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SUCCESSFUL AGING AND ASSOCIATED MIDLIFE FACTORS

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ACADEMIC DISSERTATION

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” The secret of living well and longer is:
Eat half, walk double, laugh triple
and love without measure.”

(Tibetan Proverb)

TABLE OF CONTENTS

LIST OF ORIGINAL PUBLICATIONS

This dissertation is based on the following original publications:

I. Urtamo A, Kautiainen H, Pitkälä KH, Strandberg TE. Association of midlife value priorities with health-related quality of life, frailty, and mortality among older men: a 26-year follow-up of the Helsinki Businessmen Study (HBS). *Qual Life Res*. 2018;27(5):1269–1275.

II. Urtamo A, Huohvanainen E, Pitkälä KH, Strandberg TE. Midlife predictors of active and healthy aging (AHA) among older businessmen. *Aging Clin Exp Res*. 2019;31(2):225–231.

III. Urtamo A, Jyväkorpi SK, Kautianen H, Pitkälä KH, Strandberg TE. Major cardiovascular disease (CVD) risk factors in midlife and extreme longevity. *Aging Clin Exp Res*. 2020;32(2):299–304.

IV. Jyväkorpi SK, Urtamo A, Strandberg AY, von Bonsdorff M, Salomaa V, Kivimäki M, Luotola K, Strandberg TE. Associations of overweight and metabolic health with successful aging: 32-year follow-up of the Helsinki Businessmen Study. *Clin Nutr*. 2020;39(5):1491–1496.

ABBREVIATIONS

AHA	Active and healthy aging
ADL	Activities of daily living
CI	Confidence interval
CCI	Charlson comorbidity index
COVID-19	Corona Virus Disease 2019
CVD	Cardiovascular disease
DNA	Deoxyribonucleic acid
DNAm age	DNA methylation age
DXA	Dual-energy X-ray absorptiometry
FI	Frailty Index
HBS	Helsinki Businessmen Study
HRQoL	Health-related quality of life
IADL	Instrumental activities of daily living
LBZs	Longevity Blue Zones
LTL	Leukocyte telomere length
MCI	Mild cognitive impairment
MHN	Metabolically healthy normal weight
MHO	Metabolically healthy overweight and obesity
MUN	Metabolically unhealthy normal weight
MUO	Metabolically unhealthy overweight and obesity
OR	Odds ratio
SARC-F	Sarcopenia risk score
SD	Standard deviation
SOC	Selective optimisation with compensation theory
SPPB	Short physical performance battery - test
SRH	Self-rated health
SRF	Self-rated fitness
UJACAS	University of Jyväskylä the Active Aging Scale
TUG	Timed up and go test
WHO	World Health Organisation

ABSTRACT

Successful aging has been defined as good physical, psychological, and social functioning in old age without major diseases. Previous studies show that life habits in midlife influence longevity, functionality, and health-related quality of life (HRQoL) in old age. However, there is a lack of longitudinal studies in homogenous cohorts exploring the association of midlife value priorities, self-rated health (SRH), and cardiovascular risk factors with successful aging.

This study, comprising four sub-studies, explores the associations of midlife factors with successful aging in the Helsinki Businessmen Study (HBS) cohort. Successful aging is defined in sub-studies as HRQoL, longevity, reaching 90 years of age, absence of frailty, and fulfilment of the Active and Healthy Aging criteria (AHA). *Study I* investigates the association of midlife value priorities with higher mortality risk, frailty, and HRQoL in old age. *Study II* explores the relation between midlife SRH, lifestyle and cardiovascular risk factors, and active and healthy aging using the AHA criteria, and *Study III* investigates how midlife cardiovascular disease (CVD) risk factors are associated with reaching 90 years of age. *Study IV* examines the associations of being overweight and associated metabolic health during later midlife with successful aging defined as longevity and HRQoL.

The subjects of the study were the participants of the Helsinki Businessmen Study (HBS) cohort, who were born between 1919 and 1934 with an original study population of 3490. The study consisted of data from surveys in 1974 and during the 2000s as well as from registries and clinical and laboratory assessments performed in 1974 and during 1985–86. In *Study I*, the businessmen responded to questions of their value priorities in 1974 and the RAND-36 questionnaire in year 2000. Their frailty phenotype and mortality were studied in 2000. In *Study II*, the midlife CVD risk factors and SRH were examined in year 1974, and the association of these factors with the AHA criteria in 2010 was analysed. The criteria of AHA were defined in 2010 (Rantanen et al. 2015) as having the following: being alive, responding to the mailed questionnaire, no subjective cognitive problems, feeling of happiness, no difficulties in activities of daily living (ADL), and no history of chronic diseases. The best AHA was fulfilling all these criteria. Fulfilling other five criteria but having chronic diseases was considered second best. *Study III* investigated the association of CVD risk factors in 1974 with extreme longevity defined as reaching 90 years of age by the 31st March 2018. *Study IV* consisted

of metabolic status data from participants' late midlife from 1985–86 and the association of metabolic health with the RAND-36 in 2000 and in 2007 and mortality until 31st March 2018.

The results of *Study I* revealed that valuing health during midlife was associated with better RAND-36 scores of physical functioning and vitality and predicted less frailty. Valuing an enjoyable and a varying life predicted higher mortality risk. *Study II* showed that a good SRH and low levels of cardiovascular risk factors in midlife are associated with active and healthy aging (AHA). The results of *Study III* indicated a linear relation between the number of CVD risk factors and reaching up to 90 years of age. *Study IV* revealed that mortality risk was the highest among the participants in the metabolically unhealthy overweight and obesity (MUO) group adjusted for age. Furthermore, men in the MUO group had, and men in the metabolically healthy overweight and obesity (MHO) group tended to have, lower odds to survive until 90 years of age.

Results of the study indicate that personal values, subjective health, and low levels of cardiovascular risk factors in midlife can predict longevity, HRQoL, health, and functionality in old age. Preventing cardiovascular risk factors early during the life course has long-term effects, and promotion of successful aging is beneficial for individuals and societies. An understanding of the long-term aspects and predictors of successful aging can be used for health promotion and the prevention of disability.

TIIVISTELMÄ

Onnistunut vanheneminen on määritelty fyysisen, psyykkisen ja sosiaalisen toimintakyvyn säilymiseksi myöhemmällä iällä ilman merkittäviä sairauksia. Aikaisemmat tutkimukset ovat osoittaneet, että keski-iän elintavoilla on yhteyttä eliniän pituuteen, toimintakykyyn ja elämänlaatuun vanhuudessa. Keski-iän arvostusten, koetun terveyden ja verisuonitautien riskitekijöiden pitkäaikaisia vaikutuksia onnistuneeseen vanhenemiseen on kuitenkin tutkittu vähän sosioekonomiselta taustaltaan yhtenevässä aineistossa.

Tutkimus sisältää neljä osatutkimusta, joiden tarkoituksena on selvittää onnistunutta vanhenemista Helsingin Johtajatutkimuksessa (Helsinki Businessmen Study, HBS). Onnistunut vanheneminen määritellään osatutkimuksissa hyvään terveyteen liittyväksi elämänlaaduksi, pitkäikäisyydeksi ja 90 ikävuoden saavuttamiseksi, gerastenian puuttumiseksi sekä aktiivisen ja terveen vanhenemisen kriteerien (AHA) täyttymiseksi. Tutkimuksessa selvitettiin keski-iän henkilökohtaisten arvostusten yhteyttä vanhuuden elämänlaatuun sekä keski-iän riskitekijöiden yhteyttä aktiiviseen ja hyvään vanhenemiseen. Lisäksi tutkittiin, mitkä keski-iän tekijät olivat yhteydessä 90 ikävuoden saavuttamiseen, sekä miten ylipaino ja metabolinen terveys olivat yhteydessä onnistuneeseen vanhenemiseen.

Aineisto koostui Helsingin Johtajatutkimukseen osallistuneista miehistä (alun perin N= 3490), jotka ovat syntyneet vuosina 1919–1934. Miehet ovat vastanneet kyselytutkimuksiin vuodesta 1974 lähtien 2000-luvulle, sekä osallistuneet myös kliinisiin mittauksiin vuonna 1974 ja 1985–86. *Ensimmäisessä osatutkimuksessa* miehet olivat vastanneet kysymyksiin arvostuksista vuonna 1974 sekä elämänlaatukysymyksiin RAND-36-mittarilla vuonna 2000. Lisäksi määritettiin osallistujien gerastenian status sekä kuolleisuus vuonna 2000. *Toisessa osatutkimuksessa* sydän- ja verisuonitautien riskitekijät sekä itsearvioitu terveys oli määritetty keski-iässä vuonna 1974 ja näiden tekijöiden yhteyttä aktiivisen ja terveen vanhenemisen kriteereihin (AHA) selvitettiin vuoden 2010 kyselyaineistosta. Aktiivisen ja terveen vanhenemisen kriteerit määriteltiin vuonna 2010 seuraavasti (Rantanen et al. 2015): on elossa, vastaaminen postikyselyyn, ei subjektiivisia kognitiivisia vaikeuksia, kokemus onnellisuudesta, ei vaikeuksia päivittäisissä toiminnoissa (ADL), ja ei merkittäviä sairauksia. Aktiivinen ja terve vanheneminen toteutui parhaiten niillä, joilla kaikki kriteerit täyttyivät. Kriteerien toteutuminen muiden kuin sairauksien osalta määriteltiin tutkimuksessa toiseksi parhaaksi vaihtoehdoksi. *Kolman-*

nessa osatutkimuksessa miesten sydän- ja verisuonitautien riskitekijöitä oli selvitetty vuonna 1974 ja tutkimuksessa selvitettiin näiden yhteyttä 90 ikävuoden saavuttamiseen 31.maaliskuuta 2018 mennessä. *Neljäs osatutkimus* tarkasteli osallistujien metabolista statusta vuosina 1985–86, ja metabolisen terveyden yhteyttä RAND-36-mittarilla mitattuun elämänlaatuun selvitettiin vuosien 2000 ja 2007 kyselyaineistoista.

Ensimmäinen osatutkimus osoitti, että terveyden arvostaminen keski-iässä oli yhteydessä parempaan elämänlaatuun fyysisen toimintakyvyn ja elinvoiman osa-alueilla RAND-36 mittarilla mitattuna ja se ehkäisi lisäksi gerasteniaa. Lisäksi tutkimuksessa tuli esille, että nautinnollisen ja vaihtelevan elämän arvostaminen ennusti aikaisempaa kuolleisuutta. *Toisen osatutkimuksen* tulokset osoittivat, että hyvä itsearvioitu terveys keski-iässä sekä vähäinen sydän- ja verisuonitautien riskitekijöiden määrä olivat yhteydessä aktiiviseen- ja terveeseen vanhenemiseen (AHA-kriteerit). *Kolmannen osatutkimuksen* tulokset toivat esille lineaarisen yhteyden sydän- ja verisuonitautien riskitekijöiden määrän sekä 90 ikävuoden saavuttamisen välillä. *Neljäs osatutkimus* osoitti, että suurin ikävakioitu kuolemanriski oli niillä osallistujilla, jotka kuuluivat metabolisesti epäterveellisesti ylipainoisten ja lihavien ryhmään (MUO). Tällä ryhmällä oli myös heikentyneet mahdollisuudet saavuttaa 90 vuoden ikä. Tulokset viittasivat myös, että metabolisesti terveillä ylipainoisilla ja lihavilla (MHO) oli heikentyneet mahdollisuudet 90 ikävuoden saavuttamiseen.

Tutkimustulokset osoittavat, että erityisesti terveyden arvostus, hyvä itsearvioitu terveys ja vähäiset sydän- ja verisuonitautien riskitekijät keski-iässä olivat yhteydessä onnistuneeseen vanhenemiseen HBS kohortissa. Tulosten perusteella terveys ja elintavat keski-iässä voivat ennustaa eliniän pituutta sekä vanhuusiän elämänlaatua, terveyttä ja toimintakykyä. Tutkimustulokset antavat vahvistusta sille, että sydän- ja verisuonitautien riskitekijöiden ehkäisy ajoissa elämänkulun aikana on monipuolisesti kannattavaa. Onnistuneen vanhenemisen ja terveyteen liittyvän elämänlaadun edistäminen ovat merkityksellisiä sekä yksilön että yhteiskunnan kannalta. Tuloksia voidaan hyödyntää terveyden edistämistyössä.

1 INTRODUCTION

As the population ages, it is important to understand which factors promote successful aging during the life course. Rowe and Kahn have defined successful aging as good physical, cognitive, psychological, and social functioning in old age without major diseases (Rowe & Kahn 1987, Rowe & Kahn 1997). They argued that age-related losses had been exaggerated and older peoples' heterogeneity ignored (Rowe & Kahn 1987). During recent decades, the definition of successful aging has developed from a biomedical approach to a wider multidimensional concept describing the quality of aging (Fernandez-Ballesteros 2019). The holistic view of successful aging includes also adaptive psychological and social mechanisms that can compensate for the limitations of physiological health (Baltes & Baltes 1990, Baltes & Cartensen 1996, Baltes 1997).

Various definitions of successful aging have been introduced in studies (Cosco et al. 2014), and the mean proportion of successful agers also varies among studies according to the definition used (Depp and Jeste 2006). On average, about one-third are successful agers, but the prevalence has a very wide variation in a review of 28 studies (Depp and Jeste 2006). Among the studies that had physical function or disability in their definition, the mean proportion of successful agers was 27%, and among those studies that included both physical and cognitive function, the mean proportion of successful agers was 20% (Depp and Jeste 2006).

The life-course approach focuses on biological, psychological, and social factors that operate from early life and influence the chance of successful aging and health in later life (Kuh et al. 2014). There is a growing interest in studying the large spectrum of health and aging and to explore what can be learnt from the "successful agers" (Kuh et al. 2014). The longitudinal cohort studies provide a powerful way to determine life course factors that can impact on successful aging (Kuh et al. 2014).

Previous studies having samples with varying age and socioeconomic profiles have shown that lifestyle and biological risk factors in midlife are related to longevity and aging successfully (Willcox et al. 2006, Sabia et al. 2012, Rantanen et al. 2012, Södergren 2013, Lafortune et al. 2016). The studies indicate that healthy lifestyles could diminish age-associated diseases and disability. However, most of the earlier studies have been conducted with varied

follow-up times and most of them provided analyses of survivors without considering the effect of mortality.

The focus of this thesis is to explore the associations of midlife factors with successful aging in the Helsinki Businessmen Study (HBS) cohort. Successful aging is defined in sub-studies as HRQoL, longevity, reaching 90 years of age, absence of frailty, and fulfilment of the Active and Healthy Aging criteria (AHA). The study examines the associations of midlife value priorities, self-rated health, self-rated fitness, and various lifestyle and cardiovascular risk factors with successful aging.

2 LITERATURE REVIEW

2.1 Definitions of successful aging

The concept of successful aging has started a debate in recent years (Bülow & Söderqvist 2014, Katz & Calasanti 2015, Calasanti 2016), and various definitions of the phenomenon have been introduced in studies (Cosco et al. 2014). The earliest definition of the concept was introduced by Robert J. Havighurst, who described successful aging as a happiness and satisfaction in a social context (Havighurst 1961). Ryff (1982) suggested that well-being in old age is related to its development over the life course. The classic definition by Rowe and Kahn defines successful aging as high physical, cognitive, psychological, and social functioning in old age without major diseases (Rowe & Kahn 1987, Rowe & Kahn 1997). Fries (1980, 1990) brought up a medical perspective of successful aging, where the focus is on optimizing life expectancy and compressing morbidity into a shorter period in old age. Baltes and Baltes (1990) introduced the model of selective optimization with compensation, which defines successful aging as adaptation to changes during the aging process. According to the definition by Baltes and Carstensen (1996), successful aging is an individual process where persons reach their own goals. Furthermore, Young, Frick, and Phelan (2009) also describe successful aging as an individualized process. They highlight an individual`s ability to compensate physiological limitations with adaptive psychological and social mechanisms (Young et al. 2009).

Several terms of the concept of successful aging have been used in the field (Fernandez-Ballesteros 2019). *Healthy aging* is defined by health and functionality, while *aging well* consists of both biomedical and psychosocial factors and refers more as a synonym to successful aging (Fernandez-Ballesteros 2019). The WHO (2001, 2002) has defined *active aging* as a "process of optimizing opportunities for health, participation and security in order to enhance quality of life as people age." In 2015, healthy aging replaced active aging in a policy framework of WHO, and the definition expanded to take into consideration also physical and cognitive functionality (WHO 2015). Rantanen and colleagues (2018) have presented active aging as a striving for well-being with activities that are related to a person's goals, functional capacities, and opportunities. *Productive aging* refers to the domain of social participation and engagement (Fernandez-Ballesteros 2019) and describes older peoples' contribution to society (O`Reilly and Caro 1995). The relation of these terms and the dimensions of successful aging are presented in Figure 1.

