has been found to be one of the leading causes of several chronic diseases and a major contributor to sarcopenia and functional deficits (Marzetti et al. 2017). The Ministry of Social Affairs and Health, together with the UKK Institute, has also created its own national recommendations for reducing sedentary behaviour. These encourage older people to take a break from sedentary behaviour and to engage in everyday and beneficial PA to make PA part of everyday life (STM & UKK-instituutti 2015). In addition to endurance exercise, the recommendations stress the importance of muscle strength, balance and mobility, and the recreational benefits of outdoor activities (STM & UKK-instituutti 2015).

### 3.3 Measurement of the amount of physical activity

PA is a multidimensional concept and complex behaviour (Silfee et al. 2018), which can be measured both subjectively and objectively. Because of the multidimensional and complex nature of PA, no single measure can capture all dimensions (Sylvia et al. 2014). Researchers should therefore carefully consider the type of data (i.e., focus group and the number of participants) they are collecting and choose the method of measuring PA accordingly (Sylvia et al. 2014).

Subjective measures are based on self-assessment and the memory of the respondent (Sylvia et al. 2014). There are several different questionnaires for self-assessment of PA and diary-type reporting can also be used (Sylvia et al. 2014). Subjective measures may also include individual observation of the PA of the respondent. The use of such direct observation is possible when the activity takes place in a closed environment (Sylvia et al. 2014). A challenge with subjective measurement methods is the risk of bias that can occur when reporting is not timely and thus dependent on the subject's memory (Sylvia et al. 2014). One study evaluating the validity of the International Physical Activity Questionnaire (IPAQ) showed that older people tend to under-report both MVPA and sedentary behaviour (Cleland, Ferguson & Hunter 2018). In addition, self-reporting has its weaknesses in detecting low-intensity PA (Skender et al. 2016; Sylvia et al. 2014). Questionnaires are considered the most cost-effective method for measuring PA (Skender et al. 2016) and the biggest advantage with self-reporting questionnaires might be, that data can be collected rather easily even in a large population.

Objective methods for measuring PA include wearable monitors such as accelerometers, pedometers, and heart rate monitors, indirect calorimetry, respiratory gas analysis, and isotope methods such as doubly labelled water (Silfee et al. 2018; Leppäluoto et al. 2012). Doubly labelled water is considered to be the gold standard for measuring energy expenditure in free-living (Sylvia et al. 2014; Leppäluoto et al. 2012). The method involves administering hydrogen and oxygen isotopes and monitoring their removal from the body, which can be used to calculate a person's total energy expenditure (Leppäluoto et al. 2012). The method is limited by its high cost, the burden on the subject and its time complexity, and that it does not consider the amount or quality of PA (Sylvia et al. 2014; Leppäluoto et al. 2012). Accelerometers have become more and more advanced and demonstrate even better validity than doubly labelled water (Sylvia et al. 2014).

Objective methods for measuring PA such as accelerometers can be rather expensive (Portegis et al. 2019) while methods based on self-reporting are considered to be cost-effective (Sylvia et al. 2014). Objective methods usually require careful preparation and expertise by the research team (Portegis et al. 2019). The advantage of objective PA measurements is that they can collect a large amount of data timely without being dependent of the subject's memory and ability to write down even the smallest amount of activity. The risk of bias for both objective and subjective measures is affected by the fact that subjects may change their behaviour when they are aware of the measurement.

Sylvia et al. (2014) highlights four essential factors that should be considered when choosing a PA measurement. The first is the quality of PA, considering activity type, duration, intensity, and repetition. The second is the objectivity of the data and the load on the individual, such as the time and/or effort required to complete the activity. The cost or other burden and any specific constraints must also be considered. The study population also contributes to the choice of PA measurement (Sylvia et al. 2014). Measurements can also be used in combination. In this thesis the focus will be on measuring PA with accelerometers, as PA data measured with accelerometers will be utilized.

The use of accelerometers in both research and everyday use has increased with technological advances. Accelerometery is based on continuous measurement of movement-induced raw acceleration signal (Troiano et al. 2014). In general, accelerometers can measure PA in three axes (vertical, horizontal, and perpendicular) and, as the name suggests, they measure the acceleration of body movements (McCullagh et al. 2016; Skender et al. 2016; Lee & Shiroma 2014). Accelerometers can be attached to the wrist, waist, or thigh (Sylvia et al. 2014; Leppäluoto et al. 2012). With an accelerometer attached to thigh, the distribution of gravity over the three axes can be interpreted using a simple equation to calculate thigh inclination, which makes the detection of position possible (White et al. 2019). Data outputs from accelerometers e.g., raw acceleration signals or filtered activity counts, offer a specific representation of acceleration due to bodily motion over short time periods (Troiano et al. 2014). Data measured by an accelerometer is typically presented in units of activity versus time (Skender et al. 2016) and the time periods are determined by device settings and are usually fractions of a second to a minute (Troiano et al. 2014). An essential part of accelerometery is interpret the processed data in a physiological context, such as MET values, which can be transformed from the accelerometer metrics (Sievänen & Kujala 2017). MET values can be categorized to establish how strenuous physical activity has been (Sievänen & Kujala 2017). Less than 1.5 MET is usually considered to be sedentary behaviour, 1.5-3 MET low and 3-6 MET moderate (Sievänen & Kujala 2017). Assessing how strenuous daily PA is, however, relative to an individual's physical capacity and therefore requires additional measurement of physical performance for individualization of the cut-points (Karavirta et al. 2020).

Nowadays, measuring devices are small and lightweight (Lee & Shiroma 2014), and therefore do not impose much of a burden on the wearer. The accelerometer can be attached e.g. to the waist, wrist, ankle, or thigh (McCullagh et al. 2016), and depending on where it is attached, a single meter will not be able to detect all the movement produced by the body, for example, a meter attached to the lower body will not detect upper limb movement (Skender et al. 2016; Lee & Shiroma 2014). Accelerometers also cannot assess the context in which activity is taking place, nor whether a person is carrying an additional load, such as a shopping bag, while moving (Skender et al. 2016; Lee & Shiroma 2014). Most devices are also not resistant to immersion in water and therefore cannot be used when participating in aquatic exercise (Skender et al. 2016).

The advantage of an accelerometer attached to a thigh is that it can accurately detect whether a person is lying or sitting down or in an upright or moving position (Portegis et al. 2019; McCullagh et al. 2016). Due to the fact that accelerometers are able to detect position changes and short movement periods, those are feasible in examining older people's PA habits. It is highlighted that even short periods of movement are meaningful for health and that older individuals can compile their physically active time from shorter bouts of activity (UKK-instituutti 2019) and accelerometery makes the assessment of these shorter bouts of activity possible (Vähä-Ypyä et al. 2015). There are no generally accepted standards for analysing accelerometer data and analysis typically requires specialised expertise (Portegis et al. 2019). The accelerometer should be worn for several days in a row (Portegis et al. 2019), with most studies setting a minimum of four valid measurement days, at least one of which should fall on a weekend (Skender et al. 2016).

# 4 ASSOCIATION BETWEEN THE COMPONENTS OF FUNCTIONAL AGE (FBIOAGE) AND PHYSICAL ACTIVITY

The sum variable fBioAge is an aging biomarker that represents functional age through five different functional measurements combined as one calculated score. The five components of fBioAge are self-reported hearing and vision, maximal isometric handgrip strength, walking speed and respiratory function. A higher fBioAge score signifies weaker performance on the five functional measures. More accurate calculation of fBioAge is presented in the chapter 6.2 of this thesis.

One proposed criterion for a good biomarker for ageing is the ability of a biomarker to measure the phenomenon underlying ageing (The American Federation of Aging Research 2016). Using several biomarkers together naturally provides a broader picture of the phenomenon under consideration. With the functional aging measure fBioAge, variations across time, gender, and individuals can be observed and both genetic and environmental factors can be taken into account (Finkel et al. 2017). This chapter will observe the association between the individual components of the sum variable fBioAge and PA in light of existing literature. Frailty and mobility limitations may influence individual's PA levels and are therefore also considered here.

## 4.1 Hearing

The available scientific research is limited on examining the association of hearing and PA. People with moderate to severe hearing loss are more likely to be less physically active as measured by self-report and accelerometer, than people with normal hearing, while mild hearing loss was not found to be associated with lower PA levels (Gispen et al. 2014). On the other hand, Choi et al. (2016) concluded in their study that hearing problems of moderate or greater severity did not increase the likelihood of lower PA measured by an accelerometer compared to individuals who reported excellent or good hearing. In a study by Tremblay et al. (2015), a higher proportion of subjects who reported hearing difficulties also reported reduced PA, among other things. Average and above average hearing problems have been found to be associated with a decrease in PA, independent of demographic and circulatory risk factors (Gispen et al. 2014).

An association between the use of hearing aids and higher self-reported PA has been found in women, but not in men (Fisher et al. 2015; Holman et al. 2021). Based on their systematic review, Holman et al. (2021) concluded that the hypothesis of an association between hearing loss and reduced PA is supported by the vast majority of existing evidence, which may contribute to perceived fatigue. However, they point out that the existing evidence is still too limited to draw conclusions about the association between hearing loss and the use of hearing aids with PA (Holman et al. 2021). Hearing problems have also been found to be associated with time spent outside the home environment and withdrawal from leisure activities in those without walking difficulties (Mikkola et al. 2016). This may contribute to reduced PA outside the home environment.

Gibson et al. (2014), drawing on original research by Tay et al. (2006), point out that sensory impairment, particularly hearing and vision, is associated with reduced functional ability and cognition. Chen et al. (2014) also found in their study that greater hearing impairment is independently associated with impaired functional ability across a range of self-reported measures, including ADL and IADL (Instrumental Activities of Daily Living), leisure and social activities, lower limb mobility, general physical activities, work limitations, gait difficulties, and memory difficulties. Findings were preserved in sensitivity analyses and after accounting for multiple confounding factors, except for those over 80 years of age with severe hearing loss (Chen et al. 2014).

In their meta-analysis, Tian et al. (2021) found that the risk of frailty was higher in older people with hearing loss compared to older people without hearing loss, regardless of study design (cohort/cross-sectional), method of determining hearing and frailty, sample size, and study quality. Significant hearing impairment experienced by older people may be associated with poorer functional capacity of the lower extremities and difficulties with mobility and ADL (Mikkola et al. 2015). Hearing impairment has also been found to be associated with poorer mobility in older people (Polku et al. 2015). Hearing impairment may in fact over time increase the limb mobility limitation in older people (Polku et al. 2015). To conclude, it seems that at least moderate or severe hearing loss and hearing problems might have a direct or indirect negative association with PA levels. However, more research is needed to investigate the association between hearing and PA.

### 4.2 Vision

Vision loss has a significant impact on the daily lives of older people (Cordeiro et al. 2021). Functional vision loss has been found to be associated with poorer physical functioning i.e., balance and physical performance in older people (Aartolahti et al. 2013), and visual acuity loss appears to be independently associated with reduced PA (Swanson et al. 2012).

The link between visual impairment and PA can be bidirectional, as vision loss can affect an individual's PA levels and increased PA can on the other hand be a protective factor against vision loss (Ong et al. 2018). For example, there is evidence that increase in walking and spending more time being moderately or vigorously physically active and less time being passive is associated with slowing of vision loss in people with glaucoma (Lee et al. 2019). It has also been suggested that, in addition to glaucoma, PA could have a protective effect on vision loss in two other common eye diseases, age-related macular degeneration and diabetic retinopathy, but more research is needed to confirm this hypothesis (Ong et al. 2018).

Ong et al. (2018) cited a study by Heinemann et al. (1988) where the participation of older people with low vision in various leisure activities was examined. The study in question found a loss of participation over time in five out of six activity categories, including participating in sports. Ong et al (2018) also highlighted a study by van Landingham et al. (2012), part of the NHANES research project, which apparently stated that people with bilateral visual field defects spent 30% less time in MVPA compared to people without a corresponding visual impairment. Another NHANES study (Willis et al. 2015) found that visual impairment was associated with almost 50% less time spent on MVPA (Ong et al. 2018).

Older people with impaired vision may have more significant age-related challenges with balance and therefore a greater need for fall prevention programmes compared to older people without vision challenges (Office of Disease Prevention and Health Promotion 2018). The available scientific evidence is currently insufficient to determine the benefits of PA for older people with vision challenges (Office of Disease Prevention and Health Promotion 2018). More research is needed to investigate the association between vision and PA.

### 4.3 Handgrip strength

A systematic review by Ramsey et al. (2021) highlights the association between higher PA and lower inactivity and improved skeletal muscle strength and muscle performance. Cooper et al. (2017) examined the cross-sectional, longitudinal, and bilateral associations between PA and muscle strength in individuals aged 60 years and older. In their cross-sectional analyses, they found a positive association between handgrip strength and MVPA (Cooper et al. 2017). In the longitudinal setting, the level of PA in the baseline measurements was only weakly associated to the handgrip strength in the follow-up measurements, whereas the handgrip strength in the baseline measurements was found to be linearly and positively associated to the level of PA in the follow-up measurements (Cooper et al. 2017). Individuals who increased their PA level after the initial measurements or maintained it at the same level did not improve their handgrip strength, whereas individuals who managed to increase their handgrip strength from the initial measurements spent more time being physically active at the follow-up measurements.

Unlike Cooper et al. (2017), Dodds et al. (2013) found that increased levels of leisure-time PA in mid-life would be associated with improved handgrip strength at age 60-64 in both men and women. Bann et al. (2015), on the other hand, found that an increase in the amount of time spent in light-intensity activity was associated with improved handgrip strength in men, but not in women. In the study by Bann et al. (2015), light intensity PA was divided into two categories (low/high intensity light activity) according to accelerometer data and the results mentioned refer to the high intensity light PA. Being physically active in leisure time throughout adulthood may prevent the deterioration of handgrip strength in early old age (Dodds et al. 2013).

Higher amount of PA and lower levels of physical inactivity have been found to be associated with higher upper body muscle strength (grip strength), upper body muscle power (elbow flexion), and lower body muscle strength and power (chair-lift test) (Ramsey et al. 2021). In people aged 85 years, poorer handgrip strength has been found to be associated with poorer functional, psychological, and social health (Taekema et al. 2010). According to Sternäng et al. (2015), PA is generally positively associated with muscle strength, but excessive inappropriate PA may lead to poor physical functioning later in life and therefore physically demanding occupations may negatively affect the body. In a study by Taekema et al. (2010), poorer handgrip strength at baseline predicted faster decline in functioning i.e., ADL and cognition. The researchers found that this contributed to an increased need for assistance in old age (Taekema et al. 2010). Also minimising muscle strength loss can be sufficient to slow the decline in attending MVPA (Cooper et al. 2017).

To add, it has been found that more time spent sitting is associated with poorer handgrip strength in middle age in both men and women (Cooper et al. 2020). This association remained after controlling for interdependence between variables and time spent in MVPA (Cooper et al. 2020), whereas Bann et al. (2015) found no association between handgrip strength and time spent inactive. The study by Cooper et al. (2020) also produced evidence that greater total time spent physically active was associated with higher handgrip strength in both sexes, but the association was dependent on the time spent sitting.

### 4.4 Walking speed

The amount of MVPA has been found to be associated with higher walking speed in women aged 75 years and older, and the association persisted after controlling for stride length and other confounding factors (Adachi et al. 2018). Adachi et al. (2018) concluded in their cross-sectional study that participation in MVPA may play an important role in preventing decline in neuromuscular function related to walking speed in older women but called for prospective studies on this topic. In healthy women aged 65-75 years, changes in gait (step width, length, frequency) have been found to be significantly negatively associated with PA levels indicating that people with more gait changes are less physically active (Ciprandi et al. 2017). However, women with high preferred walking speed and moderate gait variability i.e., step width variability, appeared to reach the recommended level of PA (Ciprandi et al. 2017).

Qiao et al (2021) examined the two-way associations of perceived physical fatigue and PA and walking speed in two generations of older adults. They found that perceived physical fatigue largely explained the association between lower PA and slower walking speed in the younger generation studied. In the older generation studied, both lower levels of PA and higher levels of perceived fatigue were equally associated with slower walking speed (Qiao et al. 2021). Based on their results, Qiao et al. (2021) concluded that perceived levels of physical fatigue may vary over the lifespan. Renner et al. (2022) also looked at two different generations (49-105 years old and their offspring aged 24-88 years) in their cross-sectional study and assessed the associations of fatigue, inflammation, and PA and walking speed. Among other things, they found that PA was significantly associated with faster walking speed in the generations examined (Renner et al. 2022). Moderate PA (walking two to nine times in two weeks' time) appeared to be associated with a faster walking speed of 0.11 m/s in the older and 0.05 m/s in the younger generation compared to participants with low PA (walking one time or less in two weeks' time). Vigorous PA (walking ten to fourteen times in two weeks' time), on the other hand, appeared to be associated with 0.15 m/s and 0.08 m/s faster walking speeds in the older and younger generations, respectively (Renner et al. 2022). Westbury et al. (2018) also found that greater accelerometer-measured activity and less time spent being passive were associated with faster walking speeds in older men and women with sarcopenia.

The results of the study by McMullan et al. (2020) also support the claim that MVPA is associated with faster walking speed. In addition, they found that MVPA were also associated with slower decline in gait speed at follow-up. Even low intensity PA were beneficial compared to inactivity. The average age of participants included in their study was 65 years. Age was found to influence walking speed; moderate intensity PA was associated with higher walking speed in those under 70 years of age and light intensity PA was associated with higher walking speed in those over 70 years (McMullan et al. 2020). Contributing factors to this difference were thought to include the fact that light intensity PA is likely to be achievable at a higher potential volume for older people, while MVPA may be unattainable for some (McMullan et al. 2020).

### 4.5 Respiratory function

A study by Dogra et al. (2018) examined the association between exercise behaviour and respiratory function in Canadians aged 45 years and older. The main finding of the study was that time spent sitting, walking, and PA of different intensities were all associated with predicted expiratory volume per second (FEV1%pred) and predicted vital capacity (FVC%pred), regardless of smoking background. Indeed, the study found that the less time per week was spent sitting and the more time was spent in being physically active, the better was the respiratory function (Dogra et al. 2018). Roman et al. (2016) on the other hand found in their review that the age-associated decline in pulmonary function is not recovered by training. Consequently, they stated that respiratory decline is likely to affect exercise tolerance and the ability to gain health benefits of PA in healthy older people, particularly those who remain physically active into old age. However, they also pointed out that the decline in muscle oxidative capacity and cardiac output in inactive older people is more significant than the decline in pulmonary function in the sense that the relatively small contribution of pulmonary function to exercise capacity limitation remains similar across a range of ages.

Establishing cause-and-effect relationships between respiratory function and functional capacity is not unequivocal and the need for longitudinal studies on this topic has been called for (Sillanpää et al. 2014; Singh-Manoux et al. 2011). McHugh et al. (2020) examined associations between respiratory function and several factors related to sociodemographic, lifestyle, chronic disease and psychosocial factors in Canadian adults aged 45-86 years. They found evidence that several sociodemographic, lifestyle and health factors are significantly associated with FEV1 and FEV1/FVC (Forced Vital Capacity) scores, and that age, gender and health status indirectly influence several of the observed associations (McHugh et al. 2020).

A study by Singh-Manoux et al. (2011) suggests that respiratory function early in the ageing process could be a good indicator of ageing, reflecting the influence of environmental factors throughout the life course. On the other hand, study by Sillanpää et al. (2014) suggested that the decline in mobility with age could be due to a decline in both muscle strength and power, but that respiratory function would also be an indirect contributor. Impaired skeletal muscle strength was found to be associated with impaired respiratory function, but the link between respiratory function and mobility was less clear in healthy older people (Sillanpää et al. 2014).

# 5 PURPOSE OF THE STUDY AND RESEARCH QUESTIONS

The purpose of this thesis is to investigate the association of functional age with PA in people aged 74 years and older. Functional age is measured with a sum variable fBioAge and another purpose is to examine the fBioAge's components' association with PA. The differences between men and women in the association between fBioAge and PA is also studied. Furthermore, this thesis examines whether the association studied is affected when the chronological age of the subjects is considered. The analyses will be adjusted for lifestyle factors, the number of chronic diseases and the use of assistive devices.

The research questions are:

1. Is fBioAge associated with objectively measured PA (total PA and absolute MVPA) in older people and what kind of association is between the components of fBioAge and PA?

2. Is there a difference in the association of fBioAge with PA between men and women?

3. Is the association of fBioAge with PA different among participants aged 75, 80 and 85 years?

# 6 METHODS

This master's thesis utilizes the data collected in the AGNES -research project (Active aging – resilience and external support as modifiers of the disablement outcome) led by Rantanen et al. since 2017. The purpose of the AGNES cohort study was to examine the connection between health, health behaviour, health literacy, functional capacity, environment and social support with active ageing and wellbeing (Rantanen et al. 2018).