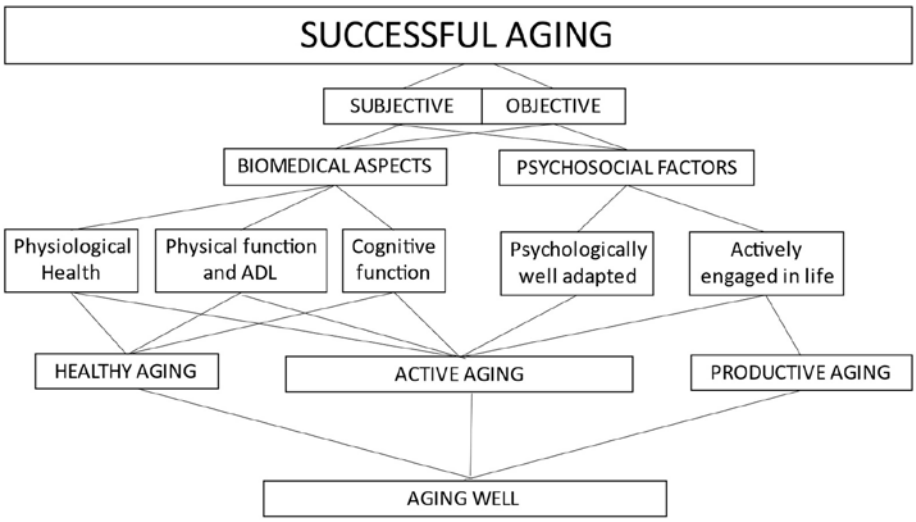

Figure 1. Dimensions of successful aging. Modified from Fernandez-Ballesteros et al. 2013 and Urtamo et al. 2019.

The main interest in the concept of successful aging is how to expand good health and disability-free years in the life span with a compression of morbidity (Fries 1980, 1989, 1990, Kivimäki & Ferrie 2011, Kuh et al. 2014). At the population and public policy level, the promoters of successful aging are discussed for the purpose of the quality of aging, whereas at the individual level, successful aging is defined by outcomes of health, functionality, and life involvement (Fernandez-Ballesteros 2019). Thus, successful aging is a multidimensional concept including domains of physiological, functional, social, cognitive, and psychological health. All these dimensions should be considered when studying the phenomenon – both from subjective and objective perspectives (Fries 1980, Depp & Jeste 2006, Cosco et al. 2014, Martin et al. 2014). Conceptual models describe the dimensions of successful aging and operational models present the practical indicators of this multidimensional concept. Table 1 shows how the dimensions of successful aging and related terms in conceptual models.

Table 1. Dimensions of successful aging and related terms in conceptual models. Modified and updated from Fernandez-Ballesteros 2019.

	Biomedical aspects			Psychosocial factors		Other constructs	
	Health constructs	**Physical constructs**	**Cognitive constructs**	**Psychological, adaptive and well-being constructs**	**Engagement and social participation constructs**	**Longevity**	**Other**
Havighurst 1961 "Successful aging"	-	-	-	Happiness, subjective well-being	Satisfaction in the social context	-	Adding life to years and getting satisfaction from life
Ryff 1982 "Successful aging"	-	Ideal functioning	-	Well-being	-	-	Well-being is related to development over the life course
Guralnik & Kaplan 1989 "Healthy aging"	Low number of chronic diseases	High level of physical functioning	-	-	-	-	-
Rowe & Kahn 1987, 1997 "Successful aging"	"Low probability of disease and disease-related disability"	High physical functional capacity	High cognitive functional capacity	-	Active engagement with life	-	-
Fries 1980, 1990 "Aging well"	Healthy lifestyles	Minimizing physical morbidity, independence	-	"To be enthusiastic, to have a good image of one`s self, to be an individual"	To be active	Optimizing life expectancy	Morbidity compression into a shorter period
Baltes & Baltes 1990 "Successful aging"	Biological health	-	Cognitive efficacy	Mental health, individual motivation, skills, life satisfaction	Social competence and productivity	Length of life	Strategies of selection, optimization, and compensation
Baltes & Carstensen 1996 "Successful aging"	"Bio-physical conditions, such as strength or vital capacity"	"Physical health, functional abilities"	-	"Subjective well-being, life satisfaction"	"Perceived social support, and involvement in life, social network, education"	-	Individual process with personal goals
Schulz & Heckhausen 1996 "Successful aging"	Cardiovascular and pulmonary functioning	Absence of disability	Cognitive and intellectual performance	-	-	-	Achievements in physical and artistic domains

Table 1 continued...

	Biomedical aspects			Psychosocial factors		Other constructs	
	Health constructs	**Physical constructs**	**Cognitive constructs**	**Psychological, adaptive and well-being constructs**	**Engagement and social participation constructs**	**Longevity**	**Other**
Yoon 1996 "Successful aging"	-	Physical health	Optimal cognitive functioning	Personal control, coping strategies, resilience, meaning of life	Family, social support networks	-	Personal income and financial stability
Reed et al. 1998 "Healthy aging"	Free of major chronic illnesses	Maintaining physical ability	Maintaining mental ability	-	-	-	-
WHO 2002 "Active aging"	Optimizing opportunities for health	-	-	Well-being, quality of life	Participation	-	Security
Young, Frick and Phelan 2009 "Successful aging"	Compensation mechanisms for physiological limitations	Adaptive psychological and social compensation mechanisms for disability	Cognitive function	Emotional vitality, well-being, high self-assessed quality of life, and a sense of personal fulfilment	Engagement with life, spirituality	-	Psychological and social compensation mechanisms
WHO 2015 "Healthy aging"	The process of developing and maintaining the functional ability.			Well-being	"Build and maintain relationships; contribute to society"	-	"Enable people to meet their basic needs, learn, grow, and make decisions, be mobile."
Rantanen et al. 2018 "Active aging"	Physiological resilience, recovery from adverse events	Physical health, mobility, physical and sensory functioning	Cognitive capacity	Psychological resilience, well-being, quality of life	Social engagement and environmental support	-	Health behavior and health literacy, physical activity

The meta-analysis exploring the correlates of successful aging describes four domains: avoiding disease and disability; having good cognitive, psychological, and physical function; actively engagement in life; and being psychologically well-adapted in later life (Kim & Park 2016). Similarly, Fernandez-Ballesteros and colleagues defined successful aging in the model of "Aging well" by the domains of health and activities of daily living (ADL), physical and cognitive functioning, social participation and engagement, and a positive affect and control (Fernández-Ballesteros et al. 2008, Fernández-Ballesteros 2013). Kok and colleagues (2015) found that there is a variation between indicators of domains of successful aging, and the combinations of successful indicators varied between individuals.

In Finland, gerontologists have been interested in this framework during recent decades. Discussion has occurred about successful aging and the changing images of old age (Ruoppila & Häivälä 2000, Jylhä & Saarenheimo 2000). A study of older people in Helsinki found that diseases, such as CVDs and diabetes, may lead to a decline of cognition among persons aged over 75 during the ten-year follow-up (Tilvis et al. 2004). Attitudes to life also seemed to have played a significant role in the need for treatment and in mortality (Pitkälä et al. 2004). Tilvis (2006) pointed out that successful aging has been studied widely based on paternalistic and biomedical assumptions. Later, older peoples' own perceptions and interpretations have become more valued topics of reviews, and it has been suggested that successful aging could be more of a personal experience and mindset than a measured multidimensional ability to function (Tilvis 2006). This debate has sought to change the traditional understanding of aging as a negative stage in life and to give a more positive context to aging that highlight the resources of older people (Koskinen 2007). Nosraty (2018) pointed out that successful aging is possible for the oldest old, despite the disability, and more attention should be paid to the individual aging process. In the AGNES study, Rantanen and colleagues (2018) have developed the Active Aging Scale (UJACAS) that evaluates the active aging of individuals, including goals, functional capacity, perceived opportunities, and activities. Recent studies investigated that during the COVID-19 pandemic and social distance restrictions, good physical function, perceived stress management ability, and not feeling lonely were important factors for maintaining a good quality of life (Koivunen et al. 2021a). Lived life during the life course affects health and functionality in old age, and people born at different times have had different opportunities to build resources that are important for resilience and successful aging (Koivunen 2021). Furthermore, during recent years, a key feature of the successful aging debate has been the diversity of the old age.

2.2 Biomedical aspects of successful aging

2.2.1 Longevity

During the past 100 years, life expectancy has doubled in all world regions, and an increase is continuing worldwide (World life expectancy 2021). In Europe, the number of people reaching a very old age, 85 years or more, is going to double in the next 30 years (Eurostat 2019). However, there remains a gap between genders with women living longer than men. On average, women aged 60 could expect to live 24.3 more years, and men of the same age could expect to live an additional 20.5 years in Europe (WHO 2020). In 2020, the average life expectancy at birth for women was 81.3 years, and for men, it was 75.1 years in the whole of Europe, and in Finland, 84.0 and 79.2 years, respectively (WHO 2020). Men's life expectancy is lower in Finland than in many other European countries (Eurostat 2019). The gender gap is relatively narrow in Iceland (3.1 years) and Ireland (3.3 years), but much larger in Russia (9.8 years), Latvia (9.3 years), and in Estonia (7.9 years) (WHO 2020).

Women live longer than men worldwide, especially due to psychosocial and behavioral factors. Men seek health care less than women, and death rates from suicides and accidents are higher in men than in women (Thorslund 2013). It is estimated that a half of the differences would be due to more common smoking and alcohol use among men (Thorslund 2013). Women's lifestyles have approached men's lifestyles that narrow this gap in life expectancy. However, in Finland, the load of cardiovascular risk factors is still higher for men (Koponen et al. 2018). Women have more sick leave and depression during their working age, and during old age, they have more frailty and disability than men, but they live longer (Oksuzyan et al. 2010, Christensen et al. 2009).

Various factors have contributed to the population's longer life span. In the early twentieth century, infant mortality decreased due to an accrued hygiene level and maternal care, whereas improved health and medical care had a high impact on increased life expectancy at the end of the century (Christensen et al. 2009). In addition, the development of antibiotics was influential (Hutchings et al. 2019). Since the 1980s, medical treatment of cancers, high cholesterol, and hypertension have developed (Klenk et al. 2016). The World Wars caused a gap in the life expectancy curve (Plumper & Neumayer 2006). During the years 1918–1920, the Spanish flu affected the mortality rate (Nickol & Kindrachuk 2019) as well as the human immunodeficiency virus (HIV) during the 1980–90s (Lai et al. 1997). The recent COVID-19 pandemic may affect life expectancy rates over the longer term (Spiers et al. 2021, Woolf et al. 2021).

Healthy life expectancy is defined as expected years of life lived in a healthy state with the measure of health usually referred to as active life (Crimmins & Hagedorn 2010). Also, the definition of disability-free life expectancy is used to describe the expected number of years without major disabilities (Imai & Soneji 2007). The theory of dynamic equilibrium, provided by Manton (1982), presents that the decline in mortality is related to an increase in the prevalence of milder chronic diseases.

Longevity has led to a growing number of older people with multimorbidities, frailty, and disability in the oldest populations (Newman & Murabito 2013). James Fries has launched the paradigm of compression of morbidity that proposes that by improving health behavior, a person may extend life but also postpone the onset of disability (Fries 1980). Until the early 2000s, the cohort trends were consistent with Fries` hypothesis (Freedman et al. 2002, Christensen et al. 2009, Karppinen 2019), but since the beginning of the 2000s, the improving functioning among older people has changed for the worse (Karppinen 2019), especially in the younger cohorts (Christensen et al. 2009, Karppinen 2019). However, a recent cohort study showed that older people born between 1938 and 1943 had better physical function than those born between 1910 and 1914 at same age (Koivunen et al. 2021b). Similar findings were found in the Helsinki Aging Study (Öhman et al. 2021).

Many studies have defined successful aging highlighting the importance of having lived a very long and healthy life (Martin et al. 2014). Andersen-Ranberg and colleagues suggested that "healthy centenarians do not exist, but autonomous centenarians do," which can be explained so that long life may have a price (Martin et al. 2014, Andersen-Ranberg et al. 2001). In addition, according to Rowe and Kahn's criteria of successful aging (Rowe & Kahn 1987, Rowe & Kahn 1997), very few of the centenarians would be classified as "successful" agers (Martin et al. 2014).

2.2.2 Health and living a life without diseases

Reaching a healthy longevity depends especially on lifestyle and environmental factors, which contribute to the homeostatic systems, such as the immune, endocrine, and nervous systems and the interactions between them (De la Fuente 2019). The maintenance of health requires a good state of these systems during the life span, and especially during the years of aging (De la Fuente 2019). Moreover, the function of the immune system is a marker of the rate of

individual aging, and its capacity is involved in reaching a healthy longevity (De la Fuente 2019).
The cohort studies have indicated that morbidity and functional limitations are associated with a lower quality of life in old age (Davis et al. 2015, Strandberg et al. 2014). The prevalence rates of diseases have increased according to the cohort studies of younger populations (Christensen et al. 2009, Karppinen 2019) that may reflect more effective diagnosing of diseases, e.g., cancers, osteoporosis, and dementia, now which have medications available (Karppinen 2019). In older cohorts with a population over age of 85, trends of morbidities are more complex and difficult to explore (Karppinen 2019, Jylhä et al. 2013).

Avoiding disease and disability are common criteria of successful aging (Kim & Park 2016). However, according to the recent studies the absence of disease and disability may not be the most important element in the concept of successful aging, and it is also possible to age successfully with chronic diseases (Nosraty et al. 2015, Pruchno & Wilson-Genderson 2015, Baltes & Baltes 1990). Treatment of chronic and severe diseases has improved and does not lead to complications that often (Karppinen 2019). The model by Young and colleagues (Young et al. 2009) and the model of selective optimisation with compensation, the SOC model (Baltes 1997, Baltes & Baltes 1990), consider adaptive psychological and social mechanisms that can compensate for limitations in physiological health. Manierre (2018) has proposed that the Young and colleagues' model provides a holistic perspective of successful aging among people with chronic diseases.

2.2.3 Physical function, sarcopenia, and frailty

Physical function is the most developed and explored component of successful aging (Anton et al. 2015). Physical function is defined as a person`s ability to perform activities that require physical actions varying from daily activities to more complex tasks (van Lummel et al. 2015). Mobility and activities of daily living are subdomains of physical function (van Lummel et al. 2015). Webber and colleagues (2010) have defined mobility as an ability to move oneself independently or with assistive devices. Mobility is usually measured with physical performance tests, e.g., the Short Physical Performance Battery test (SPPB) and the Timed Up and Go test (TUG) (Billot et al. 2020). The ability to carry out daily activities can be measured with questionnaires of activities of daily living (ADL) and instrumental activities of daily living (IADL) (Katz 1983, Lawton 1991, Graf 2008).

Muscle mass and muscle strength decrease due the aging processes, but also chronic diseases and lifestyle, especially poor diet quality, insufficient protein intake, and physical inactivity contribute to the decline (Billot et al. 2020, Strandberg 2019). The definition of *sarcopenia* emphasizes decreased muscle function, and it is also characterized by low muscle mass and low muscle quantity and quality (Cruz-Jentoft et al. 2019). Probable sarcopenia is identified if person has a low muscle strength, and if, in addition to that, a low muscle quantity or quality are present, diagnosis is confirmed (Cruz Jentoft et al. 2019). If the previous criteria are all met, and there is also a decline in physical performance, sarcopenia is severe (Cruz-Jentoft et al. 2019). Sarcopenia can be identified with the SARC-F questionnaire, muscle strength tests (e.g., chair stand and grip strength tests), muscle mass assessment (e.g., Dual-energy X-ray absorptiometry and DXA), and physical performance tests (e.g., gait speed, SPPB, and TUG) (Cruz-Jentoft et al. 2019). Sarcopenia is a muscle disorder that is associated with an increased risk of severe outcomes, e.g., falls, fractures, physical disability, a decline in quality of life, and mortality (Landi et al. 2012, Marzetti et al. 2017, Cruz Jentoft et al. 2019). Physical activity, especially the physical multicomponent exercise, has positive effects on the sarcopenic process and physical function (Pahor et al. 2014, Marzetti et al. 2017, Steffl et al. 2017).