## 6.1 Participants and Study design

The participants of the AGNES-study were recruited by drawing personal detail from the population register. Three age cohorts (75-, 80- and 85-year-olds at baseline) living independently at home in central Finland (postal code within ten kilometres from the centre of Jyväskylä or subject's residence accessible by local transport) were all invited to the study (Rantanen et al. 2018). The exclusion criteria were unwillingness to participate in the study and inability to communicate.

Data collection carried out in the AGNES-study started with an invitation letter to the participants informing them of the study. Within a week from receiving the letter, participants received a phone call from a trained interviewer and their willingness and eligibility to participate were assessed. If an individual was willing and eligible to participate, home interview was scheduled. Before the home interview, participants received a postal questionnaire. The home interviews were conducted by trained research staff who collected data on activity, health, functioning and wellbeing with several questionnaires. In addition, two brief performance tests were conducted and willingness to participate in the PA surveillance was assessed. Participants willing to participate in the PA surveillance wore an accelerometer attached to a thigh and a single-channel electrocardiogram (EEG) recorder for five days (three weekdays and a weekend). Lastly participants visited the research centre, the Faculty of Sport and Health Sciences of the University of Jyväskylä, and data were collected using clinical examination, cognitive and physical performance tests, interviews and PA monitors. The baseline data collection was carried out during the years 2017 and 2018.

The AGNES-study protocol was approved by the ethical committee of the Central Finland Health Care District (Rantanen et al. 2018). There were no invasive or potentially physically or psychologically harmful aspects in the study beyond what one might encounter in daily life. At the beginning of the home visit, participants were asked to sign a written consent and they were allowed to withdraw their consent at any time throughout the study or for any individual part of the study.

For this thesis a data processing agreement was made for the utilization of the data collected in the AGNES-study. A pseudonymised SPSS-file containing only the necessary variables was released for use during the completion of this thesis. The data is stored and processed in accordance with the information security policy of the University of Jyväskylä. After the thesis is completed, the data concerning the sum variable created will be handed over to the AGNES-study group for further application and all the unnecessary data will be extinguished.

A minimum of three full valid measurement days was used in a study of Karavirta et al. (2020), who supplied the accelerometer data used in this thesis. Therefore, only participants who had worn the accelerometer at least three whole days and had all the elements of fBioAge measured were included in the analysis (n=407).

### 6.2 Variables

*Physical activity* was measured with tri-axial accelerometer attached to the thigh and measured seven to ten days in a row. At least three whole successful measuring days was required to be included in the analyses. Thigh worn accelerometer data gives information about how much time a participant has spent lying or sitting down or in an upright or moving position (Portegis et al. 2019; McCullagh et al. 2016). In this thesis, two different PA values were calculated based on the accelerometer data. First value used in this thesis is *mean total physical activity (total PA)* which is the mean high pass filtered magnitude (HPFVM, in gravity units [g]). This variable reflects the average intensity of all movement and non-moment during the measurement period. After applying autocalibration, HPFVM was calculated from the raw accelerometery records in five-second non-overlapping epochs, after which the mean of all 5 second epochs were calculated (Karavirta et al. 2020). Second value is *the absolute moderate to vigorous physical activity (absolute MVPA)* in minutes per day, which is based on the number of epochs at or above the acceleration that corresponds to three METs (metabolic equivalent of task) (Karavirta et al. 2020). The three MET cut-point was based on a previous study that evaluated the association between energy expenditure and HPFVM measured on the thigh (White et al. 2019).

*Functional biological age.* A slightly modified version of the sum variable fBioAge developed by Finkel et al. (2017) was used in this thesis, consisting of:

- self-reported hearing and vision
- maximal isometric handgrip strength
- walking time (3m)
- respiratory function

In the AGNES-study participants chose a number from 0 (very poor) to 10 (excellent), which they thought reflected their hearing. Self-reported vision was assessed with three questions as follows: “Are you able to read a normal newspaper text?” (near vision), “Are you able to watch television from normal watching distance (three meters distance, far vision) and also the use of spectacles was asked and if yes, what kind of spectacles (Rantanen et al. 2018). Response options for the first two questions were: one (yes, without difficulty), two (yes, with some difficulty), three (yes, with a great deal of difficulty) and four (no, not at all). Question about far vision also had a fifth option (I do not watch television), which was recoded as missing data in this thesis because these two questions were combined to one variable. By summing the questions concerning near and far vision up, it was possible to get a one variable that combined near and far vision so that the sum variable fBioAge would be similar to the one developed by Finkel et al. (2017).

Maximal isometric handgrip strength was measured in the AGNES-study both in the home interview and at the research centre (Rantanen et al. 2018). In this thesis measurement made during the home interview was used. Measurement was made with handheld dynamometer (Jamar Plus digital hand dynamometer, Patterson Medical, Cedarburg, WI, USA) in a seated position with elbow flexed in an angle of approximately 90 degrees. Three to five attempts were made with the dominant hand to achieve the maximum score, which was expressed as kilograms and used in the analyses. Participants were allowed to rest 30 seconds in-between the attempts.

Lower extremity function was assessed with SPPB measurement (Short Physical Performance Battery, Guralnik et al. 1994) in the AGNES-study. One element of the SPPB is walking speed measurement (Pavasini et al. 2016). In the AGNES-study this element was measured by asking the participants to walk three meters distance with their habitual moderate pace. In the test protocol of SPPB, participant is guided to wear shoes that are fit for walking, sturdy and non-slippery when the walking speed is recorded (THL 2023a). In the AGNES-study time spent in walking the three meters distance was recorded once (in seconds) with a stopwatch. This value was used in this thesis as a component of the sum variable.

Respiratory function was assessed in the AGNES-study with spirometry using Medikro Pro Spirometer, by Medikro Oy, Kuopio, Finland. The measurement was made in standing position and a nose clip was used to block nasal passages. Forced vital capacity (FVC) manoeuvre was performed at least two times (eight times maximum) and the highest volume of FVC and forced expiratory volume in the first second (FEV1) were recorded in litres. FEV1-value was used in this thesis as a component of the sum variable.

Finkel et al. reported in their article that before calculation of fBioAge FEV1 was corrected with body volume through division by individual's squared height ($m^2$). Same kind of correction was made in this thesis so that the fBioAge sum variable would be as similar as it could the one Finkel et al. (2017) created. Before the creation of the sum variable fBioAge scaling of the variables concerning vision and walking time (3m) were reversed to be comparable with the other variables (smaller values indicate better functioning). The five variables of fBioAge were z-transformed separately and to correct for sex in handgrip strength scores, the z-transformation was made separately for men and women. Z-scores are standardized scores that indicate how far from the mean a data point is and value zero is the mean value (University of Connecticut 2023). Z-scores are a way to compare data even when the data measurements vary in measurement scaling (University of Connecticut 2023). After converting raw measurement data to z-scores, the z-scores were summed to create a composite score. The composite score was then z-transformed and then t-transformed with following same methods as Finkel et al. (2017) had used in their study. A t-score is a conversion of a z-score which can be calculated with following formula: T= (Z x 10) + 50 (University of Connecticut 2023). T-scores and z-scores both represent standard deviations from the mean only with different mean values (University of Connecticut 2023). T-score 50 indicates the mean and a t-score above 50 is therefore above average and a t-score below 50 is below average.

*Background variables*

- chronological age (three age cohorts)
- sex (men and women)
- weight and height, BMI (Body Mass Index)
- number of chronic diseases
- smoking history (self-reported, never/former/current)

- alcohol use (self-reported, four items)
- assistive devises (walking aids)

The AGNES-study had three age cohorts: 75-, 80- and 85-year-olds (Rantanen et al. 2018). Exact chronological age varied slightly depending on how participation to the study was scheduled and, in the data, chronological age consequently varied between 74-75-years, 78-80-years, and 83-85-years. To follow a consistent line with the previous studies that have used this data, age cohorts will be referred to as 75, 80 and 85 years of age. Because of the three age cohorts, *chronological age* was not used as a continuous variable and was recoded into dummy-variables for the analyses. 75-year-olds was used as a refence group in the analyses.

*Sex, smoking history, and the use of assistive devices* were also recoded into dummy-variables, female-sex being a reference group and male-sex got the value of 1. Smoking history was assessed by asking whether participant smoke or have smoked daily or nearly daily for a year minimum and whether participant has quit smoking and if so, at what age. Smoking history was recoded into two different dummy-variables, one being non-smoker (0=non-smoker, 1=former smoker/smoker) and the other current smoker (0=non-smoker/former smoker, 1=current smoker). Participants were asked whether they used any assistive devices listed (walking stick, crutches, Nordic walking sticks, rollator, kicksled/kickcycle, wheelchair, electric scooter) or other. These questions where first summed and the sum variable was recoded into a dummy-variable (0=does not use assistive devices, 1=uses assistive devices).

*Alcohol consumption* was assessed separately for distilled beverages, wine and beer and cider using five-point scales. For distilled beverages the response option ranges from zero (not at all) to four (more than two bottles a month), for wine from zero (not at all) to four (more than two bottles a week) and for beer and cider from zero (not at all) to four (more than 12 bottles a week). To sum these three questions, all response options were changed to describe the number of doses per week. However, due to the fact that some of the original response options were not unambiguous (for example response option two meant one to four bottles per week) the summation of these questions also produced only indicative results on total alcohol consumption. After summation, total alcohol consumption was interpreted from the data as follows: zero (not at all), one (less than one to less than one and a half doses per week), two (less than two to eight and a half doses per week), three (less than two to 12 doses per week), four (two to over 12 doses per week), five (three and a half to over 24 doses per week), six (five and a half to over 24 doses per week), seven (eight to over 24 doses per week) and eight (12 to over 24 doses per week).

*Number of chronic diseases* was based on participant self-reporting during the home interview where information was gathered whether the participant had been diagnosed with chronic conditions by a physician. The conditions were categorised to ten categories and specified under each category. Categories were: respiratory conditions (chronic obstructive pulmonary disease, chronic bronchitis, asthma, other), cardiac conditions (heart failure, atrial fibrillation or other arrhythmias, myocardial infarction, coronary heart disease, other), vascular conditions (hypertension, thrombosis or intermittent claudication, other), brain injury or cerebrovascular condition (brain injury, stroke or cerebral infarction, other), musculoskeletal condition (chronic back pain or problems, chronic neck pain or problems, osteoporosis, rheumatic arthritis, osteoarthritis, other), visual or auditory impairment (cataract, not surgically repaired, glaucoma, macular degeneration, hearing disorder, hearing injury or other hearing debilitating condition), malignant cancer, diabetes mellitus, neurological condition (Alzheimer or dementia, Parkinson's disease, epilepsy, other), and depression. Moreover, an open-ended question about any other physician diagnosed chronic conditions was asked.

*BMI* was calculated in the original AGNES-data as weight in kilograms divided by height squared in meters (kg/m2).

### 6.3 Data Analysis

IBM SPSS Statistics 28 program was used for the data analysis. The limit of statistical significance was set at $p<0.05$. The normality of the sample was analysed with Kolmogorov-Smirnov test and skewness and kurtosis of the distributions were also observed. Some of the variables were not normally distributed according to the Kolmogorov-Smirnov test. When absolute values of skewness and kurtosis exceeded two, a statistician was consulted before the actual analyses. After consulting the statistician, a decision was made to not use variable transformations. Correlations between fBioAge and the amount of PA (total PA and absolute MVPA) was examined using Pearson's correlation coefficient. Also, correlation between all the independent components of the sum variable with total PA was examined using Pearson's correlation coefficient. The variables were in basic form when examining the correlations meaning that small values in vision and walking time (3m) and large values in hearing, handgrip strength and respiratory function indicated good functioning ability. The difference in basic characteristics between sexes were tested using Independent Samples T-Test for continuous variables and Chi Square Test for discrete variables.

Linear regression was used to analyse the association of functional age (fBioAge) with PA (total PA and MVPA). Initially, PA was explained only with the fBioAge. Background variables were then added to the regression analysis to examine whether the association between fBioAge and PA was maintained. Table 1 presents the models used in the analyses. Interaction terms were made for age and sex and used in the basic models. Chronological age variable consisted of three age groups and was therefore recoded into dummy-variables for the creation of the interaction terms. No joint effect was found and therefore no further modelling was made for these measures.

TABLE 1. Linear regression models to investigate the association of fBioAge with physical activity.

| Model 1 | no adjustments |
|---|---|
| Model 2 | adjusted for sex and chronological age |
| Model 3 | Model 2 + adjusted for lifestyle factors (smoking and alcohol consumption) |
| Model 4 | Model 3 + adjusted for BMI, a number of chronic diseases and the use of assistive devices* |

BMI = Body Mass Index, *Walking aids

Multicollinearity of the variables was examined using VIF (the variance inflation factor) and tolerance -values as well as the condition index and correlation matrix. Some condition index values were suspicious, yet only weak correlations were found when the correlation matrixes were examined. Consequently, the interpretation of multicollinearity was based on tolerance-values. The number of outliers did not exceed five percent of the total number of cases studied. However, it was confirmed by manual observation that all outliers were reasonable values and there was no reason to suspect any measurement errors.

# 7 RESULTS

## 7.1 Descriptive information of the participants

The data applied in this thesis consists of 407 participants in total. Majority (61.7%) of the participant were women. Descriptive information of the participants is presented in table 2. The participants represent three age cohorts: 75-year-olds, 80-year-olds, and 85-year-olds. Mean chronological age of the participants was 77.7 years (standard deviation, SD 3.4). Percentages of participants for different age cohorts were 51.8% for 75-year-olds, 31.9% for 80-year-olds and 16.2% for 85-year-olds. There was no statistically significant difference in the chronological age between men and women (77.8 (SD 3.4) vs. 77.7 (SD 3.4), p=0.829). FBioAge of the participants was calculated in t-scores and values ranged between 24.2 to 98.7 with the mean of 49.4 (SD 9.8). Women's fBioAge scores were higher on average compared to men (women 50.6 (SD 9.3) and men 47.4 (SD 10.1), p=0.001). Of the components of fBioAge, self-reported hearing, handgrip strength and respiratory function varied between men and women at statistically significant level. Self-reported hearing on a scale of one to ten had the mean of 7.0 (SD 2.0.) for men and 7.5 (SD 2.0) for women (p=0.036). Men's mean handgrip strength was 41.8kg (SD 9.1) and women's 26.3kg (SD 7.1) (p<0.001). Mean respiratory function (FEV1) was 2.6 (SD 0.6) for men and 1.8 (SD 0.4) for women (p<0.001).

Men were more physically active compared to women based on both PA variables. Men's total PA had the mean of 0.057 g/day (SD 0.015) whereas women's total PA had the mean of 0.053 g/day (SD 0.014) (p = 0.008). The mean of absolute MVPA was 95.81 min/day (SD 35.34) for men and 84.45 min/day (SD 34.80) for women (p = 0.002). Men also had more individual diseases on average than women and their alcohol consumption was heavier on weekly basis compared to women. Women on the other hand had higher BMI on average and the use of assistive devices was more common for women than for men. Smoking history also varied between sexes at statistically significant level. Greater proportion of men were past or current smokers than women.

TABLE 2. Descriptive information of the participants presented as mean and standard deviation (SD) unless stated otherwise.

| **Variable** | **All** | **Female** | **Male** | **p-value** |
|---|---|---|---|---|
| | n = 407 | n = 251 | n = 156 | |
| **Chronological age** | 77.7 (3.4) | 77.7 (3.4) | 77.8 (3.4) | 0.778[a] |
| 74–75, n (%) | 211 (51.8) | 133 (53.0) | 78 (50.0) | 0.829[a] |
| 78–80, n (%) | 130 (31.9) | 76 (30.3) | 54 (34.6) | |
| 83–85, n (%) | 66 (16.2) | 42 (15.4) | 24 (15.4) | |
| **fBioAge, t-scores** | 49.4 (9.8) | 50.6 (9.3) | 47.4 (10.1) | **0.001**[a] |
| Self-reported hearing, 1-10* | 7.3 (2.0) | 7.5 (2.0) | 7.0 (2.0) | **0.036**[a] |
| Self-reported vision, 1-4* | 1.1 (0.3) | 1.1 (0.3) | 1.1 (0.3) | 0.291[a] |
| Handgrip strength, kg | 32.2 (10.9) | 26.3 (7.1) | 41.8 (9.1) | **<0.001**[a] |
| Walking time (3m), s | 3.2 (1.1) | 3.3 (1.1) | 3.1 (1.2) | 0.051[a] |
| Respiratory function, FEV1 | 2.1 (0.6) | 1.8 (0.4) | 2.6 (0.6) | **<0.001**[a] |
| **Total PA, g/day** | 0.055 (0.015) | 0.053 (0.014) | 0.057 (0.015) | **0.008**[a] |
| **Absolute MVPA, mins/day** | 88.80 (35.40) | 84.45 (34.80) | 95.81 (35.34) | **0.002**[a] |
| **Number of chronic diseases** | 3.1 (2.0) | 3.3 (2,0) | 2.9 (2.0) | **0.046**[a] |
| **Alcohol consumption*** | n = 406 | n = 251 | n = 155 | |
| | 2.2 (1.8) | 1.7 (1.4) | 2.9 (2.0) | **<0.001**[a] |
| **BMI** | n = 406 | n = 251 | n = 155 | |
| | 27.6 (4.4) | 28.1 (4.8) | 26.6 (3.7) | **<0.001**[a] |
| **Assistive devices** | n = 406 | n = 251 | n = 155 | |
| No, n (%) | 334 (82.1) | 187 (74.5) | 147 (94.2) | **<0.001**[b] |
| Yes, n (%) | 73 (17.9) | 64 (25.5) | 9 (5.8) | |
| **Smoking** | n = 405 | n = 251 | n = 154 | |
| Non-smoker, n (%) | 303 (74.8) | 217 (86.5) | 86 (55.8) | **<0.001**[a] |
| Former, n (%) | 96 (23.7) | 32 (12.7) | 64 (41.6) | |
| Current, n (%) | 6 (1.5) | 2 (0.8) | 4 (2.6) | |

[a]) Independent Samples T-Test. [b]) Chi Square Test. *Self-reported hearing: 1(very poor)-10(excellent), Self-reported vision: 1(excellent)-4(very poor), Alcohol consumption: value 1 meaning less than 1-1.5 doses per week. BMI = Body Mass Index. fBioAge = the sum variable of functional biological age. FEV1 = forced expiratory volume in one second. MVPA = Moderate to Vigorous Physical Activity. PA = Physical Activity.

## 7.2 The association of functional age with total physical activity

There was a negative correlation between fBioAge and total PA (r=-0.243, p<0.001). Apart from hearing, all the components of the sum variable also had statistically significant correlations with total PA (p<0.05, Table 3). Maximal isometric hand-grip strength, walking time (3m) and respiratory function (FEV1) had the greatest correlation with total PA (p<0.001, Table 3). The variables were in basic form when examining the correlations i.e., small values in vision and walking time (3m) and large values in hearing, handgrip strength and respiratory function indicated good functioning ability. Negative correlation between walking time (3m) and total PA for example indicates that the faster the walking time (3m) the more physical activity.

TABLE 3. Correlation between self-reported hearing, self-reported vision, handgrip strength, walking time (3m), respiratory function, and total physical activity.

| Variable | Total PA | Self-reported hearing | Self-reported vision | Handgrip strength (kg) | Walking time, 3m (s) | Respiratory function (FEV1) |
|---|---|---|---|---|---|---|
| Total PA | 1 | | | | | |
| Self-reported hearing (1-10) | -0.021 | 1 | | | | |
| Self- reported vision (1-4) | -0.100* | -0.159** | 1 | | | |
| Handgrip strength (kg) | 0.213** | -0.026 | -0.137* | 1 | | |
| Walking time, 3m (s) | -0.307** | -0.062 | 0.119* | -0.249** | 1 | |
| Respiratory function (FEV1) | 0.228** | -0.002 | -0.178** | 0.563** | -0.265** | 1 |

FEV1 = forced expiratory volume in one second, PA = Physical Activity, Pearson's correlation coefficient; **p<0.001; *p<0.05. The variables were in basic form when examining the correlations: small values in vision and walking time (3m) and large values in hearing, handgrip strength and respiratory function indicate good functioning ability.

Linear regression analysis showed that fBioAge associated with the total PA at statistically significant level (Model 1, Table 4: standardized coefficient (β) = -0.245, $p<0.001$). Adjusting the model with sex and chronological age in model 2 did not attenuate the association of fBioAge and total PA nor did the adjustment for lifestyle factors in model 3 (Table 4). A minimal attenuation in the association was detected in the fully adjusted model, but the association of fBioAge and total PA remained statistically significant (β= -0.125, $p=0.008$).