Frailty is a geriatric syndrome associated with aging, and it is characterized by diminished resistance to stressors (Fried et al. 2001, Strandberg & Pitkälä 2007, Clegg et al. 2013). There are two widely used distinctive ways to definite frailty: the Fried criteria presents the phenotype of frailty (Fried et al. 2001), and the Frailty Index (FI) describes the criteria for deficit accumulation (Mitnitski et al. 2001). The symptoms of physical frailty include a feeling of weakness, a slow walking speed, involuntary weight loss, fatigue, and inactivity (Fried et al. 2001, Perttilä 2018). The Frailty index (FI) by Rockwood (Rockwood et al. 2004, Rockwood et al. 2005) is constructed by problems and declines in various physiological systems, e.g., the circulatory system, nervous system, and cognitive functioning. The Frailty index is a quantitative measure of frailty considering various items from cognitive, physical, social, and psychological dimensions (Perttilä 2018, Mitnitski et al. 2001). Frailty is associated with negative health-related outcomes (Cesari et al. 2016), such as disability, a decline in quality of life, and hospitalizations (Xue Qian-Li 2011). Despite aging, a sedentary lifestyle, malnutrition, and diseases are major factors causing the frailty syndrome (Cesari et al. 2016, Cesari et al. 2017, Dent et al. 2019). In addition, a risk of developing frailty is higher among older people with comorbidities and a low socioeconomic status (Hoogendijk et al. 2019). Physical activity (Pahor et al. 2014) and nutrition (Cruz-Jentoft et al. 2017) are

key elements in preventing frailty. A multicomponent exercise and nutrition intervention was associated with a decrease in the incidence of disability in mobility in older adults with sarcopenia and physical frailty, and who had lower scores in physical performance testing (SPPB 3-7) at baseline (Bernabei et al. 2022). Furthermore, aging successfully delays the onset of frailty (Mor 2005, Gordon et al. 2020).

There has been a debate that successful aging and frailty could be opposite sides of the same coin (Woo et al. 2016). Successful aging includes similar components to define its concept as frailty (Cesari et al. 2016). In addition, both concepts have a life-course basis, biomedical explanations, functional aspects, and multidimensional characteristics (Rolfson 2018). Frailty may represent a transitional state between successful aging and disability (Cesari et al. 2016). In successful aging, biomedical and psychosocial factors are optimized, but the frailty syndrome has a decline of these factors, which can lead to disability (Figure 2).

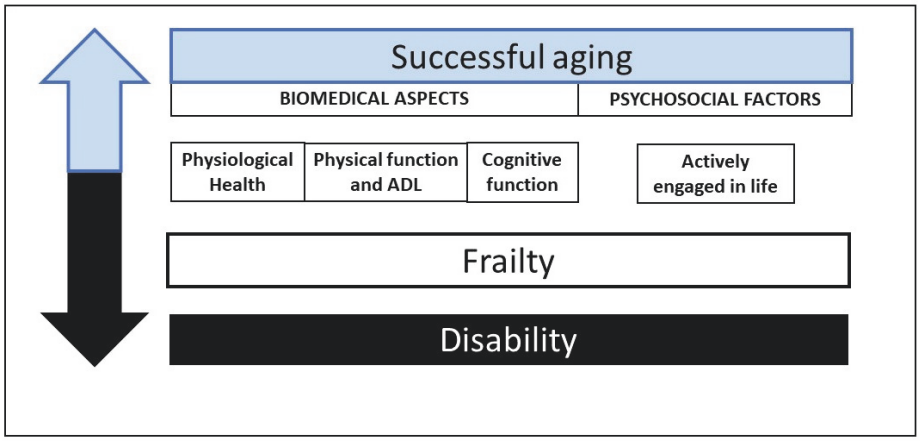

Figure 2. The relation between successful aging, frailty, and disability.

2.2.4 Cognitive function

Cognitive functioning comprises explicit memory (e.g., episodic memory, knowledge) and procedural memory functions (e.g., performing tasks) and other higher functions such as attention, problem solving, reasoning, and executive functioning (Harvey 2019). The study of Salthouse (2006) showed changes in various dimensions of cognitive performance in aging. The deepest decline was in processing speed, and episodic memory and reasoning also declined, but there were no changes in crystallized intelligence (Salthouse

2006). Longitudinal studies have revealed that middle age is a critical period for the onset of the pathology of cognitive disorders (Zanto & Gazzaley 2019, Irwin et al. 2018). However, indicators of this pathology process are still poorly understood (Irwin et al. 2018).

Hartley et al. (2018) have suggested that maintaining cognitive abilities and preventing memory disorders are key aims in old age, and therefore, a good cognitive functioning should be a central component of successful aging. Cognitive development in old age varies individually, and higher cognitive functioning in old age might be explained by a cognitive reserve and a compensation for age-related changes (Hartley et al. 2018). Cognitive reserves are dependent on lifetime brain challenges and education, and relatively higher function may reflect relatively more successful aging (Hartley et al. 2018). Jessberg and Gage (2008) have stated that the brain retains a high level of plasticity even at an old age. Kinugawa (2019) suggests that successful aging could be achieved by boosting and recruiting this plasticity. The latest cohort studies suggest that in later born cohorts, cognitive decline is postponed to older age (Munukka et al. 2021, Christensen et al. 2009).

Depp and Jeste (2006) found that standards for successful cognitive aging have large differences in studies. Hartley and colleagues (2018) have proposed that the clinical cognitive measurements often indicate only a particular dimension of cognitive functioning, and, therefore, may not be the most optimal for indicating successful cognitive functioning (Hartley et al. 2018).

2.3 Psychosocial factors of successful aging

2.3.1 Actively engaged in life

Personal and societal circumstances contribute to individual development processes, including aging processes (Baltes & Baltes 1990). Social participation is a key factor in successful aging (Douglas et al. 2017). Social functioning includes indicators of social activity, emotional and instrumental support given to others, and a feeling of loneliness (Jopp et al. 2014). Social function has been identified as an important factor in aging, especially by older people themselves (Jopp et al. 2014). This reflects a wish for being involved with other people and to retain a meaningful role in society (Jopp et al. 2014). Meaningful social roles during old age improve health and psychological well-being (Oh et al. 2021), and friendships during old age are associated with higher levels of life satisfaction and happiness (Fiori et al. 2007). Social participation includes

factors of social connections, informal social participation, and volunteering, and all of these are positively associated with health in older adults (Douglas et al. 2017). Furthermore, researchers suggest that the effect on health is mediated by social cohesion and social support (Douglas et al. 2017). The will to be active, the ability and power to choose and manage their own intentions is called "active agency," and it is constructed in a relation with social and societal structures and the environment (Jyrkämä 2008).

The experience of loneliness varies depending on age, life events, and cultural backgrounds (Victor 2015). In a Finnish study, more than one-third of older people suffered from loneliness (Routasalo et al. 2006). The feeling of loneliness was not related to the number of contacts with relatives and friends, but rather to expectations and satisfaction with these meetings (Routasalo et al. 2006). A recent study showed that group interventions increased self-direction and relieved loneliness (Jansson 2020). These findings are consistent with other studies indicating that emotional loneliness and social isolation are different concepts (Routasalo et al. 2006, Ong et al. 2016).

2.3.2 Psychologically well adapted in later life

Aging is a process of development that entails "an inherent dynamic between gains and losses," as Paul Baltes (1987) has pointed out. The main issue in successful development is how do people adapt to the changes during their life course (Nikitin & Freund 2019).

Subjective well-being is a key element in the psychology of aging, and it reflects adaptation to the cognitive, physical, and social strains that people may face in old age (Rott & Jopp 2006).

Psychological well-being can be viewed from three aspects: life satisfaction, hedonic well-being such as feelings of happiness, and eudemonic well-being that reflects sense of purpose and meaning in life (Steptoe et al. 2014). The definition of well-being by Seligman (2011) considers hedonic and eudemonic aspects, and it is defined as a subjective sense of functioning across the five domains of Positive emotion, Engagement, Relationships, Meaning, and Accomplishment (PERMA-model). According to this approach, well-being considers more than the absence of psychological distress and highlights adaptive behaviors and thoughts (Bartholomaeus et al. 2019). A positive life orientation includes the following factors: satisfaction with life, seldom feeling lonely or depressed,

feeling of being needed, having zest for life, and having plans for the future (Pitkälä et al. 2004).

The studies with single-item measures of well-being have presented that happiness across the life span follows a U-curve with well-being being highest during the 20s, decreasing in midlife, and rising again in old age (Galambos et al. 2021). Recently, this approach has been under debate, and studies on subjective indicators of well-being have had mixed results and challenged the U-curve (Galambos et al. 2021, Laaksonen 2018). Happiness varies within age groups, and the consequences of unhappiness in old age would need further studies (Galambos et al. 2021). However, psychological well-being and feelings of happiness increase physical health and longevity (Ryff 2014).

Kim and Park (2016) have suggested that it is possible for older adults to age successfully even with a decline of physical and cognitive function, if they are psychologically well adapted and socially active. The model of selective optimization with compensation (SOC) by Baltes and Baltes (1990) explains adaptation to deficits of aging with successful psychological and behavioral processes. According to Baltes and Lang (1997), in the SOC model, successful aging is a process of balancing between losses and gains. The SOC model reflects people`s capacity to make choices that suit best to individual resources but consists of both objective and subjective perspective (Baltes & Baltes 1990).

Resilience is defined by the American Psychological Association (APA) as "the process of adapting well in the face of adversity, trauma, tragedy, threats, or significant sources of stress" (MacLeod et al. 2016). This definition describes resilience as a process which differs from a stable personality trait called resiliency (MacLeod et al. 2016). Resiliency emphasizes capability of people to demonstrate resilience, but a common perspective suggests that resilience is an adaptive process that can be developed (MacLeod et al. 2016). Resilience is a multidimensional concept including mental, social, and physical components (MacLeod et al. 2016). High resilience in old age is associated with increased quality of life, self-perceptions of aging successfully, and reduced mortality risk (Jeste et al. 2013).

Coping strategies can be defined as individual`s behavioral and cognitive efforts to face with a demanding situation which exceeds resources (Lazarus & Folkman 1984). Coping strategies play an important role in aging process, and resilient coping seems to be a predictor of well-being among older adults (Tomás et al. 2012). Resilience and social participation may have a mediating role within the relation of coping strategies and quality of life (Palmes et al. 2021).

Studies emphasize resilience as one of the major contributors to successful aging (Palmes et al. 2021, Hildon et al. 2009), while social participation plays a role in improving the mental health and quality of life in old age (Takagi et al. 2013).

2.4 Associates and predictors of successful aging

Studies on successful aging vary depending on methods and follow-up time. It is challenging to distinguish the associations from the predictors when researchers present results related to successful aging, especially in studies with a short follow-up time. In addition, the dimensions of successful aging and the associates and the predictors of the concept include similar factors (e.g., physical function and psychosocial factors) that may cause confusion. Longitudinal studies with over 10 years of follow-up on predictors of successful aging are presented in Table 2.

Table 2. Longitudinal studies with over 10 years of follow-up on predictors of successful aging.

Study Country	Setting	Participants	Successful aging definition	SA %	Follow-up rate %	Physical inactivity	Physical function	Diseases	Obesity, BMI	High cholesterol	Smoking	Alcohol	Loneliness	Cognitive activity Education	Other associates, notes
Haveman-Nies et al. 2003 The SENECA study Europe	10 years follow-up	n=2586, aged 70–75 years at baseline	Healthy aging			↓					↓				↑ high quality diet
Tilvis et al. 2004 The Helsinki Aging Study Finland	10 years follow-up	n=629, mean age 79 at baseline	Cognitive function		39			↓					↓		↓ APOE4 (Apolipoprotein E)
Willcox et al. 2006 the Honolulu Heart Program/ Honolulu Asia Aging Study	40 years follow-up	n=5820, mean age 54 at baseline	Overall survival (to 85 years) and exceptional survival (85 years, no diseases)				↑	↓	↓		↓	↓			↑ physiological reserve ↑ physical fitness ↑ grip strength ↑ lower levels of glucose and triglycerides
Britton et al. 2008 the British civil service-based cohort study United Kingdom	17 years follow-up	n= 5963 (1823 women), mean age 44 at baseline	Old age without disease and good functioning	men 12.8 women 14.6		↓					↓			↑ (men)	↑ midlife socioeconomic position ↑ height ↑ diet ↑ moderate alcohol consumption (women) ↑ work support (men)
Swindell et al. 2010 the study of Osteoporotic Fractures (SOF) U.S.	19 years follow-up	n=4097, (women 65–69 years of age)	Cognitive function, no depression, ADL, grip strength	60			↑	↓			↓				↑ contrast sensitivity scores in visual exam ↑ self-rated health assessments

Table 2. continued...

Study Country	Setting	Participants	Successful aging definition	SA %	Follow-up rate %	Physical inactivity	Physical function	Diseases	Obesity, BMI	High cholesterol	Smoking	Alcohol	Loneliness	Cognitive activity Education	Other associates, notes
Sabia et al. 2012, the Whitehall II study United Kingdom	16 years follow-up	n=5100, mean age 51.3 at baseline, 29.5% women	Mental, cognitive, physical, physiological health	18.7		↓					↓	↓		↑	↑ being married, ↑ moderate alcohol consumption, ↑ consuming fruits and vegetables daily
Hodge et al. 2013 & 2014 Melbourne Collaborative Cohort Study Australia	12 years follow-up	n=5512, aged 70 and over	Aged 70 or over, absence of major diseases, physical function, low risk of psychological stress			↓	↑	↓	↓		↓				↓ diabetes ↑ dietary pattern including plenty of fruit ↓ dietary pattern with meat and fried foods
Gopinath et al. 2018 The Blue Mountains Eye study (BMES) Australia	10 years follow-up	n=3654, >49 years				↓					↓				↑ married ↓ live alone ↑ high levels of physical activity (>5000 MET minutes/week)
Bosnes et al. 2019 the Nord-Trondelag Health Study (HUNT) Norway	22 years follow-up	n=4497, mean age 52.7 at baseline	Rowe & Khan			↓			↓		↓			↑	↑ female gender ↑ social support

2.4.1 Socioeconomic factors

Socioeconomic factors during the life span contribute to successful aging (Khalatbari-Soltani et al. 2020). The study of Ferdows et al. (2018) found that favorable conditions in childhood significantly improved healthy aging. A higher socioeconomic status in childhood is significantly associated with higher cognitive function in late midlife (Kaplan et al. 2001, Beck et al. 2018). The study of Beck et al. (2018) explained the relationship through an indirect association with general cognitive ability in early adulthood but also with engagement in cognitive leisure activities and socioeconomic status in midlife. Zhang et al. (2020) showed that educational achievement also plays a role. Furthermore, education and occupation have been found to be predictors of successful aging (Doménech-Abella et al. 2018, Cosco et al. 2017, Willcox et al. 2006). Higher education prevents age-related declines in psychosocial functioning, and it is associated with a sense of control and hope (Mitchell et al. 2016). In addition, higher education provides cognitive and relational resources throughout life (Mitchell et al. 2016). Also, a high socioeconomic status provides resources for maintaining and promoting health. Among other things, highly educated people have better health literacy and financial opportunities to take care of health (Doménech-Abella et al. 2018, Mitchell et al. 2016).

Marital status predicts successful aging and being single is more harmful for men (Pruchno & Wilson-Genderson 2015, Domenech-Abella et al. 2018). The living environment also matters and living in an urban environment seems to be more favorable for successful aging (Domenech-Abella et al. 2018). In most populations, women live longer than men, and men have a higher mortality rate at all ages, especially due to behavioral and psychosocial factors (Brooks-Wilson 2013, Thorslund 2013). Furthermore, many studies have revealed that successful aging is more likely for women (Bosnes et al. 2019, Kim et al. 2019, Rinaldi et al. 2018), but there are also studies that report higher odds for men (Pruchno & Wilson-Genderson 2015), and also review studies that show no association with gender (Depp & Jeste 2006). Behavioral and socioeconomic factors may explain gender differences at least partly (Thorslund 2013). The study of Park et al. (2010) revealed that a higher level of education was associated with higher physical functioning among women. In addition, culture and ethnic background are associated with successful aging being more likely for white ethnicity (Pruchno & Wilson-Genderson 2015, Troutman-Jordan et al. 2013, Strawbridge et al. 1996). The SHARE study (Hank 2011) compared successful aging, as defined as Rowe and Kah's conceptualization and according to the study of McLaughlin et al. 2010, in 14 European countries and Israel and revealed that the prevalence of successful agers varies across the nations with

a mean of 8.5% being the highest in Denmark (21.1%) and the lowest in Poland (1.6%).