FBioAge explained 6% of the variation in total PA ($p<0.001$) (Model 1, Table 4), thus the effect size was rather low in the first model. The degree of explanation in the linear regression model grew gradually when the background variables were added to the model (Table 4). The fully adjusted model explained 29% of the variation in total PA and was suitable for the data – F (10, 394) = 16.096, $p<0.001$.

TABLE 4. The association of fBioAge with total physical activity.

| | Model 1 (fBioAge) | | | Model 2 (age and sex) | | | Model 3 (lifestyle factors) | | | Model 4 (fully adjusted) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $R^2$ | β | p | $R^2$ | β | p | $R^2$ | β | p | $R^2$ | β | p |
| **Model fit** | .060 | | **<.001** | .078 | | **<.001** | .106 | | **<.001** | .290 | | **<.001** |
| **fBioAge** | | -0.245 | **<.001** | | -0.205 | **<.001** | | -0.174 | **<.001** | | -0.125 | **.008** |
| **Chronological age** | | | | | | | | | | | | |
| 75$^{ref}$ | | - | - | | ref | ref | | ref | ref | | ref | ref |
| 80 | | - | - | | 0.018 | .723 | | 0.008 | .880 | | 0.018 | .688 |
| 85 | | - | - | | -0.092 | .082 | | -0.105 | **.046** | | -0.072 | .133 |
| **Sex** | | | | | | | | | | | | |
| Women$^{ref}$ | | - | - | | ref | ref | | ref | ref | | ref | ref |
| Men | | - | - | | 0.096 | .050 | | 0.083 | .126 | | 0.018 | .718 |
| **Smoking history** | | | | | | | | | | | | |
| Never smoked$^{ref}$ | | - | - | | - | - | | ref | ref | | ref | ref |
| Former smoker | | - | - | | - | - | | -0.077 | .144 | | -0.039 | .407 |
| Current smoker | | - | - | | - | - | | -0.091 | .064 | | -0.126 | **.004** |
| **Alcohol consumption*** | | - | - | | - | - | | 0.144 | **.005** | | 0.069 | .139 |
| **A number of chronic diseases** | | - | - | | - | - | | - | - | | -0.217 | **<.001** |
| **Assistive devices** | | - | - | | - | - | | - | - | | -0.035 | .451 |
| **BMI** | | - | - | | - | - | | - | - | | -0.350 | **<.001** |

BMI = Body Mass Index (kg/m$^2$), PA = physical activity, ref = refence group, $R^2$ = Correlation of coefficient, β = standardized coefficient, *value 1 meaning less than 1-1,5 doses per week

## 7.3 The association of functional age with total physical activity according to sex and age groups

No interaction for age and sex was found in the basic models of linear regression analysis and therefore no further modelling was considered for these measures (sex*80years: p=0.744, sex*85years: p=0.774, age group of 75 years as a reference group). Figure 1 illustrates the association of fBioAge and total PA separately for men and women. Higher fBioAge was associated with lower level of total PA in both sexes at statistically significant level (men: r=0.303, p<0.001, women: r=0.176, p=0.005) (Figure 1).

FIGURE 1. The association of fBioAge and total physical activity for men (n=156) and women (n=251).

Figure 2 illustrates the association of fBioAge and total PA separately for age groups of 75, 80 and 85 years. Higher fBioAge was associated with lower level of total PA in age groups of 75 and 85 years at statistically significant level (75: r=0.241, p<0.001, 85: r=0.319, p=0.009, respectively) (Figure 2). This association was not found in the group of 80-year-old participants (r=0.118, p=0.180)

(Figure 2). FBioAge explained 9,2% of variation in total PA in 85-year-olds, which was the highest degree of explanation between different age groups (Figure 2).

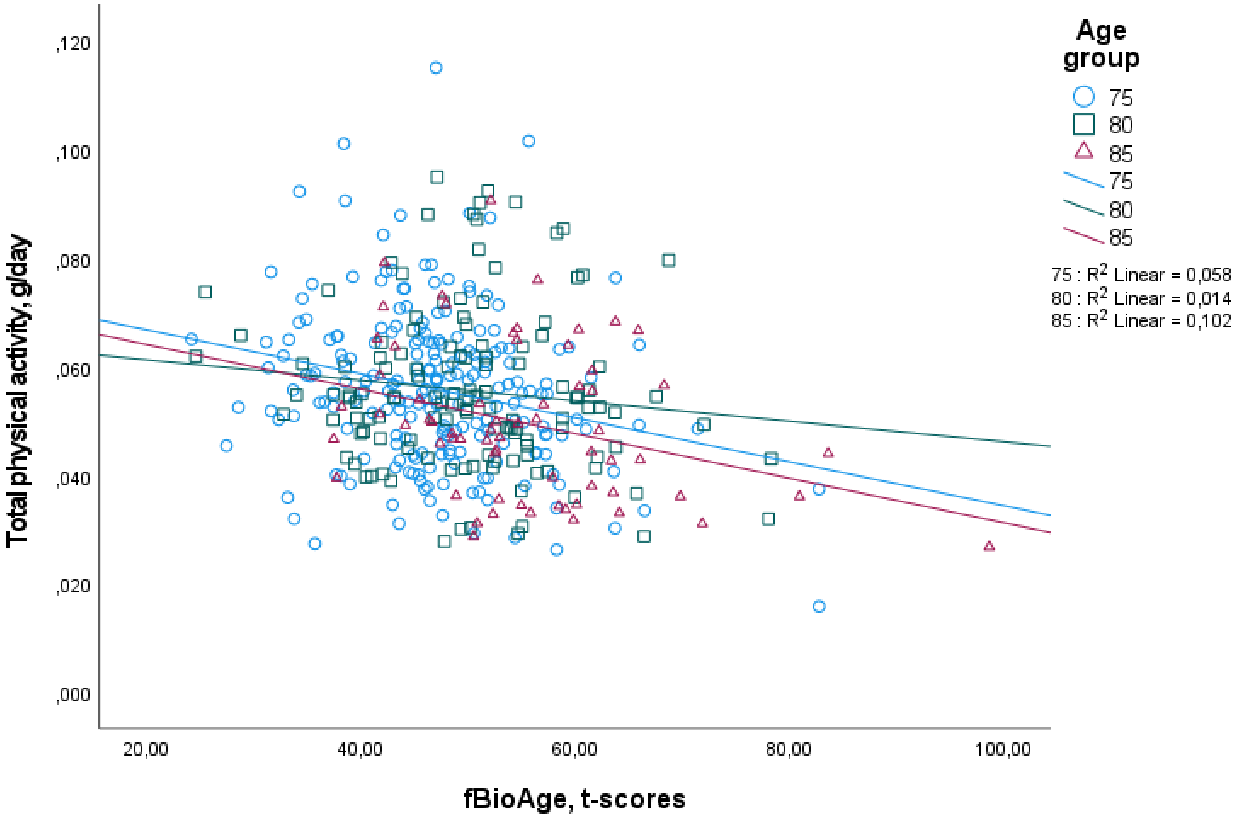

FIGURE 2. Association of fBioAge and total physical activity in age groups of 75-year-olds (n=211), 80-year-olds (n=130), and 85-year-olds (n=66).

### 7.4 The association of functional age and moderate to vigorous physical activity

There was a negative correlation between fBioAge and absolute MVPA ($r=-0.235$, $p<0.001$). Apart from hearing, all the components of the sum variable also had statistically significant correlations with absolute MVPA ($p<0.05$, Table 5). Maximal isometric hand-grip strength, walking time (3m) and respiratory function (FEV1) had the greatest correlation with absolute MVPA ($p<0.001$, Table 5). The variables were in basic form when examining the correlations i.e., small values in vision and walking time (3m) and large values in hearing, handgrip strength and respiratory function indicated good functioning ability. Negative correlation between walking time (3m) and absolute MVPA for example indicates that the faster the walking time (3m) the more physical activity.

TABLE 5. Correlation between self-reported hearing, self-reported vision, handgrip strength, walking time (3m), respiratory function and absolute MVPA.

| Variable | Absolute MVPA | Self-reported hearing | Self-reported vision | Handgrip strength (kg) | Walking time, 3m (s) | Respiratory function (FEV1) |
|---|---|---|---|---|---|---|
| Absolute MVPA | 1 | | | | | |
| Self-reported hearing (0-10) | -0.021 | 1 | | | | |
| Self- reported vision (1-4) | -0.126* | -0.159** | 1 | | | |
| Handgrip strength (kg) | 0.235** | -0.026 | -0.137* | 1 | | |
| Walking time, 3m (s) | -0.292** | -0.062 | 0.119* | -0.249** | 1 | |
| Respiratory function (FEV1) | 0.243** | -0.002 | -0.178** | 0.563** | -0.265** | 1 |

FEV1 = forced expiratory volume in one second. MVPA = Moderate to Vigorous Physical Activity. Pearson's correlation coefficient; **p<0.001; *p<0.05. The variables were in basic form when examining the correlations: small values in vision and walking time (3m) and large values in hearing, handgrip strength and respiratory function indicate good functioning ability.

Linear regression analysis showed that fBioAge associated with absolute MVPA (Model 1, Table 6: β = -0.235, p<0.001). Adjusting the model with sex and chronological age in model 2 (Table 6) did not attenuate the association of fBioAge with absolute MVPA. A minimal attenuation in the association was detected after adjusting the model with lifestyle factors (β= -0.154, p=0.003) and further in the fully adjusted model, but the association remained statistically significant (β=-0.105, p=0.027).

Linear regression analysis showed that fBioAge explained 5,5% of the variation in the absolute MVPA (p<0.001) (Table 6), thus the effect size was rather low in the first model. The degree of explanation in the linear regression model grew gradually when the background variables were added to the model (Table 6). The fully adjusted model explained 27.8% of the variation in total PA and was suitable for the data – F (10, 394) = 15.203, $p<0.001$.

TABLE 6. The association of fBioAge with moderate to vigorous physical activity.

| | Model 1 (fBioAge) | | | Model 2 (age and sex) | | | Model 3 (lifestyle factors) | | | Model 4 (fully adjusted) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $R^2$ | β | p | $R^2$ | β | p | $R^2$ | β | p | $R^2$ | β | p |
| **Model fit** | .055 | | **<.001** | .083 | | **<.001** | .112 | | **<.001** | .278 | | **<.001** |
| **fBioAge** | | -0.235 | **<.001** | | -0.183 | **<.001** | | -0.154 | **.003** | | -0.105 | **.027** |
| **Chronological age** | | | | | | | | | | | | |
| $75^{ref}$ | | - | - | | ref | ref | | ref | ref | | ref | ref |
| 80 | | - | - | | 0.000 | .997 | | -0.006 | .910 | | 0.006 | .901 |
| 85 | | - | - | | -0.120 | **.024** | | -0.128 | **.015** | | -0.093 | .054 |
| **Sex** | | | | | | | | | | | | |
| $\text{Women}^{ref}$ | | - | - | | ref | ref | | ref | ref | | ref | ref |
| Men | | - | - | | 0.125 | **.010** | | 0.093 | .083 | | 0.033 | .504 |
| **Smoking history** | | | | | | | | | | | | |
| $\text{Never smoked}^{ref}$ | | - | - | | - | - | | ref | ref | | ref | ref |
| Former smoker | | - | - | | - | - | | -0.033 | .524 | | 0.002 | .968 |
| Current smoker | | - | - | | - | - | | -0.098 | **.046** | | -0.130 | **.004** |
| **Alcohol consumption*** | | - | - | | - | - | | 0.157 | **.002** | | 0.084 | .075 |
| **A number of chronic diseases** | | - | - | | - | - | | - | - | | -0.232 | **<.001** |
| **Assistive devices** | | - | - | | - | - | | - | - | | -0.035 | .458 |
| **BMI** | | - | - | | - | - | | - | - | | -0.314 | **<.001** |

BMI = Body Mass Index ($kg/m^2$), ref = refence group, $R^2$ = Correlation of coefficient, β = standardized coefficient, *value 1 meaning less than 1-1,5 doses per week

### 7.5 The association of functional age with moderate to vigorous physical activity according to sex and age groups

No interaction for age and sex was found in the basic models of linear regression analysis and therefore no further modelling was considered for these measures (sex*80years: p=0.818, sex*85years: p=0.940, age group of 75 years as a reference group). Figure 3 illustrates the association of fBioAge and absolute MVPA separately for men and women. Higher fBioAge was associated with lower level of absolute MVPA in both sexes at statistically significant level (men: r=0.278, p<0.001, women: r=0.017, p=0.006) (Figure 3).

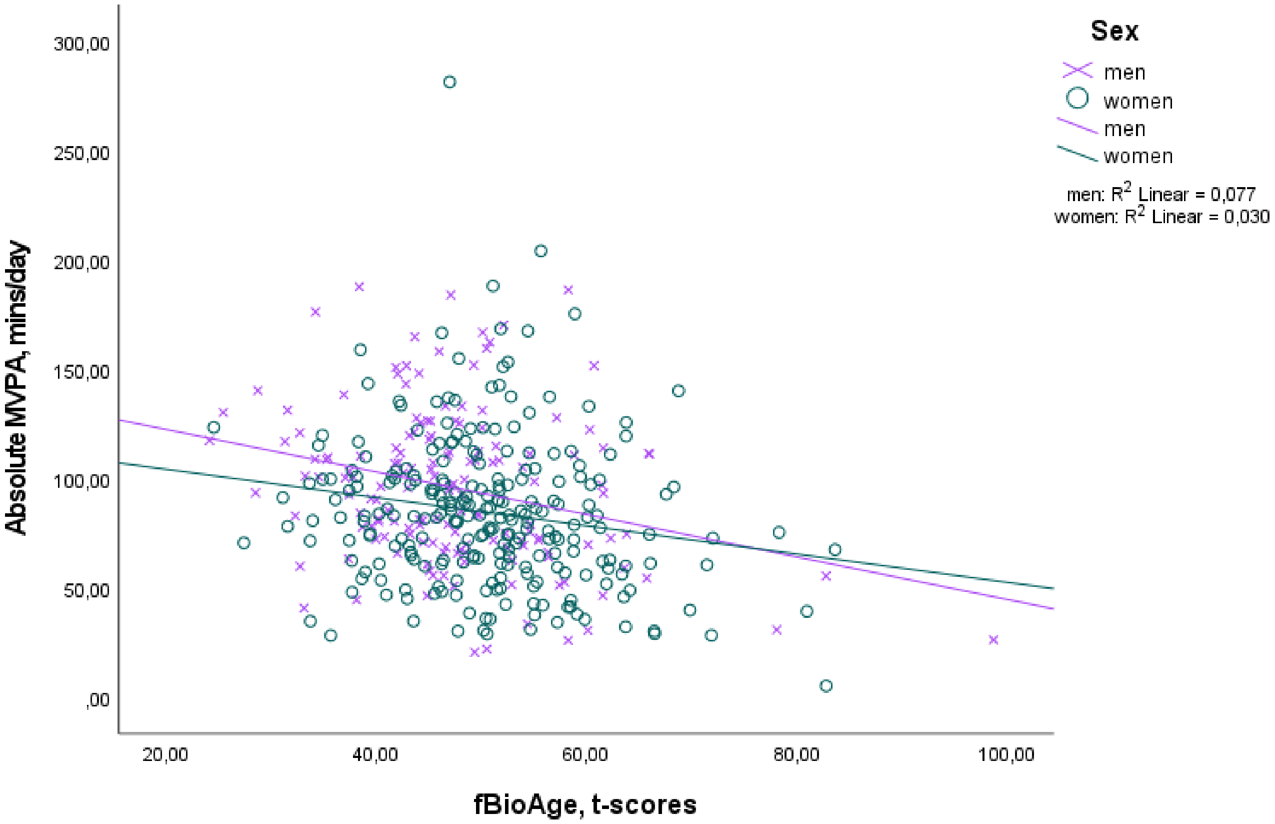

FIGURE 3. Association of fBioAge and absolute MVPA for men (n=156) and women (n=251).

Figure 4 illustrates the association of fBioAge and absolute MVPA separately for age groups of 75, 80 and 85 years. Higher fBioAge was associated with lower level of absolute MVPA in age groups of 75 and 85 years at statistically significant level (75: r=0.235, p<0.001, 85: r=0.293, p=0.017) (Figure 4 This association was not found in the group of 80-year-old participants (r=0.095, p=0.283) (Figure 4). FBioAge explained 10,2% of variation in absolute MVPA in 85-year-olds, which was the highest degree of explanation between different age groups (Figure 4).

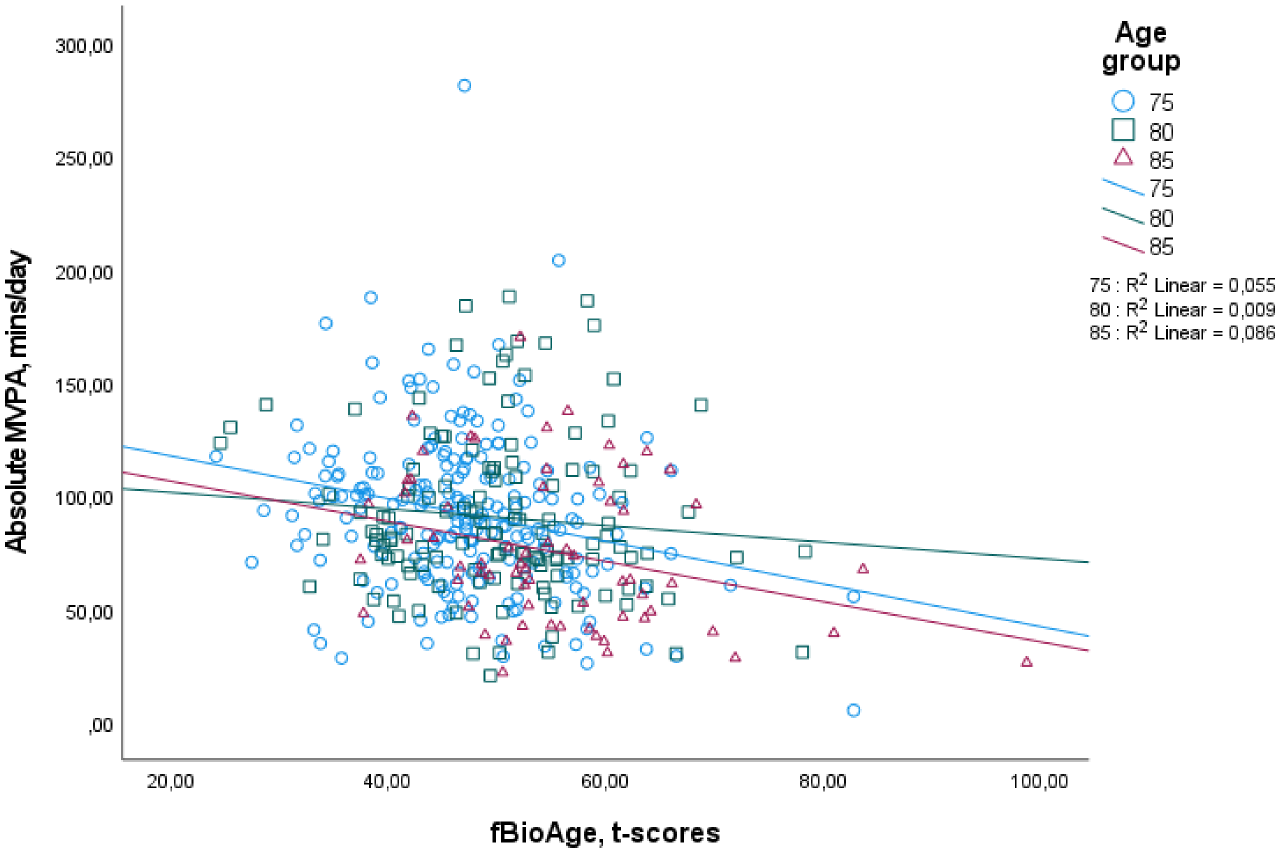

FIGURE 4. Association of fBioAge and absolute MVPA in age groups of 75-year-olds (n=211), 80-year-olds (n=130), and 85-year-olds (n=66).

# 8 DISCUSSION

This thesis investigated the association of a sum variable of functional age (fBioAge) with PA in 74-year-old and older individuals living at home. It was also under examination whether the possible association between functional age and PA differed between men and women or between age groups of 75, 80 and 85 years of chronological age. This thesis is the first study known to be published that examines the association of the sum variable fBioAge to PA. According to the results, fBioAge is associated to objectively measured PA and the association turned out to be marginally stronger with total PA than absolute MVPA. The higher the participant's calculated fBioAge was, the less physically active they were.