There are a few areas in world called "Blue Zones," where people live healthier, happier, and exceptionally long lives. These areas currently include five regions across the world: Ikaria in Greece, the Barbagia region of Sardinia, the Nicoya Peninsula in Costa Rica, Okinawa in Japan, and Loma Linda in California (Buettner 2021). Research of the Blue Zone areas have provided information on aging mechanisms in humans (Buettner & Skemp 2016). All these areas have in common are that the most people living in these regions have lifestyles that includes physical activity, a healthier diet, less stress, social connections, belonging, and a sense of purpose (Buettner 2021).

Longevity Blue Zones (LBZs) have extremely high proportion of the oldest old (Poulain et al. 2021). The study of Poulain et al. (2021) showed that in the LBZ regions of Sardinia and Ikaria, self-rated health, and self-perceived optimism scores were significantly higher than in compared other regions in Italy and Greece. In this study, the impact of genetic factors was less important than behavioral and health factors (Poulain et al. 2021).

Robine et al. (2010) has studied the emergence of centenarians in Japan where the life expectancy at birth has been the highest in the world. The number of centenarians in Japan increased during years 1996–2006 almost three times faster compared with Sweden and Denmark, and two times faster compared with France and Switzerland (Robine et al. 2010). These differences are explained by the increased rate of the oldest old in the countries studied, especially the differences in mortality among older age groups (Robine et al. 2010).

2.4.2 Genetics and heredity

Epigenetics provide biological insights of longevity and healthy aging and give an understanding of desirable traits of aging (Brooks-Wilson 2013). Longevity runs in families, though the role that genetics plays in life span longevity is about 15–30% (Ruby et al. 2018). Studies of longevity show that heritability plays the greatest role at the oldest ages of ages of 90 years and over (Caruso et al. 2019, Brooks-Wilson 2013). For centenaries, it is even higher, up to 48% for men and 33% for women (Caruso et al. 2019). The study of Reed & Dick (2003) showed that healthy physical aging among older males exhibited significant

heritability. Longevity may correlate either with the absence of harmful alleles or the presence of protective alleles (Caruso et al. 2019).
Biomarkers of biological aging, such as leukocyte telomere length (LTL) and DNA methylation age (DNAm age), associate significantly with chronological age across the life span (Marioni et al. 2016, Horvath S 2013, Muezzinler et al. 2013). Telomeres consist of DNA repeats, and they form the end of eukaryotic chromosomes (Blackburn 2001). The function of telomeres is to protect the genomic DNA by telomerase that replicates the DNA sequences and lengthens telomeres (Blackburn 2001). Telomere length is a marker of biological age, and it is associated with morbidity and higher mortality risk (Benetos 2018). Studies have indicated that male gender is associated with shorter telomere length than women (Gardner et al. 2014) as well as physical inactivity and smoking (Aviv et al. 2009). A recent study showed that frail persons had shorter telomeres than non-frail persons at the mean age of 71, which may indicate leukocyte telomere length being a biomarker of frailty (Haapanen 2019). Further, the accelerated DNA age has been found to be associated with lower grip strength, which predicts a decline in physical functioning and mortality risk (Sillanpää et al. 2018). An analysis by Föhr et al. (2021) showed that faster epigenetic aging was associated with a higher risk of mortality irrespective of shared genetic factors in a longitudinal twin design. In addition, the results of this study indicated that smoking had an important role in the association between epigenetic aging and mortality.

2.4.3 Lifestyle

Many lifestyle factors are associated with successful aging (Lafortune et al. 2016, Södergren 2013, Westermeyer 2013, Sabia et al. 2012). The review of Södergren (2013) included studies (n=20) of various designs, and indicated that men with healthy life habits, such as physical activity, a healthy diet, non-smoking, and low alcohol consumption do live longer, and they also have better health and less disabilities during old age.

Previous studies are consistent with the adverse effects of smoking and its harmful consequences on healthy aging (Lafortune et al. 2016, Södergren 2013, Willcox et al. 2006). In the longitudinal study of Willcox et al. (2006), non-smoking was associated with overall survival to 85 years of age. The study of Bosnes et al. (2019) showed that non-smoking was a significant predictor of successful aging (defined according to Rowe & Khan 1987, 1997). In the Whitehall II study, the participants who had never smoked had higher odds for

successful aging, defined as good mental, cognitive, physical, and physiological health (Sabia et al. 2012).

Heavy consumption of alcohol is significantly associated with poor health and higher mortality risk (Willcox et al. 2006). Sabia et al. (2012) found that moderate consumption was associated with higher odds of successful aging than no or heavy alcohol consumption. These findings are similar with the studies of Pruchno et al. (2010) and Sun et al. (2011). However, a systematic review of Lafortune et al. (2016) showed that results on the relation between alcohol consumption and successful aging are mixed.

Nutrition plays a role in achieving successful aging. According to the previous studies, a high- quality diet is associated with healthy aging (Hodge et al. 2014, Haveman-Nies et al. 2003). In an Australian study, a diet including plenty of fruits was positively associated, and a diet with meat and fried food was inversely associated with successful aging, defined as an absence of major diseases, disabilities, and psychological stress (Hodge et al. 2014).

The Mediterranean diet consists mainly of fresh vegetables and fruits, nuts, beans, whole grains, olive oil, fish, and small amounts of dairy products, which all contribute to health benefits (Foscolou et al. 2020). The Mediterranean diet has been associated with health outcomes in various studies (Ventriglio et al. 2020, Capurso et al. 2019). It plays a significant role in improving metabolic and cardiovascular health and reducing an incidence of major cardiovascular events (Guasch-Ferré et al. 2017, Martínez-González et al. 2015, Martínez-Lapiscina et al. 2013). The results of the PREDIMED study revealed that the Mediterranean diet, supplemented either with extra-virgin olive oil or nuts, improved cognition compared with a low-fat control diet (Martínez-Lapiscina et al. 2013). In addition, polyphenol consumption in the Mediterranean diet is associated with mental health outcomes, such as lower depression risk and reduction of depressive symptoms (Bayes et al. 2020). A Mediterranean diet is associated with a lower mortality risk (Trichopoulou et al. 2005) and successful aging (Britton et al. 2008). A recent study found that adherence to a Mediterranean diet was associated with high levels of successful aging, as defined with a validated index for successful aging by Tyrovolas et al. in 2014 among people with the same genetic background despite living in different environments (Papadimitriou et al. 2022). A review of cohort and case-control studies by Capurso et al. (2020) showed that following the Mediterranean diet slows down the aging process and helps to prevent the onset of frailty. Findings of the Finnish cohort study showed that a higher Mediterranean diet score was associated with decreased onset of pre-frailty and frailty in

older women (Alaghehband et al. 2020). In addition, the same study revealed a tendency between a higher Baltic Sea diet score and the decreased onset of frailty (Alaghehband et al. 2020).
Coffee drinking was associated with a decreased risk of dementia in the Finnish CAIDE study (Eskelinen et al. 2009). A recent study by Zhang et al. (2020) showed similar results and showed that drinking tea or coffee or a combination of both was associated with a lower risk of developing stroke or dementia. Previous studies have also had mixed results about these associations (Larsson & Orsini 2018, Panza et al. 2015). In the study of a HBS cohort (Jyväkorpi et al. 2021), higher coffee consumption was independently associated with better physical performance and measured as a faster gait speed in older men. Naumovski et al. (2019) found that green tea consumption was associated with higher odds of successful aging than black tea consumption. In this study, successful aging was defined as higher values in successful aging index that included scores of physical activity, BMI, depression, cardiovascular disease risk factors, and the adherence to a Mediterranean diet, for example. The authors suggested that the results of the study might be explained by higher levels of catechins in green tea compared with black tea (Naumovski et al. 2019).

Physical activity contributes to successful aging. According to a systematic review and meta-analysis of 15 cohort studies (Lin et al. 2020), physical activity is associated with successful aging, following the biomedical model in most studies, among middle-aged and older adults. These results were consistent with the systematic review and meta-analysis of 23 longitudinal studies that showed a positive association between physical activity and healthy aging despite of definition or measurements (Dascalopoulou et al. 2017). The study of Almeida et al. (2014) revealed that a sustained physical activity promotes survival and healthy aging with a Patient Health Questionnaire score less than 10 in older men. They also found that vigorous physical activity seems to increase the odds for healthy aging and should therefore be encouraged when feasible and safe. The study of Gopinath et al. (2018) had similar results and showed that physical activity above the minimum level was associated with a greater likelihood of successful aging 10 years later. In this study, successful aging was defined according to Sabia et al. (2012) that classified successful agers as survivors without major diseases.

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) found that earlier life leisure-time physical activity reduced the risk of pre-frailty and frailty in later life (Lorenzo-López et al. 2017).The FINGER trial showed also that lifestyle intervention including dietary counselling, physical exercise, cognitive training, and CVD risk factor

monitoring benefits cognition in older people with an increased risk of dementia (Kivipelto et al. 2018, Ngandu et al. 2015).

Long working hours and a stressful life have an influence on health outcomes. A systematic review of epidemiological studies (n=19) concluded that long working hours were associated with coronary heart disease, a sleep condition, anxiety, and depression (Bannai & Tamakoshi 2014). A Danish study found that permanent night workers and workers with moderately longer regular working hours had a higher risk of dementia (Nabe-Nielsen et al. 2019). A cross-sectional study of U.S. veterans showed that psychological distress and physical health difficulties were most negatively related to scores of successful aging, including measurements of self-rated successful aging; quality of life; and physical, cognitive, social, and psychological function (Pietrzak et al. 2013).

The findings of the Nurses` Health Study showed that both long and short sleep durations at midlife were associated with decreased odds for healthy aging in later life compared to 7 hours of sleep (Shi et al. 2021). Although, the results of the MEDIS study revealed that 8–9 total hours of sleep per day, including midday napping, was proposed as optimal in achieving the best successful aging score including clinical, lifestyle, and social indicators (Foscolou et al. 2019).

2.4.4 Other CVD risk factors

Lifestyle factors were presented in the previous paragraph, and this paragraph presents intermediate risk factors that indicate that the disease process is already underway.

Life habits that influence cardiovascular health have shown to be associated with poorer cardiovascular health and further survival (Clarke et al. 2009). Being overweight and obese promote cardiovascular morbidity and mortality (Arnlov et al. 2010), especially due to the associations with various risk factors, including dyslipidemia, hyperglycemia, hypertension, and metabolic syndrome. CVD risk factors are associated with an increased risk of developing disabilities, frailty, and dementia (Krivanek et al. 2021, Lafortune et al. 2016). Longitudinal studies have shown that midlife hypertension, high cholesterol, and smoking impair cognition in old age, and over the decades, the better treatment of these risk factors may have reduced the decline in cognition in the elderly population (Baumgart et al. 2015).

In addition, a higher BMI was associated with significantly shorter healthy and chronic disease-free life expectancy both in men and women in four European cohort studies (Stenholm et al. 2017). The Whitehall II study showed that midlife BMI starting already at ≥23.5 kg/m^2 and waist circumference over 82/68 cm in men/women, respectively, were associated with lower odds of successful aging as defined as absence of major chronic diseases and mental problems, good physiological, physical, and cognitive functioning in a 16-year follow-up (Singh-Manoux et al. 2014).

In the National Health and Aging Trends study (U.S.), men with abdominal obesity had lower odds for healthy aging than males with a normal abdominal waist status. The healthy aging score was based on the WHO (2020) and Assmann et al. (2015) definition, including indicators of physical and cognitive function, major chronic diseases, well-being, depression, anxiety, function limiting pain, health-related limitations in social life, and perceived health, and IADL (Xu et al. 2020). On the contrary, in the Chinese oldest olds (80+ years of age), a higher waist circumference and higher BMI predicted better survival in both genders, but these results might not apply to other ethnic groups (Lv et al. 2018).

Metabolic syndrome (MetS) is characterized by abdominal obesity, dyslipidemia, hypertension, and increased blood glucose (Punthakee et al. 2018). The definitions of the syndrome vary, but the definition according to the International Diabetes Federation is commonly used in studies (Ortega et al. 2016). Metabolic syndrome was negatively associated with successful aging, as defined as the dimensions of physiological, psychological, and sociological and economic aspects among community-dwelling older adults (Lin et al. 2021).

The phenotype of being metabolically healthy overweight (MHO) has become an area of interest in recent studies (Mongraw-Chaffin et al. 2018, Lavie et al. 2015, Bell et al. 2015, Pajunen et al. 2011). The prevalence of MHO varies depending on the criteria, and it is suggested that 9%–16% of obese persons could be metabolically healthy (Pajunen et al. 2011, Velho et al. 2010). MHO is related to cardiorespiratory fitness and physical activity, and according to short-term studies, prognosis of MHO could be similar with metabolically healthy normal weight (MHN) persons (Ortega et al. 2013, Frisard et al. 2007). However, MHO may turn into being metabolically unhealthy overweight (MUO) along with aging (Bell et al. 2015). The evidence of the association between MHO and CVD has been mixed (Ortega et al. 2016). Criticism of the concept has been demonstrated indicating that MHO, not only obesity, is associated with less successful aging (Pajunen et al. 2011).

The obesity epidemic is a main contributing factor of the rising prevalence of type 2 diabetes mellitus in most developed countries (Bradley & Hsueh 2016). The review and meta-analysis by Lu et al. (2009) showed prospective associations between diabetes and a decline in cognition and mobility. An Australian study revealed that diabetes was inversely associated with successful aging, as defined as an absence of major diseases, physical function, and a low risk of psychological stress in a 12-year follow-up (Hodge et al. 2013).

One of the paradoxes in aging is the reversal of direction of some risk factors in old age (Orkaby 2020). For example, body mass index (BMI) above the normal weight and higher cholesterol levels may be protective among the oldest olds (Orkaby 2020). These associations may be explained by "terminal decline," which indicates that some years before death, a person loses weight, cholesterol and blood pressure levels decline, and thus "normal values" appear to be a risk factors (Strandberg et al. 2009).

The Cardiovascular Health study examined survival up to 90 years of age and healthy aging outcomes among participants aged 67–75 years at baseline (n=3613) in the U.S. (Odden et al. 2020). Surprisingly, the results of the study showed that higher levels of high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol were associated with better odds of greater survival (Odden et al. 2020). These results are inconsistent with a general consensus of risk factors (ESC Committee for Practice Guidelines 2019), and Odden et al. (2020) suggested that during the life span, some risk factors may switch over time from a cause of disease to a consequence of disease, although the timing of this switch may depend on the health and longevity of the individual. However, in the meta-analysis of Silverman et al. (2016), lower LDL cholesterol levels achieved with treatments were associated with decreased risk of major coronary events. Benn et al. (2019) found that genetically low LDL cholesterol levels were associated with a low risk for CVD mortality. A meta-analysis by Prospective Studies Collaboration (2007) showed that total cholesterol was inversely associated with ischemic heart disease mortality during middle and old age.

In addition, the associations between total cholesterol and cognition differ in studies according to the age when cholesterol is measured (Silverman & Schmeidler 2018). The Framingham Heart Study revealed that the association of high total cholesterol on cognitive decline diminished with increasing outcome age (Silverman & Schmeidler 2018). However, there is consistent evidence among the studies that LDL cholesterol is associated with the risk of

atherosclerotic cardiovascular disease (ASCVD) and lowering LDL cholesterol reduces this risk (ESC Committee for Practice Guidelines 2019).

The meta-analysis of Hughes et al. (2020) showed that the treatment of blood pressure reduces the risk of cognition decline even in the oldest old. In the Cardiovascular Health study, higher systolic blood pressure was associated with a lower likelihood of survival to age 90, but the association was attenuated at older ages (Odden et al. 2020). The findings of the Taiwanese study showed that the absence of hypertension was the strongest predictor of physiological successful aging (Lin et al. 2021). A systematic review and meta-analysis by Bundy et al. (2017) assessed the association of systolic blood pressure levels with the risk of CVD and mortality. The findings indicated that the lowest risk was at a systolic blood pressure of 120 to 124 mmHg (Bundy et al. 2017). In addition, a recent study revealed that threating hypertension contributes to better cognitive function and prevents mild cognitive impairment MCI/ dementia (SPRINT MIND 2019).

Overall, the large cohort studies indicate that CVD risk factors are predictors for various geriatric syndromes (Atkins et al. 2019).