Participant's chronological age and sex was not found to influence the association between fBioAge and PA. Examining the age groups separately, the association of fBioAge and both PA variables was similar and statistically significant for the age groups of 75- and 85-years. However, there were couple of individuals in these age groups who had very high fBioAge and had low PA values, which might have affected the results. No association between fBioAge and PA variables was found in the group of 80-year-olds which might be due to them being more functionally homogenous group compared to 75- and 85-year-olds. Higher chronological age has been associated with decline in PA levels in scientific literature (Husu et al. 2016; Troiano et al. 2008).

In the sample of this thesis, 85-year-olds were less physically active in moderate to vigorous level compared to younger counterparts. This same phenomenon has been noticed in previous literature as leisure-time PA has been found to decrease with age, especially for women (Koponen et al. 2018). On the other hand, it has been argued that due to the age-related decrease in physical performance, activities such as walking become more intensive for older adults compared to younger people (Karavirta et al. 2020; Goodpaster et al. 2006; Fleg et al. 2005). The association of fBioAge with total PA and absolute MVPA seemed to be the strongest for the age group of 85 even though chronological age did not have an effect on the association after adjusting with other background variables. Participants in the age group of 85 may have had higher heterogeneity in functional ability compared to the younger age groups, which could explain the stronger association between fBioAge and PA. Physical functioning varies greatly in later life and functional limitations become more common with advancing age since they usually develop slowly (von Bonsdorff & Rantanen 2011). It is possible that in the age group of 85 there have been more functional limitations compared to younger age groups which could at least partially explain the differences in the association. However, the association was the weakest for the age group of 80 years, hence the differences between age groups cannot be explained only with age-induced functional limitations.

The results of this thesis are in line with these previous studies, since women had a significantly higher fBioAge on average compared to men ($p<0,001$). The rate of change in fBioAge has been indicated to be similar between men and women, but women seem to have a higher fBioAge than men (Finkel et al. 2017). The results of the study of Liang et al. (2008) also showed that women experience a faster decline in functional status after 50 years of chronological age and have a higher level of functional impairment compared to men. In line with result of Finkel et al. (2017) women's fBioAge had the mean above 50 and men had the mean under 50 in the sample of this thesis. FBioAge was calculated in t-scores where 50 is the mean so the results indicate that women's fBioAge is above average whereas men's fBioAge is below average. The sum variable fBioAge has been shown to differ in the rate of increase through the lifespan and that the rate of increase is twice as fast after 75 years of chronological age (Finkel et al. 2017). This is not surprising since functional impairments are shown to be more common in older age (Liang et al. 2008). It is noted before that men perform better in physical function measurements and that women are frailer and have worse health in late life (Hägg & Jylhävä 2021; Liang et al. 2008), which would explain the differences in fBioAge. Interestingly, biological ageing has shown to differ between sexes in a way that men age biologically faster than women (Kankaanpää et al. 2022; Hägg & Jylhävä 2021). In general, women live longer than men, which is in line with the evidence of sex differences in biological ageing but not with the evidence of functional ageing. There seems to be some kind of a paradox in sex differences in ageing that has also been recognized before (Hägg & Jylhävä 2021).

Men were more physically active than women when comparing both the total PA and absolute MVPA variables. This is in line with previous study findings (Hickey & Mason 2017; Troiano et al. 2008). Despite the detected differences between sexes in fBioAge and in PA on their own, sex did not affect the association of fBioAge with PA according to the results of this thesis. As Hägg & Jylhävä have stated (2021) it is important to try to understand the sex-driven characteristics of ageing, since there is increasing body of evidence about the significance of biological sex in ageing process, and therefore the research question about sex differences was highly relevant. Sex differences of two out of five components of fBioAge was faded before the actual creation of the sum variable following the methods of Finkel et al. (2017). The z-transformation for handgrip strength was made separately for men and women and respiratory function (FEV1) was corrected with body volume through division by individual's squared height ($m^2$). Finkel et al. (2017) justified this with the aim to examine sex differences beyond the trivial fact that men have grater body mass and stronger muscles in general than women. Descriptive statistics of these two variables varied between men and women on the sample of this thesis. Without the corrections that were made before the creation of the sum variable, the differences on the association of fBioAge and PA could have been grater between men and women, and this might have resulted in further modelling separately for men and women.

Apart from hearing, all the components of fBioAge correlated with both PA variables. Self-reported hearing was still included in the sum variable because the aim was to follow the methods of Finkel et al. (2017) as closely as possible. Dropping the self-reported hearing out of the sum variable might have however resulted in different results found in the association of fBioAge and PA. The association could have been greater if all the components of the sum variable had individually correlated with PA. The components of the sum variable fBioAge have all been at least moderately examined in the research literature in relation to physical activity. The strongest evidence appears to be for the relationship of handgrip strength to PA, and it can be stated with some confidence that better muscle strength is related to higher PA levels.

The results of this thesis also showed that stronger handgrip strength was associated with greater amount of PA. The use of handgrip strength measurement in research and clinical work is relatively easy and inexpensive, which is why it has gained much support as a measure of muscle strength (e.g., Taekema et al. 2010). Based on their findings, Taekema et al. (2010) concluded that measuring handgrip strength can be a useful tool in geriatric clinical work to identify older people at risk of more rapid decline in functional capacity for activities of daily living and cognition. However, the use of handgrip strength to assess total body muscle mass has also been criticised and the need to measure lower limb muscle strength as part of geriatric assessment has been identified instead (Ramsey et al. 2021). Drawing on this, one might therefore think that a more accurate and comprehensive picture of functional age could be obtained by slightly different muscle strength measurements. On the other hand, however, handgrip strength has been found to be strongly associated with lower limb muscle strength in older individuals and is therefore an adequate and useful measure of muscle strength in older people (Strandkvist et al. 2021). Some gender differences in the relationship of handgrip strength with physical activity have been observed (Bann et al. 2015), which supports the relevancy of processing the data of handgrip strength separately for men and women in calculation process of the sum variable fBioAge.

The relationship between walking speed and PA has also been studied quite extensively, and the association seems to be bidirectional. Negative changes in gait (step width, length, speed) have been found to indicate reduced level of PA (Ciprandi et al. 2017) and it would also seem that being more physically active would also lead to a faster walking speed (Renner et al. 2022; McMullan et al. 2020; Adachi et el. 2018). In this thesis, faster three-meter walking time with participant's habitual moderate pace was associated with greater amount of PA. This in line with previous studies which have noted that preferred walking speed seem to contribute to the level of PA (Karavirta et al. 2020; Ciprandi et al. 2017). Age has also been found to influence the association between walking speed and physical activity (McMullan et al. 2020) and it is therefore important to acknowledge different level of intensities when studying PA among older people.

Moderate to severe hearing loss has been shown to reduce PA (Tremblay et al. 2015; Gispen et al. 2014), but the results of studies have been somewhat contradictory. Gender differences have also been found in relation to hearing and PA (Holman et al. 2021; Fisher et al. 2015). The relationship between hearing loss and PA levels may depend on the hearing measurement methods used. Choi et al. (2016) found in their study that when using self-reporting as a measure, the association of hearing loss with lower PA levels, among other things, may be weaker compared to audiometry. Drawing on other research literature, they suggested that the result may be influenced by the fact that older people may underestimate their level of hearing impairment, thinking it is part of the normal ageing process, or deny the existence of hearing impairment altogether in order to not be stigmatised for it. Older people may not report mild hearing difficulties because age-related hearing loss develops gradually (Choi et al. 2016). It is possible that this sort of under-reporting has happened among the participants of this. Self-assessed hearing has been shown to correlate with the Whispered voice test and the question "Is your hearing (with or without a hearing appliance)/Excellent; Very Good; Good; Fair; Poor?" has been found to be the most accurate in terms of sensitivity (55.56%) and specificity (94.67%) for detecting hearing loss (Gibson et al. 2014). Similarly, in the sample of this thesis, hearing was assessed with a scale 0 (very poor) to 10 (excellent).

In the light of existing literature vision and respiratory function seem to be components of fBioAge that have been studied less in association with PA or the results are at least less evident. Evidence on the association of vision with PA is currently insufficient to draw conclusions, but it has been speculated that the association may be bidirectional; vision loss may influence an individual's PA level and increased PA may be a protective factor against vision loss (Ong et al. 2018). The results of this thesis showed that better self-reported vision was associated with greater amount of PA.

Similar correlation was also found between respiratory function and PA. The causal relationship between respiratory function and PA is not unequivocal and the need for longitudinal studies on this topic has been called for (Sillanpää et al. 2014; Singh-Manoux et al. 2011).

The need for further research was highlighted for a number of individual variables of the sum variable fBioAge, and in particular high quality longitudinal experimental studies would be needed to establish causal relationships. FBioAge considers only measurements of physical function, which can be seen as a weakness in its ability to reflect functioning and ageing as multidimensional phenomena. Measurements of social, mental, and cognitive function could offer important insight to functional ageing. In fact, associations between fBioAge and cognition among older adults has been studied and compared with chronological age. A study of Sternäng et al. (2019) found that fBioAge was a stronger predictor of cognition than chronological age during a wide range of the old adult life span. This supports the potential of fBioAge as a useful ageing indicator.

In this thesis, components of the fBioAge sum variable vary slightly from the ones that Finkel et al. (2017) included in their sum variable. This is due to the original AGNES-study protocol, which had all the elements of fBioAge measured but with marginally varying methods. In the AGNES-study, participants chose a number from 0 (very poor) to 10 (excellent), which they thought reflected their hearing. Finkel et al. (2017) used a similar question, but their scale was from 1 (nearly deaf/deaf) to 5 (excellent). For assessing self-reported vision, they used comparable scaling, 1 (nearly blind/blind) to 5 (excellent). In the AGNES-study, self-reported vision was assessed with three questions as described earlier in this thesis. Finkel et al. (2017) measured walking speed by recording the time spent in walking three meters distance, turning, and walking back. In the AGNES-study, walking speed was measured more than once, one being part of the SPPB measurement where participant was asked to walk 3 meters distance with their habitual moderate pace. SBBP-measurement was selected to this thesis because of the similar distance used by Finkel et al. (2017) that was three meters back and forth. Another possibility would have been using the walking time recorder from 10 meters distance, which could have resulted in slightly greater variation in this study sample. SPPB-measurement has the benefit for future research use of the sum variable used in this thesis, since SPPB-measurement could be recorded even from participants who might not have been able to walk ten meters distance.