2.4.5 Self-rated health

Self-rated health (SRH) is a comprehensive measure of health status, and it offers a subjective perspective of perceived health and function (Jylhä 2009). SRH has showed a graded association with biomarkers as haemoglobin and HDL cholesterol (Jylhä et al. 2006). A recent study investigated that SRH may reflect a biological condition of the human organism beyond diagnoses, and it can be an indicator of physiologic states (Kananen et al. 2021).

The studies show that the cohort trends of SRH in old age have not been consistent, and during the 2000s, the results have indicated either a stable or worsening trend of SRH among the oldest age groups (Jylhä et al. 2013, Karppinen 2019). A longitudinal study of women revealed a linear decline in SRH during three decades of the follow-up in a younger cohort being those born between 1945 and 1954 and reported a lower SRH and a more rapid decline per year than the older cohort being those born between 1935 and 1944 (Chen et al. 2007).

SRH is a consistent predictor of health care utilization, morbidity, need of medication, and disability (Lee 2000), and it also predicts mortality risk (Idler

& Benyamini 1997, Lee 2000, Giltay et al. 2012) in older people. Self-rated health has been found to be predictive of mortality in controlled analyses, especially in healthy individuals (Schoenfeld al. 1994). The longitudinal study of Swindell et al. (2010) showed that the self-rated health assessments were one of the strongest predictors of healthy aging.

2.4.6 Psychosocial factors, participation, loneliness

Psychosocial factors contribute to successful aging over the long term. Previous studies show that social conditions and behavioral factors (Wright & Patterson 2006, Khaw et al. 2008, van Dam et al. 2008) as well as personality (Pocnet et al. 2020) and resilience (Palmes et al. 2021) are associated with health and well-being in later life. There is a consistent association between well-being and survival with high well-being having a protective role (Steptoe et al. 2014). In a Japanese study, subjective well-being predicted longevity among middle-aged and older people of both genders (Iwasa et al. 2006). The study of Hsu (2011) investigated the impact of life events on successful aging and found that a loss of offspring increased the risk of decline in physical and psychological health and life satisfaction. Also, being recently widowed was associated with increased incidence of depressive symptoms (Hsu 2011). Findings of the study by Tomioka et al. (2017) indicated that participating in social activities promoted successful aging among community-dwelling older adults. Antonucci et al. (2019) stated that social networks provide a resource for achieving more successful aging also among people who have experienced greater challenges in life.

The study of Rius-Ottenheim et al. (2012) showed that dispositional optimism was associated with lower feelings of loneliness among older men over time despite of negative life events.

In Finnish studies, lonely older people had higher risk for dementia, disabilities, and mortality during the follow-up than older persons who did not feel lonely (Tilvis et al. 2000, Tilvis et al. 2012). The review of Ong et al. (2016) found that both the quantity and quality of social relationships are associated with morbidity and higher mortality risk. Psychosocial group interventions among older adults suffering from loneliness have been associated with better cognition (Pitkälä et al. 2011), less use of health services, and lower mortality risk (Pitkälä et al. 2009).

2.4.7 Personal values, purpose in life

Values are desirable goals that serve as guiding principles in person`s life (Schwartz 1994) that drive decision making and behavior (Schwartz 2012, Schwartz 1992, Rokeach 1973). Schwartz`s value model consists of ten value domains, including the domains of power, achievement, hedonism, stimulation, self-direction, universalism, benevolence, tradition, conformity, and security (Schwartz 1994). Several values are included within these domains (Schwartz 1994). Moreover, health as a value has been recently located in the value model (Aavik & Dobewall 2017). The value of health can be positioned in the value domain of security, but also in achievement, hedonism, and universalism (Schwartz 1992, Aavik & Dobewall 2017).

Health values, combined with other values, influence attitudes, intentions, and health-related behaviors, and therefore, they may relate to perceived and objective health outcomes (Aavik & Dobewall 2017). In a Finnish study, value domains of tradition, benevolence, and conformity were associated with health (Sortheix et al. 2013). In a European study, the value domains of hedonism and benevolence contributed to life satisfaction (Sortheix &Lonnqvist 2014). The value of security has been reported to support health behavior (Aavik et al. 2014). Furthermore, the values indicating openness to change were related to non-adherence to doctors` instructions (Ahola 2015). The findings of cross-sectional study showed that valuing health was associated with health benefits and a health-related quality of life (Dobewall et al. 2017).

Experiencing a purpose in life, life satisfaction, and perception of the aging process contribute to aging successfully (Kivimäki & Ferrie 2011). A cross-sectional study revealed that a purpose in life was associated with higher levels of happiness and a better health status (Zhang et al. 2018). A positive life orientation had long-term impact on survival prognosis during old age (Tilvis et al. 2011, Pitkälä et al. 2004). Also, the study of Fagerström (2010) revealed that a positive life orientation is an inner health resource for older people. In addition, religion and spirituality have been found to be associated with well-being (Fry 2000, Daaleman et al. 2001), physical and mental health (Koening 2001), and mortality risk (McCullough et al. 2000) among older people.

2.5 Summary of the literature

Successful aging is a multidimensional concept including biomedical and psychosocial aspects, and it is most commonly defined as a good physical, cognitive, psychological, and social function during old age without major diseases (Rowe & Khan 1987). Though, definition and assessment methods of the concept vary among the studies. The main interest in the concept is how to expand good health and disability-free years in the life span with a reduction of morbidity (Fries 1990).

Biomedical factors of successful aging encompass a long and healthy life and a high physical and cognitive function. Longevity and good function during old age depend especially on lifestyle and environmental factors. Psychosocial factors of successful aging comprise elements of an active and engaged life and adaptive processes to changes in later life. All these dimensions should be considered from subjective and objective perspectives when studying successful aging (Fries 1980).

Previous studies on successful aging show the influence of socioeconomic factors, genes, life habits, and cardiovascular disease risk factors on longevity, physical and cognitive function, and quality of life. Also, psychosocial factors and personal values have shown to be related with later life well-being. Most of the earlier longitudinal studies on predictors of successful aging have been conducted with varied follow-up times and samples and without considering the effect of mortality in analyses.

Based on this literature review, the longitudinal studies exploring successful aging and related midlife factors in homogenous cohorts and with over 26 years of follow-up are rare.

3 AIMS OF THE STUDY AND RESEARCH QUESTIONS

The aim of this study was to explore midlife factors associated with successful aging among a socioeconomically homogenous Helsinki Businessmen Study (HBS) cohort.

The research questions were:

1. How do the personal value priorities in midlife associate with a health-related quality of life, frailty, and mortality in old age? *Study I*

2. How do the CVD risk factors, self-rated health, and self-rated physical fitness in midlife associate with active and healthy aging? *Study II*

3. What are the midlife predictors of reaching 90 years of age? *Studies III and IV*

4. How does the metabolic health in late midlife associate with a health-related quality of life and mortality in old age? *Study IV*

4 METHODS

4.1 The participants and the study design

The study population consisted of participants from the Helsinki Businessmen Study (HBS) cohort (original, n=3490) who were born between 1919 and 1934. This is a longitudinal prospective study with repeated assessments over 44 years. The flow chart of the studies is presented in Figure 2. The participants were all men who had worked as executives or businessmen. They had participated in volunteer health check-ups in the 1960s and early 1970s organized by Finnish Institute of Occupational Health. These health check-ups aimed to diminish the cardiovascular risk among the participants. The Helsinki Businessmen Study cohort profile has been described in detail (Strandberg et al. 2015).

In 1974, the men (n=3309, the survivors and those whose addresses were available) were invited to be assessed with questionnaires, clinical, and laboratory examinations. They were also asked to participate in a prevention trial. This prevention trial was a 5-year, randomized, controlled multifactorial primary prevention study between 1974–1980 including an intervention that consisted of intensive lifestyle modification in their smoking, exercise, diet, alcohol, and contemporary drug treatment habits. Of the original sample, 1606 had a clinical disease or did not respond or were deceased. Of the rest, 1815 participated in the trial in 1974–1980. They were clinically healthy but had a risk of cardiovascular disease (CVD). These men were randomized into an intervention (n=612), a control (n=610), and a low-risk control group (n=593). Both control groups were in usual care. Of the participants, 1695 completed the trial. The post-trial examinations after ten years revealed no benefits in CVD or mortality between groups. In 1985–86, the participants of the trial (n=1399, 82%) responded to a mailed questionnaire and underwent laboratory examinations.

From 2000 on, the study aim shifted from cardiovascular prevention to gerontological aspects. In 2000, a mailed questionnaire was sent to survivors of the original cohort (n=2286), and 81.5% of survivors responded (Strandberg et al. 2015). Of responders, 970 responded both to the 1974 questionnaire concerning personal values and RAND-36 in 2000, which were used in *Study I*.

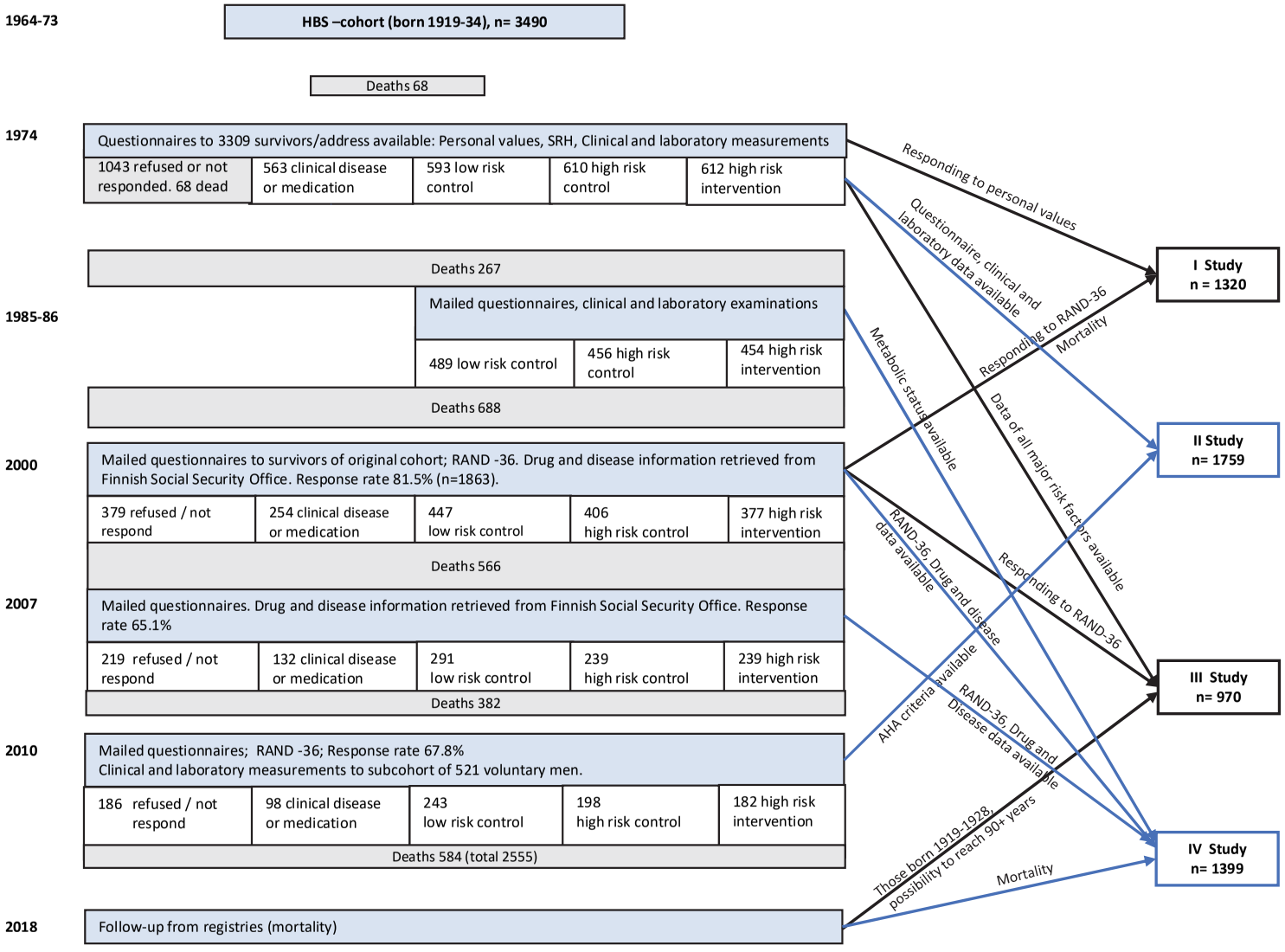

Figure 3. Flow chart of the study.

In 2007, a mailed questionnaire was sent to those men who were alive and participated in the 1985–86 mailed questionnaires and laboratory examinations. *Study IV* used responses of those who had information on metabolic health in 1985–86 and had responded to the year 2000 and 2007 RAND-36 questionnaires and gave information concerning their drug use and diseases concerning diabetes and hypertension. In addition, information concerning their prescribed drug use and diseases, i.e., hypertension, diabetes, was retrieved from the Finnish Social Security Office register.

In 2010, a questionnaire was sent to survivors. *Study II* used the information concerning census status, clinical examinations, and laboratory measurements in 1974 and questionnaire data in 2010 resulting in a sample of 1759, of which, 533 responded to the questionnaire, 920 were deceased, and 306 were non-responders.

On 31.3.2018, a follow-up of those participating in 1974 in clinical examinations and laboratory measurements and having all major risk factor data available and a possibility to reach the age of 90+ years (n=970) (*Study III*) was conducted. Their mortality was retrieved from national registries and see Table 3 for the characteristics of the studies.

Table 3. Characteristics of studies.

Study, N	Participants, mean age at baseline	Explanatory variables	Outcome
Study I n=1320	Those providing their personal value priorities in 1974, mean age 48 years.	Personal value priorities, Keys risk equation[1]	RAND-36[2], frailty phenotype, mortality until year 2000
Study II n=1759	Those providing clinical and laboratory data in 1974, mean age 47 years.	BMI[3], systolic and diastolic blood pressure, cholesterol, triglycerides, smoking, consumption of coffee and alcohol, SRH[4], SRF[5]	Active and healthy aging (AHA)[6] criteria defined in 2010
Study III n=970	Those providing data of all major risk factors in 1974, mean age 50 years.	BMI, systolic blood pressure, cholesterol, 1-h post-load glucose, smoking, consumption of alcohol, SRH, SRF, RAND-36, Charlson[7]	Extreme longevity defined as reaching 90 years of age by 31st March 2018
Study IV n=1399	Those providing their metabolic status in 1985–86, mean age 60 years.	BMI, weight gain, waist circumference, consumption of alcohol, smoking, exercise, blood pressure, blood glucose cholesterol, HDL cholesterol, LDL cholesterol, triglycerides. Metabolic syndrome and metabolically healthy overweight/obesity were defined.[8]	RAND-36 in 2000 and in 2007 and mortality until 31st March 2018

[1]Keys et al. 1972; [2]RAND-36 (Aalto et al. 1999); [3]BMI=body mass index; [4]SRH=self-rated health; [5]SRF=self-rated functioning; [6]AHA=Active and Healthy Aging (Rantanen et al. 2015); [7]Charlson comorbidity index (Charlson et al. 1987); [8]Ortega et al. 2016.

4.2 Ethical considerations

The Ethics Committee of the Helsinki University Hospital, Department of Medicine has approved the follow-up studies of HBS, and all participants have provided written informed consent. The study has been registered as ClinicalTrials.gov identifier: NCT02526082.

4.3 Measurements

The study consisted of data from mailed questionnaires in 2000, 2007, and 2010, registries (mortality from the population register of Finland in 2018, prescriptive medicine from the Social Insurance Institution of Finland in 2000

and 2007), and clinical and laboratory assessments in 1974 and 1985–86. In the clinical assessments administered in 1974 and 1985–86, participants were interviewed for their lifestyle and risk factors and measured for their blood pressure, height and weight, and waist circumference. Laboratory assessments in 1974 and 1985–86 included blood samples (i.e., serum lipids and fasting blood glucose levels). The questionnaires in 2000, 2007, and 2010 included questions about anthropometry, lifestyle, diseases, medications, well-being, and the health-related quality of life. The participants completed the questionnaires independently.

4.3.1 Demographic data

The mailed questionnaires included demographic details such as age and marital and socioeconomic status.

4.3.2 Cardiovascular risk factors and lifestyle

Studies I, II, III. In 1974, the participants provided data on their smoking status ("Have you ever smoked regularly (yes/no)?," "Do you smoke at the moment?" (yes/no), coffee consumption (cups/day), and alcohol consumption (type and amount). Their blood pressure was measured with a mercury sphygmomanometer (mmHg) with the subject in a sitting position after a 10-minute rest. Participants' weight (kg) and height (cm) were measured, and the body mass index (BMI) was calculated (kg/m^2). The waist circumference was measured (cm). Furthermore, fasting blood samples were taken, and fasting plasma glucose (mmol/L), total cholesterol (mmol/L), LDL-cholesterol (mmol/L), HDL-cholesterol (mmol/L), triglycerides (mmol/L) were measured. In addition, one-hour post-load glucose (mmol/L) was measured.

The Keys risk equation was calculated (Keys et al. 1972). It has been constructed to demonstrate a correlation between cholesterol levels and cardiovascular disease (Keys et al. 1972). It includes age, smoking, BMI, total cholesterol, and systolic blood pressure.

Study IV. In 1985–86, the participants were measured, and blood samples were taken to determine if the participant had metabolic syndrome. Metabolic syndrome (MetS) was determined according to the International Diabetes Federation definition: MetS: ≥ 3 of the following components (Ortega et al. 2016) each giving one point if the cut point was reached:

- triglycerides ≥ 1.69 mmol/L (150 mg/dL)
- HDL cholesterol < 1.04 mmol/L (40 mg/dL)
- systolic blood pressure ≥ 130 mmHg, or diastolic blood pressure ≥ 85 mmHg, or diagnosis of hypertension
- fasting glucose ≥ 5.55 (100 mg/dL) or diagnosis of diabetes
- waist circumference (men) > 102 cm

Metabolic status groups were determined as follows:

- metabolically healthy normal weight (MHN) BMI < 25 kg/m^2, not MetS
- metabolically healthy overweight and obesity (MHO) BMI ≥ 25 kg/m^2, not MetS
- metabolically unhealthy normal weight (MUN) BMI < 25 kg/m^2 with MetS
- metabolically unhealthy overweight and obesity (MUO) BMI ≥ 25 kg/m^2 with MetS

Studies I, III, IV. In 2000 and 2007 (*only Study IV*), the questionnaires included self-reported data on weight (kg) and height (cm), smoking status (current smoker yes/no), alcohol consumption (type and amount), and exercise behavior (*Study IV*) ("Do you exercise regularly weekly?" (yes/no, if yes "How many hours weekly?").

4.3.3 Health and diseases

Studies II, III. Self-rated health (SRH) was assessed in 1974 with similar wording as used in the Whitehall II study (Marmot & Shipley 1996). SRH was assessed by asking: "What do you think about your present state of health;" is it "very good," "fairly good," "average," "fairly poor," or "very poor." The statuses such as "very good" and "fairly good" were combined in the analyses of SRH.

Studies II, III. The chronic diseases and diagnoses were self-reported in questionnaires with yes/no questions in 2000 (*Study III*) and in 2010 (*Study II*). Diagnoses were confirmed from the register of Social Insurance Institution of Finland. The Charlson Comorbidity Index (CCI) was used as a measure of burden of disease (Charlson et al. 1987) in *Study III*.

4.3.4 Frailty, cognition, and functioning

Study I. The phenotypic frailty status was defined in 2000 by the modified Fried criteria, which have been validated in our cohort (Sirola et al. 2011). The walking speed was not measured in our study, so the four following criteria were used: (1) Shrinking was based on a weight loss of ≥ 5% from midlife or current BMI < 21 kg/m^2, (2) Physical weakness was based on self-reported difficulty carrying a grocery bag, (3) Exhaustion was based on self-reported low energy during the preceding 4 weeks (item in RAND-36), (4) Physical inactivity was based on a question: "Do you exercise regularly weekly?" The answer "No" indicated physical inactivity. The sum of fulfilled criteria classified a person to be "not frail" (zero criteria), "pre-frail" (1–2 criteria), or "frail" (3–4 criteria) (Sirola et al. 2011).

Study II. Cognitively healthy was defined as "no subjective cognitive problems" and was self-reported in the survey in 2010 according to the memory item in the Clinical Dementia Rating.

Studies II, III. Self-rated fitness (SRF) was assessed in 1974 by asking "What do you think about your present state of fitness:" is it "very good," "fairly good," "average," "fairly poor," or "very poor" (Marmot & Shipley 1996). The statuses such as "very good" and "fairly good" were combined in the analyses indicating good SRF.

Study II. Social functioning was defined in 2010 as "responding to the mailed questionnaire survey."

Study II. Difficulties in activities of daily living (ADL) were self-reported in the 2010 survey reflecting physical functioning (help needed, yes/no).

Study III. The RAND-36 (Aalto et al. 1999) was used in the survey 2000. The Physical and Mental health summary scores of the RAND-36 Health Survey were calculated and used in the analyses (Ware & Kosinski 2001).

4.3.5 Health-related quality of life

Study II. Psychological functioning was defined as "feeling of happiness." This was self-reported in the survey (RAND-36 item) in 2010.

Studies I, II, III, IV. RAND-36 was used in the 2000 and 2010 surveys. It consists of 36 items that evaluates the eight domains of HRQoL: physical functioning,

role limitations caused by physical health problems, role limitations caused by emotional problems, social functioning, emotional well-being, vitality, pain, and general health perception (Aalto et al. 1999), see Appendix 2. All scale scores ranged from 0 to 100 with 100 presenting the most favorable state of functioning or well-being (Ware & Kosinski 2001).

4.3.6 Mortality

The dates of death were retrieved from the population register of Finland in 2000, 2010, and 2018.

4.3.7 Life values in Study I

Study I. Personal values were assessed by a 12-item questionnaire. Personal value priorities (PVP) were considered as the priorities of one's subjective values. The PVP questionnaire was based on Rosenberg's value assessment (Rosenberg 1957). It was slightly modified by adding items of health and environment. The scale based on this questionnaire was originally created by the Finnish Institute of Occupational Health.

Personal values were assessed by asking in 1974: "How do you prioritize the following issues in your personal value system?" The items were: (1) a pleasant working environment, (2) a pleasant living environment, (3) a job with appropriate challenges, (4) effective health services, (5) an active social life, (6) exercise, (7) good possibilities for traveling, (8) a variable life, (9) good health, (10) effective environmental protection, (11) a long life, and (12) the ability to spend a vacation at the countryside. The participants were invited to evaluate all these issues using a scale as follows: 1 = not important, 2 = desirable, 3 = important, 4 = very important, 5 = imperative (Appendix 1).

4.3.8 Active and healthy aging in Study II

Active and healthy aging (AHA) was determined by the following items (Rantanen et al. 2015): 1. being alive, 2. responding to the survey, 3. not subjective cognitive problems according to the CDR memory item (Hughes et al. 1982), 4. a feeling of happiness by RAND-36 item (Aalto et al. 1999), 5. no difficulties in ADL, and 6. no significant self-reported chronic diseases (e.g., cardiovascular diseases, Parkinson disease, Alzheimer disease, rheumatoid

arthritis, cancer, obstructive pulmonary disease, diabetes). The AHA was constructed by the number of positive responses in items: AHA 0: deceased, AHA 1: alive but not responding to the mailed survey, AHA 2–4: responding to the mailed survey plus one to two positive responses in not having subjective cognitive problems, feeling of happiness, and no ADL difficulties. AHA 5 was all above the criteria plus having possible chronic diseases, and AHA 6 was all above but not having chronic diseases.

4.3.9 Extreme longevity in Study III

In *Study III*, the association of midlife factors to extreme longevity was explored. Extreme longevity was defined as reaching at least 90 years of age as suggested by Yates et al. 2008.

4.4 Statistical analyses

The data are presented as means with standard deviations (SD), as medians with interquartile range (IQR), or as counts with percentages. Statistical comparisons between the groups were made using the t test, Chi square test, or analysis of variance (ANOVA, ANCOVA). Statistical significance for the unadjusted hypothesis of linearity was evaluated using the Cochran–Armitage test for trend or analysis of variance with an appropriate contrast. In the case of a violation of the assumptions (e.g., non-normality), a bootstrap type test was used. The normality of the variables was tested using the Shapiro–Wilk W test. All analyses were performed using STATA 14.0–15.1 (StataCorp LP, College Station, TX) or NCSS statistical software (Kaysville, UT, www.ncss.com, Version 8).

In *Study I*, an exploratory factor analysis with a principal component method for factoring and oblique rotations on a polychoric correlation matrix was performed to identify related items of the PVP questionnaire. The strategies used to extract the number of factors were: (1) the Kaiser criteria, which determines that components with eigenvalues lower than one should be excluded. Factor scores were computed for the rotated loading matrix using a regression scoring method. Internal consistency was estimated by calculating Cronbach's alpha internal consistency with bias-corrected bootstrap at 95% confidence intervals. By using adjusted standardized regression coefficients, Beta (β) linear regression analyses were performed to identify how the PVP

factors scores in 1974 were associated with the HRQoL in 2000. Models included age at year 2000 as covariates. The β Value is a measure of how strongly each predictor variable influences the criterion (dependent) variable and measured in units of SD. The Cohen's standard for β values above 0.10, 0.30, and 0.50 represent small, moderate, and large relations, respectively. The associations between PVP factors in midlife and frailty in 2000 were analysed using logistic regression analysis. A Hazard Model was used to estimate the association of PVP with mortality risk (adjusted for age and the Key's risk equation for adjusted risk). The proportional hazards assumption was tested graphically and by use of a statistical test based on the distribution of Schoenfeld residuals.

In *Study II,* to determine characteristics associated with AHA 6 or AHA 5–6, univariate and multivariate forward stepwise logistic regression analyses were applied.

In *Study III, the* Kaplan–Meier method with age was the time scale used to estimate the cumulative survival. To determine characteristics associated with reaching 90 years of age, multivariate logistic regression analysis was applied.

In *Study IV*, cumulative mortality up to March 15, 2018, in MHN, MHO, and MUO groups were compared using Kaplan-Meier curves and log-rank testing. Mortality in the groups was further compared using Cox's regression analysis, after ensuring the proportional hazards assumption, and hazard ratios (HR) with 95% confidence intervals (CI) were calculated. Logistic regression was used to compare metabolic groups reaching 90 years of age. To adjust for multiple testing, Bonferroni correction was applied.

5 RESULTS

5.1 Baseline characteristics

Table 4 shows the characteristics of the participants at baseline in 1974 (*Studies I, II, III*) and in 1985–86 (*Study IV*). The businessmen were at their midlife in 1974 with a mean age of 48–50 years.

Table 4. Baseline characteristics of participants in each substudy.

Characteristics	Study I in 1974 (n=1320)	Study II in 1974 (n=1759)	Study III in 1974 (n=970)	Study IV in 1985-86 (n=1309)
Age, years, mean (SD)	48 (4)	48 (4)	50 (3)	60 (4)
Current smokers (%)	369 (28)	590 (34)	341 (35)	226 (17)
Alcohol consumption (g/week), mean (SD)	112 (56 to 224) median (IQR)	164 (155)	161 (169)	mean 118.4, SD 140.8 median 84 (IQR 28-154)
BMI (kg/m^2), mean (SD)	25.8 (2.8)	26.0 (2.8)	26.1 (2.8)	26.0 (3.0)
Systolic blood pressure (mmHg), mean (SD)	142 (19)	143 (19)	146 (20)	140 (17)
Diastolic blood pressure (mmHg), mean (SD)	91 (11)	92 (12)	94 (12)	88 (10)
Total cholesterol (mmol/L), mean (SD)	6.2 (1.1)	6.3 (1.1)	6.4 (1.1)	6.5 (1.1)
Triglyceride (mmol/L), mean (SD)	1.6 (0.9)	1.7 (1.0)	1.7 (0.9)	1.5 (0.9)
Fasting plasma glucose (mmol/L), mean (SD)	4.7 (0.7)	4.8 (0.8)	7.3 (2.3) (1-h postload)	4.9 (1.1)
Self-rated health good, n (%)	n.a.	927 (53)	461 (49)	n.a.
Self-rated fitness good, n (%)	n.a.	597 (34)	317 (34)	n.a.

SD=standard deviation, BMI=body mass index, IQR=interquartile range

5.2 The associations of personal value priorities in midlife with a health-related quality of life, frailty, and mortality in old age

Study I examined the association of midlife personal value priorities (PVP) with HRQoL, frailty, and mortality during old age. At baseline (Table 4), the participants' mean age was 48, and 28% were current smokers. Their mean blood pressures were 142 (systolic) and 91 (diastolic), and total mean total cholesterol was 6.2 mmol/L. The Keys' risk equation mean was 1.99%.

The participants responded to a survey concerning their personal value priorities (PVP), and an explanatory factor analysis was performed to explore the PVP questionnaire. In the factor analysis of the 12-item value questionnaire, three factors were loaded based on the participants' scores of each question. The factors were: (1) valuing health ("Health"), loading "Effective health services, '' "exercise," "good health," "effective environmental protection," and "long life;" (2) valuing an enjoyable and varying life ("Enjoyment"), loading "Active social life," "Good possibilities for traveling," and "Variable life;" and (3) valuing comfort and a work-oriented life ("Work-life balance"), loading "Pleasant working environment," "Pleasant living environment," and "Job with appropriate challenges." Of these factors, 51% were explained in the analysis. The item "an ability to spend a vacation at countryside" was left out from the analyses because it did not get enough scores in Cronbach's alpha test to fit on the factors (See Article I, Table 2).

In linear regression analyses, a significant positive association, when adjusted for age, was found between valuing "Health" in midlife and the RAND-36 domains of Physical functioning (β 0.07, 95% CI 0.01 to 0.14) and Vitality (β 0.10, 95% CI 0.03 to 0.16) in old age. A significant negative association, when adjusted for age, was found between valuing "Enjoyment" in midlife and the RAND-36 domains of Role participation influenced by physical health problems (β -0.07, 95% CI -0.13 to 0.00) and Role participation influenced by emotional problems (β -0.06, 95% CI -0.13 to 0.00). In addition, there was a trend for a positive relation, when adjusted for age, between the "Health" factor and the RAND-36 domain of General health (β 0.06, 95% CI -0.00 to 0.13), and a trend for a negative relation, when adjusted for age, between the "Enjoyment" factor and the RAND-36 domain of Bodily pain (β -0.05, 95% CI -0.11 to 0.01). The associations are shown in Figure 3.

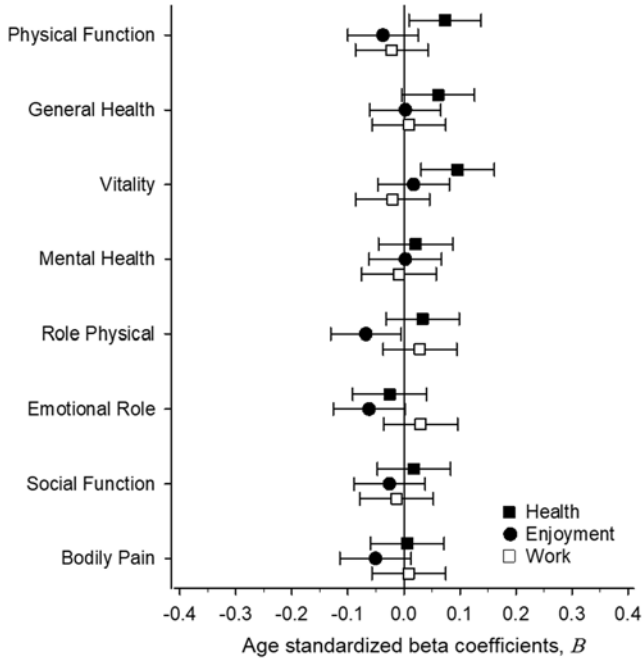

Figure 3. Associations between factors of personal value priorities and HRQoL.

The frailty status according to modified Fried's criteria was measured in 1025 participants in 2000. Of them, 460 were "robust," 436 were "pre-frail," and 68 were "frail." In logistic regression analysis, when adjusted for age and the Key`s risk equation, the "Health" factor of PVP predicted less frailty (OR per 1-SD: 0.84, 95% CI 0.75 to 0.95) and see Figure 4.

Of the 1320 participants, 295 men died before the follow-up survey in 2000. The association of personal value priorities in midlife with mortality was estimated during the 26 years of follow-up using the Hazard Model, and the "Enjoyment" factor predicted mortality (HR per 1-SD: 1.15, 95% CI 1.02 to 1.30, adjusted for age and the Key`s risk equation) and see Figure 5.