In both the present and Finkel et al. (2017) studies, maximal handgrip strength was measured with a handheld dynamometer and expressed as kilograms. The only difference was that in the AGNES-study handgrip strength was measured only from the dominant hand (3-5 attempts) whereas in the study by Finkel et al. (2017) participant made three attempts with both hands to achieve the maximum score. Respiratory function was assessed with spirometry in both studies using different spirometers (AGNES-study: Medikro Pro Spirometer, Medikro Oy, Kuopio, Finland; Finkel et al.: Vicatest spirometers, Mijnhardt, Bunnik, The Netherlands & ML 330 spirometer, Micor Medical, Kent, United Kingdom). In the AGNES-study the measurement was made in standing position whereas in the study of Finkel et al. measurement was made in seated position. Finkel et al. (2017) used forced expiratory volume in the first second (FEV1) in their analyses and so similar values from the AGNES-study were used in this thesis.

Even though the components of the fBioAge in this thesis, varied slightly from the ones that were included in the one developed by Finkel et al. (2017), the results are comparable due to the methodological alignment in converting the variables to z- and eventually t-scores which are standardized scores. Finkel et al. (2017) examined Swedish twins and the total time span of the measurements was 19 years. Their participants mean chronological age varied from 65 to 74 years of age with 7.7 to 9.3 standard deviations (Finkel et al. 2017), hence the age distribution was greater than in the sample of this thesis which had three older age cohorts (75-, 80- and 85-year-olds). With greater age distribution, the fBioAge would also most likely have greater variation which might provide different results about the association of fBioAge with PA. The association could possibly be stronger if the study sample would have had more variation in chronological age and functioning.

The results of this thesis were in line previous studies examining fBioAge as an ageing indicator. FBioAge was associated with PA and the association seemed to be independent from chronological age. Therefore, it can be assumed that fBioAge is more strongly associated with PA levels than chronological age as it has been shown to be in other ageing-sensitive functions such as cognitive ability (Sternäng et al. 2019). This thesis was a cross-sectional study, therefore, any conclusions about the causality of the association of fBioAge with PA cannot be drawn. The participants of the AGNES-study all had to match certain conditions and it is likely that older individuals with great difficulty in functioning have not participated in the study and therefore the heterogeneity of older people in general may have faded in the study sample. The study population was geographically narrowed to the region 10 kilometres from Jyväskylä centre and only individuals who were living at home were included in the study. Initial contact to the study cohorts was a letter and after that, a phone call. This might have excluded some individuals with poor hearing who therefore or who otherwise have trouble in communicating, which consequently might have some rate of explanation to the fact that no correlation was found between self-reported hearing and PA levels. Participants who were willing to take part in the accelerometery measurement and committed to wear the accelerometer at least three whole days are possibly more interested about PA and their own health in general. This group have most likely been in better condition in the means of functioning (i.e., cognitive, and physical abilities) than older individuals in general. Portegis et al. (2019) compared correlations between a range of measures of physical performance and physical activity assessing the same underlying construct in a home visit and in a highly standardized setting of the research centre or accelerometer recording. They found that self-reported PA of at least moderate intensity was greater and walking speed was faster in a group of participants who took part also in the subsequent physical assessments at the research centre and in the accelerometery-based PA assessments compared to those who only participated in the home interview. Greater deal of participants taking part in the subsequent physical assessments at the research centre and/or in the accelerometery-based PA assessments also rated their health good or excellent and reported no limitations due health and functioning compared to those who only participated in the home interview (Portegis et al. 2019). To add, greater deal of participants taking part in the home interview only or in the subsequent physical assessments at the research centre had low PA level (less than three hours) compared to those who participated in the accelerometery-based PA assessments (Portegis et al. 2019).

Participants included in this thesis seem to represent an older population whose functional ability is above average since results from all the five functional measurements included in the sum variable of fBioAge indicate normal or better functional ability when looking at mean results. For example, the mean handgrip strength in women and in men was above average comparing the reference values based on FinTerveys2017-study. It might be that examining a more heterogenous group of older people in the means of their functional ability a stronger detectable association between fBioAge and PA would be found. Comparing the amount of PA and MVPA to previous studies, participants of this study also seem to represent an exceptionally active group of older individuals. Mean amount of MVPA activity minutes in this study sample was nearly 90 minutes per day while in previous studies accelerometer measured MVPA minutes have been under fifty minutes per day (Aaltonen et al. 2020; Giné-Garriga et al. 2020). Considering that the current recommendations of weekly movement for people over 65-years are moderate intensity movement for at 150 minutes per week or vigorous intensity movement for at least 90 minutes per week, it can be assumed that participants of this study represent an exceptionally active group of older individuals since only about a half of the Finland's population aged 50-59-years reaches the meet the current recommendations for PA, and both endurance exercise and leisure-time PA decrease with age, especially in women (Koponen et al. 2018). Hence, conclusions in generalizing the results of this study to older population should be made with caution.

PA has been shown to reduce functional ability decline resulting in maintaining better functioning in older age (Paterson & Warburton 2010). Like noted before, decrease in physical performance might affect how intensive an activity is experienced. Older people with functional limitations might experience barriers in attending PA and mobility limitations have shown to diminish the amount of PA (Rasinaho et al. 2006). Frequent falls have also been associated with decline in household, common leisure, and walking activities (Stahl & Albert 2014). In this thesis the association of fBioAge with PA have been examined, however it is not clear whether functional age affects PA or other way around. The association might be bidirectional, and it is possible that higher functional age can result in diminished PA and that functional aging can be slowed down with PA.

Study limitations considering measuring of PA with accelerometery are that a thigh-worn accelerometer cannot distinguish movement of the upper body. The time participants spent in sitting position might not necessarily have been passive or inactive. If an individual has a limitation that prevents them from walking for longer periods of time or at all, they might compensate by being physically active in a way that meets their personal abilities. In addition, accelerometers do not detect if a person is carrying a load that increases the intensity of the activity, hence accelerometery data does not accurately reflect the intensity of the activity. On the other hand, measuring PA with accelerometer also contributes as an advantage of this study. Accelerometer is an objective and a rather accurate way to measure PA (Sallis 2010) as it makes gathering even the short periods of movement possible (Troiano et al. 2014). Subjective PA measurements such as self-reports have lower rate of accuracy because of the reporting is not timely and is dependent on the subject's memory (Sylvia et al. 2014) and the detection of low-intensity PA is weak (Skender et al. 2016; Sylvia et al. 2014) which might be one cause of older people’s tendency to under-report the amount of participated MVPA and sedentary behaviour (Cleland, Ferguson & Hunter 2018). With thigh-worn accelerometer, large amounts of accurate data about body position and lower-body movement can be gathered and even the short periods of activity will be recorded. This is an advantage especially when examining older individuals who may compile their physically active time from shorter bouts of PA during daily tasks such as house and garden work (Peeters et al. 2014).

Other strengths of this thesis include the large sample of older individuals that participated in the AGNES-study. The sum variable fBioAge was created during the process of this thesis following the methods used by Finkel et al. (2017) and it will be available for use of other researchers utilizing the AGNES-study data. The AGNES-study has continued after the initial data collection that contributes to this thesis. Therefore, it is also possible to examine longitudinal aspects of the association between fBioAge and PA in the future. Moreover, other associations of fBioAge can be examined with the AGNES-study data that includes a wide range of different measurements considering activity, health, and functional ability in wellbeing in old age.

*Ethics and reliability of the thesis.* In the process of this thesis, ethics have been appropriately taken into account and both the thesis and the AGNES-study have been carried out in accordance with research integrity (Tutkimuseettinen neuvottelukunta 2023). The AGNES-study protocol has been approved by the ethical committee of the Central Finland Health Care District (Rantanen et al. 2018). Before participating in the study, subjects received information about the study and the possible associated risks and discomforts. There were no invasive or potentially physically or psychologically harmful aspects in the AGNES-study beyond what one might encounter in daily life. At the beginning of the home visit, participants were asked to sign a written consent and they were allowed to withdraw their consent at any time throughout the study or for any individual part of the study.

For this thesis a data processing agreement was made for the utilization of the data collected in the AGNES-study and only the data required for this master's thesis was released for utilization as a pseudonymised SPSS-file. The data was stored and handled carefully in accordance with the information security policy of the University of Jyväskylä and after the completion of the thesis, the data concerning the sum variable created will be handed over to the AGNES-study group for further application and all the unnecessary data will be extinguished. The author of this thesis was not involved in the data collection, which can be seen as an advantage for objectivity. However, the author was involved in the data collection later in the AGNES-study during the years 2021-2022, so it should be acknowledged that enough comprehensive information about the data collection process and the different stages of the research has been gathered for this thesis. Being part of the data collection process later, can also be seen as an advantage for study reliability. The author was given guidance when needed by the thesis supervisor, the research team, and statisticians in different phases of this thesis. Additionally, peer review was available during the whole process of this thesis.

*Conclusions and recommendations for future research.* FBioAge is associated with objectively measured total PA and absolute MVPA irrespective of sex and chronological age. The association appears to be stronger in men than in women and in the age group of 85 years. The components of fBioAge correlated with PA apart from self-reported hearing. This can be due to the fact that most part of the study sample considered their hearing rather good. It could be worthy to create a sum variable without hearing aspect and compare the result with this thesis. It would also be important to examine other associations of fBioAge and health and functional ability in wellbeing in old age to find out whether fBioAge is a good biomarker of ageing that correlates with multiple aspects of ageing.

As far as I know, this thesis is the first study that examines the association of the sum variable fBioAge to PA. More high-quality research and especially longitudinal research is needed to examine the causal relations of fBioAge with PA. Since the sum variable created for this thesis will be available for further research use, the longitudinal aspects can now be examined through the follow-up data of the AGNES-study. It is known that PA improves physical functioning and reduces the risk of age-related physical disability (Office of Disease Prevention and Health Promotion 2018) so it would be highly important to understand why the current recommendations for PA are not met. The results of this thesis are meaningful because they support the previous research considering fBioAge as an ageing biomarker that does not assume the same rate of ageing for heterogenous group of individuals as chronological age does. FBioAge seems to be able to capture a small amount of variation of PA levels in older people living at home. The sum variable fBioAge shows promise as an ageing biomarker, however further research is needed for comparing different set of biomarkers of functional age and for standardizing a sum variable for future use.

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