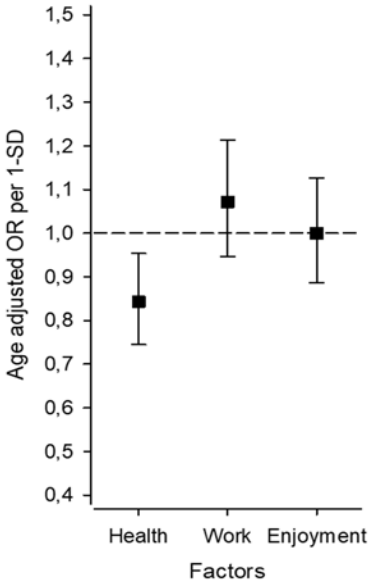

Figure 4. Association between three factors of personal value priorities and frailty.

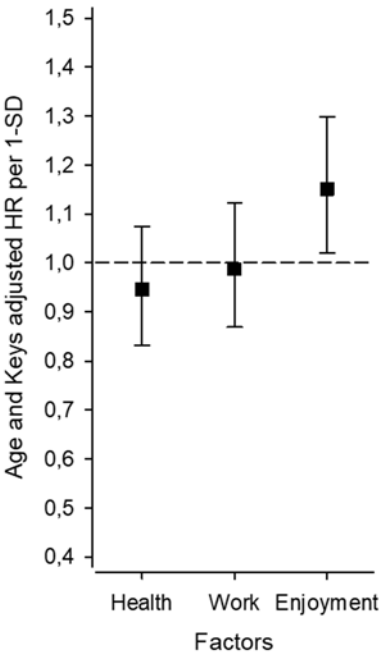

Figure 5. Association between three factors of personal value priorities and mortality.

5.3 The associations of CVD risk factors, self-rated health, and self-rated physical fitness in midlife with active and healthy aging

Study II explored the midlife variables in 1974 and how they predicted active and healthy aging (AHA) in 2010 among older businessmen.

Table 5 shows the characteristics of participants according to the AHA groups in 1974. According to AHA criteria, participants' mean age, BMI, blood pressures, total cholesterol, triglycerides, and alcohol consumption decreased linearly from AHA 0 to AHA 6. The proportion of non-smokers with good self-rated health and good self-rated fitness increased from AHA 0 to AHA 6.

Table 5. Age-adjusted characteristics of study population (n=1768) in 1974.

AHA in 2010 Variable in 1974	AHA 0 n= 920	AHA 1 n=306	AHA 2-4 n= 334	AHA 5 n=115	AHA 6 n=84	p value for difference between AHA groups
Age, y, mean (SD)	49 (4)	47 (4)	47 (4)	46 (4)	46 (4)	*<0.001*
BMI, kg/m^2, mean (SD)	26.3 (2.9)	25.8 (2.7)	26.0 (2.8)	25.2 (2.4)	25.2 (2.7)	*<0.001*
Non-smokers, n (%)	545 (59)	219 (72)	246 (74)	90 (78)	69 (82)	*<0.001*
Blood pressure, mmHg, mean (SD)						
Systolic	146 (20)	140 (17)	140 (18)	141 (20)	139 (16)	*<0.001*
Diastolic	94 (12)	91 (11)	91 (11)	90 (12)	89 (10)	*<0.001*
Serum lipids, mmol/L, mean (SD)						
Cholesterol	6.42 (1.05)	6.32 (1.03)	6.19 (1.06)	6.17 (0.98)	6.01 (1.05)	*<0.001*
Triglycerides	1.77 (1.03)	1.59 (0.73)	1.69 (1.02)	1.46 (0.71)	1.50 (0.73)	*<0.001*
Alcohol, g/week	178 (171)	158 (140)	150 (134)	126 (111)	139 (134)	*<0.001*
Coffee, cups/day	4.2 (2.6)	3.7 (2.3)	4.3 (2.6)	3.9 (2.3)	3.7 (2.1)	*0.082*
SRH, n (%)*	438 (48)	173 (57)	178 (53)	80 (70)	58 (69)	*<0.001*
SRF, n (%)*	287 (31)	125 (41)	104 (31)	43 (37)	38 (45)	*0.020*

BMI=body mass index; SRH=self-rated health; SRF=self-rated fitness. AHA was classified as follows: AHA 0=deceased; AHA 1=being alive, but not responding the survey; AHA 2–4=responding to the survey, and one to two of following criteria: no subjective cognitive problems, feeling happy, no ADL difficulties; AHA 5: all above criteria but may have possible chronic diseases; and AHA 6=as above, but no major chronic diseases.
*Assessed as excellent or very good. Continuous variables are mean (SE).

In 2010, 47.7% (839/1759) of the study population was alive. Of the survivors, 13.7% (n=115) and 10.0% (n=84) fulfilled the AHA 5 and AHA 6 criteria, respectively. This was 11.3% of the total study group.

A higher BMI (OR 0.73, 95% CI 0.61 to 0.86), smoking (OR 0.52, 95% CI 0.36 to 0.77), and higher consumption of alcohol (OR 0.73, 95% CI 0.60 to 0.90) in midlife were inversely associated with fulfilling criteria of healthy aging with chronic diseases (AHA 5). SRH rated as "very good" or "fairly good" in midlife was significantly associated with increased odds of fulfilling AHA 5 criteria (OR 1.90, 95% CI 1.37 to 2.63) and see Table 3 in Article II.

In logistic regression analysis, when adjusted for age, the midlife factors negatively associated with healthy aging (AHA 6) were smoking (OR 0.44, 95% CI 0.25 to 0.77), a higher BMI (OR 0.75, 95% CI 0.59 to 0.96), and higher total cholesterol (OR 0.76, 95% CI 0.60 to 0.97). Furthermore, a good SRH (OR 1.73, 95% CI 1.07 to 2.80) (rated "very good" or "fairly good" in midlife) was significantly associated with increased odds of fulfilling all criteria of healthy aging (AHA 6) and see Table 2 in Article II.

5.4 The associations of CVD risk factors in midlife with extreme longevity

Study III explored the major cardiovascular disease (CVD) risk factors during midlife and extreme longevity. Those with a possibility to reach 90 years of age were included in the study. Thus, the study sample consisted of those men who were born between 1919 and March 1928 and had data on midlife risk factors available (n=970). Of them, 244 men survived to the age of 90 representing 25.2% of the study sample.

Table 6 shows the baseline characteristics of participants according to reaching or not reaching very old age. The mean age of survivors and non-survivors was 50 at baseline. The survivors had a less risk factor burden in midlife: there were less smokers, they used less alcohol, and they had lower BMI, blood pressures, cholesterol, triglycerides, and 1-hour post load glucose.

In 2000, the survivors had less comorbidities according to Charlson comorbidity index than non-survivors (1.1 vs. 1.8, $p<0.001$) and a higher Physical health summary score in RAND-36 (46 vs. 43, $p<0.001$). The Mental health summary

score did not differ between the groups (54 vs. 53, p=0.39). See Table 1 in Article III.

Table 6. Characteristics of participants (n=970) according to reaching or not reaching 90 years of age.

Characteristics in 1974	Surviving until 90 n=244	Deceased before reaching 90 n=726	p value
Mean age (SD)	50 (2.7)	50 (2.7)	0.90
Smoking, n (%)	58 (24)	283 (40)	<0.001
BMI, kg/m^2 (SD)	25.4 (2.6)	26.3 (2.9)	<0.001
Blood pressure, mmHg (SD) Systolic Diastolic	 143 (20) 92 (12)	 147 (20) 94 (12)	 0.023 0.004
Laboratory values, mmol/L (SD) Total cholesterol Triglycerides 1-h post-load glucose	 6.13 (1.03) 1.55 (0.75) 7.15 (2.12)	 6.47 (1.11) 1.74 (0.93) 7.80 (2.33)	 <0.001 0.004 <0.001
Alcohol consumption, g/week (SD)	136 (133)	170 (178)	0.008
Good self-rated health, n (%)	120 (52)	341 (48)	0.69
Good self-rated fitness, n (%)	87 (38)	230 (32)	0.069

SD=standard deviation, BMI=body mass index

In stepwise logistic regression analysis, single risk factors reducing odds of reaching 90 years were smoking (OR 0.48, 95% CI 0.34 to 0.67, p <0.001), glucose (OR 0.66, 95% CI 0.49 to 0.88, p=0.006), BMI (OR 0.63, 95% CI 0.46 to 0.86, p=0.003), and cholesterol (OR 0.71 95% CI 0.53 to 0.96, p=0.027). Alcohol consumption, systolic blood pressure, SRH, or SRF did not predict reaching a very high age and see Table 2, Article III.

Of those with five major risk factors being smoking, BMI, blood pressure, serum lipids, fasting glucose, only 7% survived up to 90 years, whereas 51% of those without any risk factors reached that age. With one major risk factor, the percentage was 33%; with two risk factors, it was 30%; with three risk factors, it was 20; and with four risk factors, it was 18%. There was a linear relation between the number of risk factors and reaching up to 90 years of age. See Figure 6.

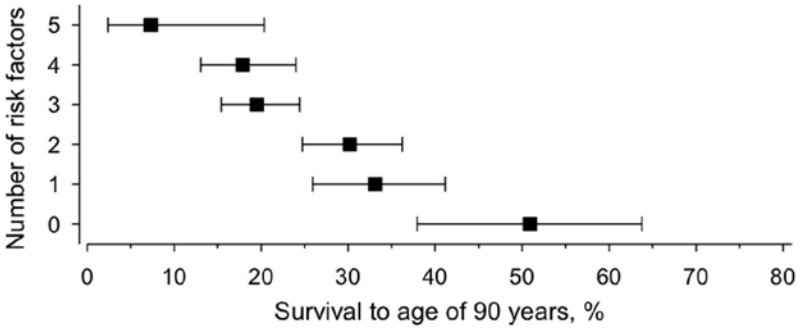

Figure 6. Relation of the amount of cardiovascular risk factors with survival to age of 90.

5.5 The association of metabolic health in late midlife with HRQoL and mortality in old age

Study IV investigated the association of metabolic health in late midlife with longevity and HRQoL in old age. Metabolic status groups were determined as follows: MHN, metabolically healthy normal weight (BMI < 25 kg/m^2, not MetS); MHO, metabolically healthy overweight/obese (BMI ≥ 25 kg/m^2, not MetS); MUN, metabolically unhealthy normal weight (BMI < 25 kg/m^2 with MetS); MUO, metabolically unhealthy overweight/obese (BMI ≥ 25 kg/m^2 with MetS). Of the participating businessmen, 469 (35.8%), 538 (41.1%), 276 (21.1%), and 26 (2.0%) were MHN, MHO, MUO, and MUN, respectively, at baseline in 1985–86.

Table 7 shows the characteristics of participants according to metabolic status groups in 1985/6, 2000, and 2007. The mean age of participants at baseline in 1985–86 was 60. The metabolically healthy normal weight (MHN) participants had a lower BMI also at the age of 25 years. They had less weight gain from young adulthood to late midlife, and their waist circumference was smaller. These participants had lower triglycerides, blood pressures, fasting glucose, and their HDL cholesterol levels were significantly better. There were also less smokers, they used less alcohol, and a larger proportion of them exercised regularly.

Table 7. Clinical characteristics of study population (n=1309, age-adjusted).

Characteristics in 1985/86	**MHN (n=469)**	**MHO (n=538)**	**MUN (n=26)**	**MUO (n=276)**	**p value**
Age years, (median, interquartile range)	60 (57–64)	59 (56–63)	60 (57–64)	60 (56–63)	0.032
BMI (kg/m^2)	23.2 (0.09)	27.1 (0.08)	23.8 (0.4)	29.0 (0.1)	<0.001
Weight gain from 25 yrs (kg)	4.1 (0.3)	12.3 (0.3)	5.4 (1.5)	18.2 (0.4)	<0.001
Waist circumference (cm)	89.6 (0.3)	98.4 (0.3)	92.7 (1.3)	105.7 (0.4)	<0.001
Ever smokers (n, %)	245 (52.2)	324 (60.2)	19 (73.1)	196 (71.0)	<0.001
Alcohol consumption (g/week)	99.6 (6.4)	118.0 (5.9)	116.8 (26.9)	150.1 (8.3)	<0.001
No regular exercise (n, %)	82 (17.5)	114 (21.2)	6 (23.1)	93 (34.4)	<0.001
Blood pressure, mmHg Systolic Diastolic	 136.0 (0.8) 84.8 (0.4)	 139.8 (0.7) 88.4 (0.4)	 147.0 (3.2) 90.2 (1.8)	 145.7 (1.0) 91.1 (0.6)	 <0.001 <0.001
Cholesterol (mmol/L) total HDL LDL Triglycerides	 6.4 (0.1) 1.52 (0.02) 4.4 (0.05) 1.16 (0.04)	 6.4 (0.05) 1.41 (0.02) 4.5 (0.05) 1.31 (0.03)	 6.3 (0.2) 1.02 (0.07) 4.4 (0.2) 2.11 (0.15)	 6.6 (0.1) 1.16 (0.02) 4.4 (0.07) 2.38 (0.05)	 0.09 <0.001 0.57 <0.001
Fasting glucose (mmol/ L)	4.68 (0.05)	4.73 (0.05)	5.62 (0.22)	5.65 (0.07)	<0.001
Characteristics in 2000	**MHN (n=361)**	**MHO (n=401)**	**MUN (n=19)**	**MUO (n=196)**	**p value**
BMI (kg/m^2)	23.4 (0.1)	26.7 (0.1)	23.4 (0.6)	27.9 (0.2)	<0.001
Smokers (n, %)	30 (8.3)	16 (4.0)	2 (11.1)	14 (7.1)	
Alcohol consumption (g/week)	103.4 (7.3)	126.0 (7.0)	89.6 (31.4)	136.3 (10.1)	0.025
No regular exercise (n, %)	48 (13.3)	74 (18.5)	2 (10.5)	46 (23.5)	0.017
Characteristics in 2007	**MHN (n=245)**	**MHO (n=247)**	**MUN (n=12)**	**MUO (n=127)**	**p value**
BMI (kg/m^2)	23.1 (0.2)	26.2 (0.2)	22.9 (0.7)	27.3 (0.2)	<0.001
Smokers (n, %)	9 (3.7)	8 (3.3)	1 (8.3)	3 (2.4)	0.71
Alcohol consumption (g/week)	86.2 (7.1)	104.0 (7.1)	77.1 (32.0)	100.3 (9.8)	0.30
No regular exercise (n, %)	34 (13.9)	45 (18.2)	2 (16.7)	25 (19.7)	0.37

MHN=metabolically healthy normal weight; MHO=metabolically healthy overweight/obese; MUN=metabolically unhealthy normal weight; MUO=metabolically unhealthy overweight/obesity. Values are means (SE) for continuous variables.

During the 21-year follow-up, there were significant differences in BMI among the different metabolic status groups. A significant decrease of BMI from 1985/6 to 2007 was shown inside the MHN (p=0.01), MHO (p<0.001), and MUO (p<0.001) groups in those men who survived to 2007. The proportion of participants reporting no regular exercise decreased linearly from MHN to MUO groups at baseline and in 2000. However, there was no significant difference among the groups in 2007. The characteristics in the MUN group

were comparable to those in the MUO group, except for BMI. The MUN group was relatively small and therefore excluded from further analyses.

During the follow-up, self-reported and drug reimbursement data regarding the prevalence of diabetes and hypertension were used to reflect metabolic health. Diabetes was present in 6.4%, 8.7%, and 28.3% of the men in MHN, MHO, and MUO groups, respectively ($p<0.001$ between the groups). 46.1%, 46.2%, and 68.6% of the men in MHN, MHO, MUO groups had hypertension, respectively ($p<0.001$ between the groups).

The HRQoL was measured in the metabolic groups with eight RAND-36 domains and was adjusted for age, baseline systolic blood pressure, log triglycerides, and smoking in 2000 and 2007. The average scores of all domains were highest in the MHN group, especially in physical domains. The scores were more similar in MHO and MUO groups (See Table 3 in Article IV).

Overall, 947 (72.3%) men died during the 32-year follow-up. The mortality curves are shown in Figure 2 in the Article IV. The MUO group had the highest mortality rate (79.7%), whereas the MHO (70.6%) and MHN (69.2%) groups had quite similar mortality rates. Of the MHN group, 25.6% men reached 90 years of age, and in MUO and MHO groups, the proportions were 15.6% and 19.1%, respectively.

The long-term mortality risk was the highest in the MUO group when adjusted for age, but differences disappeared after adjusting with baseline smoking, systolic blood pressure, and log triglycerides. However, men in the MUO group had, and men in the MHO group tended to have lower odds to survive until 90 years of age after all adjustments (See Table 8).

Table 8. Hazard ratios (multivariate-adjusted) of total mortality and odds ratios of reaching 90 years of age during the 32-year follow-up of the HBS.

Hazard ratio (95% CI) of total mortality during 32-year follow-up[a]			
	MHN	**MHO**	**MUO**
Model A[b]	1.0	1.17 (1.01–1.36)	1.53 (1.29–1.82)
Model B[c]	1.0	1.08 (0.93–1.27)	1.18 (0.95–1.47)
Odds ratio (95% CI) of reaching 90 years of age			
Model A[b]	1.0	0.78 (0.57–1.06)	0.59 (0.39–0.87)
Model B[c]	1.0 (1.05–2.46)	0.82 (0.59–1.14)	0.62 (0.41–0.95)

MHN=metabolically healthy normal weight; MHO=metabolically healthy overweight/obese; MUO=metabolically unhealthy overweight/obesity.

CI=confidence interval, HR=hazard ratio, OR=odds ratio

[a] HR was calculated using the Cox regression analysis with MHN as reference (HR=1.0).

[b] Model A: adjusted for age at baseline in 1985/86

[c] Model B: adjusted for age, systolic blood pressure, log triglycerides, and smoking in 1985/86

[d] Odds ratio was calculated using logistic regression with MHN as reference (OR=1.0)

6 DISCUSSION

6.1 General observations

In this study, the associations of midlife factors with successful aging were explored in the Helsinki Businessmen Study (HBS) cohort, which is a longitudinal study with a up to 44 years follow-up taking into consideration mortality during the follow-up years.

Study I showed that personal value priorities assessed in midlife had long-term associations with HRQoL and frailty in old age, and they also predicted mortality risk. Valuing health in midlife was positively associated with RAND-36 domains of Physical functioning and Vitality in later life. Moreover, valuing health in midlife was associated with protection of frailty in old age. Valuing an enjoyable and varying life in midlife predicted a higher mortality risk.

Studies II and *III* showed that CVD risk factors in midlife were associated with AHA and reaching 90 years of age in the HBS cohort. Midlife predictors of AHA were non-smoking, lower BMI, total cholesterol, and a higher SRH. Whilst, non-smoking, a lower BMI and alcohol consumption, and a higher SRH in midlife predicted fulfilling five AHA criteria. In addition, a fulfilment of the criteria suggested active and healthy aging despite having a possible chronic disease. A lack of the five major CVD risk factors in midlife strongly increased the odds of reaching 90 years of age and predicted successful aging in later life. Of those who had five major risk factors being smoking, BMI, blood pressure, serum lipids, fasting glucose, only 7% survived up to 90 years, whereas 51% of those without any risk factors reached that age. There was a linear relation between the number of risk factors and reaching up to 90 years of age.

Study IV examined the associations of being overweight and metabolic health in later midlife with successful aging defined as longevity and HRQoL. Results showed that MHO compared to MHN in late midlife was not associated with higher long-term mortality risk. Although, both MHO and MUO tended to lower the odds for successful aging.

6.2 Methodological considerations

In *Study I*, the baseline assessment of PVP relied on a value assessment by Rosenberg (1957), which has been applied in several earlier studies of values and work (Pine & Innis 1987, Smithers 1969). The questions of health and work environment in PVP instrument were added by the original HBS investigators. One limitation is that the PVP does not capture the full Schwartz value circle that has been used in most of the previous studies (Aavik & Dobewall 2017, Ahola 2015, Dobewall et al. 2017, Aavik et al. 2014, Sortheix & Lonnqvist 2014, Sortheix et al. 2013). The men in this study had given values for items of each factor in the PVP assessment, and they had the possibility to give high values on several factors. Thus, the linear regression analyses shed light on how the factors of Health, Work-life balance, and Enjoyment were associated with domains of HRQoL in the factor analysis. The results are significant, although the effects are small. The factor of "Work-life balance" was less meaningful than the two other factors. In addition, the assessment of values reflects the values in the 1970s with the lack of the questions of family values, which would have been explored today.

Well-constructed operationalization of successful aging includes measurements of health, well-being, and social engagement with both subjective and objective aspects (Kleinedam et al. 2018). In *Study II*, the criteria of AHA was based on self-reports in mailed questionnaires, which included subjective and objective indicators. The AHA was determined by the following items (Rantanen et al. 2015): 1. being alive, 2. responding to the mailed questionnaire reflecting a social functioning and contribution to the society, 3. not subjective cognitive problems according to CDR memory item (Hughes et al. 1982) reflecting cognitive function, 4. feeling of happiness by RAND-36 item (Aalto et al. 1999) reflecting psychological function, 5. no difficulties in ADL reflecting physical function, and 6. no significant self-reported chronic diseases reflecting physiological health. The AHA criteria capture dimensions of successful aging, but these indicators may have left out participants who would have fulfilled other indicators of successful aging. In addition, the analyses of reaching an extreme longevity (*Study III*) did not take into account the variables of the social networks.

Study I included the assessment of the 1-hour postload glucose, which has not been commonly used in practice until lately, thus, recent findings support the earlier suggestions that 1-h glucose would predict cardiovascular morbidity and mortality risk better than fasting or 2-h glucose over the long term (Saunajoki et al. 2021).

The baseline assessments of cholesterol levels included only the measurements of total cholesterol, because the differential of LDL and HDL cholesterol levels were not used at the beginning of 1970s. Alcohol consumption was asked repeatedly, also by quality, so it is likely that the participants have told the truth about their consumption without underestimating it. In *Study III,* cumulative CVD risk factors were assessed at an average age of 50, and quality of life and morbidity were not reported until the mean age of 73.

The levels of physical fitness (*Study II*) and physical activity (*Study IV*) were self-reported in this study, so there could be a possibility that participants overestimated these levels.

6.3 Strengths and limitations

The strength of this study was its length with up to 44 years of follow-up of initially healthy men. The HBS cohort has been followed up from early midlife to old age approaching a life course study. Most of the previous longitudinal studies on successful aging and extreme longevity have had varied samples and follow-up times. This male cohort was socioeconomically and ethnically homogenous representing Caucasian upper-class men. This ensures that some important confounders were intrinsically avoided. Also, another strength was that this prospective study had considered the effect of mortality in the analyses, whereas most of the earlier studies have provided analyses of survivors.

Other strengths of this study included good participation in the surveys and a reliable retrieval of data from national registers. The follow-up of mortality was reliable by using individual social security numbers. The high socioeconomic and educational status may have given credence to the self-reported questionnaires. Measurements used in the study have been widely accepted and validated, which makes the comparison to other studies feasible. Moreover, the long follow-up time combined with the robust results between the midlife factors and old age health outcomes enhanced the significance of this study.

A main limitation is that the cohort of male survivors in a long-term observational study was selected. The participants were surviving Caucasian men from the highest socioeconomic group, and their health and characteristics probably differed from those of the general population, which was a limitation in the generalizability of the results. The HBS cohort lived in a different world

from today`s society, amongst other factors, and they have lived their childhood or younghood during the Finnish war time.

Successful aging is a multidimensional concept, and this study has investigated it with HRQoL, longevity, with reaching 90 years of age, absence of frailty, and fulfilment of AHA criteria. These indicators may have left out participants who would have fulfilled other indicators of the concept.

6.4 Comparison of the findings with previous literature

6.4.1 Association of personal values with health outcomes

In *Study I*, the associations of values raised a question about the differentiation between values considered to be healthy and unhealthy. Studies of Sagiv et al. (2000, 2004) have suggested that no particular values are inherently healthy or unhealthy, and personal values depend on environment and culture. In this study, the associations of the "Enjoyment" factor showed that the values of an enjoyable and varying life could be identified as "unhealthy lifestyle" values. However, the psychological mechanism underlying the association between health values and a health-related quality of life and other objective health outcomes remains unclear and should be further studied. This is important because value surveys have traditionally not included a measure of health that is supposed to load in the middle of Schwartz's value circle and is important to most individuals (Aavik & Dobewall 2017). To my knowledge, this may be the first study exploring how personal values predict important outcomes longitudinally in old age. Although some studies have been published in much younger populations (Berson & Oreg 2016).

The literature is also scarce in explaining the link between PVP and frailty. Personal values mayaffect behavior (Aavik & Dobewall 2017, Sortheix et al. 2013, Bardi & Schwartz 2003, Roccas et al. 2002). Therefore, our results are in line with a systematic review (Lafortune et al. 2016) indicating that midlife health behavior is associated with successful aging and prevention of disability and frailty. Behavioral studies have suggested that subjective values influence choices made in everyday life (Feather 1995). Previous studies have also shown that values only affect behavior if they are cognitively activated and essential for persons themselves, which may answer the question of why people do not always live up to values (Verplanken & Holland 2002). One explanation for our results may be that a person who values health tries to make healthy choices

and adopts a health-related behavior. A healthy lifestyle can be defined as a comprehensive sense of health-related lifestyle and behavior (Abel 1991).

6.4.2 Association of midlife CVD risk factors with successful aging

Previous studies with varying age profiles have indicated that lifestyle and biological risk factors during the life course are associated with longevity and various aspects of healthy life in old age (Bosnes et al. 2019, Lafortune et al. 2016, Hodge et al. 2013 & 2014, Södergren 2013, Sabia et al. 2012, Willcox et al. 2006). Results of this study on successful aging and related midlife factors are in line with these previous studies indicating the importance of behavioral and biomedical factors in earlier life.

Study II showed that non-smoking in midlife was a very strong predictor of AHA in the HBS cohort. These results are in line with previous longitudinal studies of Bosnes et al. (2019) and Sabia et al. 2012. Smoking was also a single risk factor reducing the odds of reaching 90 years of age in *Study III*. Similarly, the study of Willcox et al. (2006) showed that smoking was significantly and inversely associated with overall survival to 85 years of age. Furthermore, the amount of smoking was inversely associated with survival to the age of 85 without major diseases (Willcox et al. 2006).

Lower levels of total cholesterol in midlife predicted AHA without diseases in *Study II*. Furthermore, higher levels of total cholesterol reduced the odds of survival until 90 years of age in *Study III*. These findings are consistent with previous studies on the relation between midlife high cholesterol and cognitive impairment or dementia in later life (Anstey et al. 2017, Rantanen KK et al. 2014) and mortality risk (Prospective Studies Collaboration 2007). A combination of high serum cholesterol and systolic blood pressure in midlife has been reported as a risk factor of Alzheimer's disease (Kivipelto et al. 2001).

Previous studies (Sabia et al. 2012, Pruchno and Wilson-Genderson 2015) suggest that moderate alcohol consumption is associated with successful aging. According to the study of Sabia et al. (2012), moderate alcohol consumption predicted successful aging better than heavy consumption or not drinking at all. Similarly, the findings of *Study II* showed that lower consumption of alcohol predicted AHA with chronic diseases. In *Study III*, levels of alcohol consumption did not reach a significance in association with reaching a very high age. Previous studies among the HBS cohort showed that over the long-term, a high consumption of alcohol was associated with worse HRQoL in old

age and affected mortality (Strandberg et al. 2004a), and it was an independent risk factor for frailty, whereas zero or moderate consumption did not show a significant association (Strandberg et al. 2018). Studies in old-aged populations have often presented benefits of moderate alcohol consumption and harms of zero consumption, which may be explained of study populations, and studies focusing on the amount of drinking, but not the drinking patterns. The abstainers in these studies may have had diseases or other health aspects that may have diluted the differences between moderate consumers and abstainers. Overall, excessive alcohol consumption has health and societal consequences (Room et al. 2003).

In contrast to various studies on longevity (Cacciatore et al. 2015, Wilhelmsen et al. 2011, Yates et al. 2008, Willcox et al. 2006, Terry et al. 2005) and also to previous studies among HBS cohort (Strandberg et al. 2014, Strandberg et al. 2004b), blood pressure was not an independent predictor of AHA in the analyses in *Study II* or of survival to the age of 90 in *Study III*. This was in contrast also to the Swedish study of Wilhelmsen et al. (2011), which showed that the greatest predictors of reaching 90 years of age were low blood pressure and other measures related to good cardiorespiratory function. However, *Study II* revealed a linear association between lower midlife blood pressure and the AHA, and the future survivors to 90 years of age had a significantly lower average systolic and diastolic blood pressure in midlife than non-survivors. These results may be explained by the lack of blood pressure data in 1974 and also by strong correlation of blood pressure with age, smoking, and BMI. These risk factors are intertwined. Furthermore, antihypertensive treatments during follow-up years have diluted the differences.

Previous studies have also indicated that midlife obesity is associated with disability in old age (Bosnes et al. 2019, Pruchno & Wilson-Genderson 2013, Willcox et al. 2006). Stenholm et al. (2017) revealed that participants with normal weight in midlife had longer healthy and chronic disease-free life expectancy than obese participants. Results of *Study II* among the HBS cohort showed that a lower BMI in midlife predicted the fulfilment of all six AHA criteria. In addition, AHA was also possible despite chronic illnesses, which implies the benefits of current health care and medical treatments for other risk factors intertwined with obesity. A higher BMI in midlife was a single risk factor that reduced the odds of reaching 90 years of age in *Study III*.

The evidence concerning the relation between MHO and CVD has been broad and mixed (Ortega et al. 2016). The results of *Study IV* support those who have criticized the concept (Pajunen et al. 2011) by showing that even already

being metabolically healthy overweight, not just obesity itself, is associated with less successful aging. One explanation for maintaining metabolic health, despite being obese, has been exercise and good cardiorespiratory fitness, which counteract metabolic disorders (Barry et al. 2018, Ortega et al. 2013). There were more men in the MHO group who did not have regular reported physical activity compared to the MHN group, but the differences were not large, as mortality was similar and HRQoL differences remained after adjustment for physical activity in analysis. On the other hand, MHO can also turn into MUO as people age (Mongraw-Chaffin et al. 2018). A recent study showed that MHO is not stable, and during 12.2 years of follow-up, half of those who had MHO progressed to MetS that increased the risk of CVD events (Mongraw-Chaffin et al. 2018, Aalto et al. 1999). Similarly, a recent study in the Nurses' Health Study found that even if metabolic health is maintained for long periods of time, obesity remains a risk factor for CVD (Eckel et al. 2018). Individuals being MHO had a higher risk of coronary heart disease, cerebrovascular disease, and heart failure as those with MHN in recent study (Caleyachetty et al. 2017). In the HBS cohort, men being MHO at baseline had slightly more diabetes, but not hypertension, than men being MHN during follow-up. In contrast, men being MUO had clearly more diabetes and hypertension up to year 2007.

The results of *Study IV* were similar to those in the Whitehall cohort study, which reported that participants being MHO at baseline had a 2-fold higher decline in physical function over 20 years and a 6-fold worsening of body pain compared to participants being MHN (Bell et al. 2017). Similarly, although not classified according to metabolic health status, a high BMI was associated with significantly shorter healthy life expectancy between the ages of 50 and 75 years, which indicates that BMI is associated with successful aging (Stenholm et al. 2017).

Previous studies report that the absence of various risk factors in middle age is associated with a longer life expectancy (Licher et al. 2019, Wilhelmsen et al. 2011, Clarke et al. 2009, Terry et al. 2005). As in *Study III*, the burden of risk factors has been studied in the Framingham Heart Study cohort, but the study population was socioeconomically more diverse, and the educational level was also found to be associated with the survival to exceptional longevity (Terry et al. 2005). Yates et al. (2008) has also studied the cumulative effect of cardiovascular risk factors, and the results were similar to those seen in *Study III*. However, the factors were measured among people who were 20 years older at baseline than the HBS cohort, and the follow-up period was much shorter being 18 years.

The earlier studies of the HBS cohort show associations between midlife cardiovascular risk factors and a health-related quality of life in old age (Hyttinen et al. 2011, Strandberg et al. 2004a, 2004b, 2004c, 2007, 2008), psychological well-being, cognitive function, frailty, and mortality (Strandberg et al. 2015, Rantanen et al. 2014, Savela et al. 2013, Savela et al. 2010, Strandberg et al. 2006). A cross-sectional study among businessmen (Rantanen et al. 2015) revealed that cardiovascular risk factors were not significantly related to AHA, which may be due to reverse causation and the effects of medications.

6.4.3 Association of midlife SRH with successful aging

In *Study II*, SRH predicted AHA in the HBS cohort, which supported the observations of SRH as an important indicator of health status, but also an independent predictor of mortality (Whitley et al. 2016, Jylhä 2009). In addition, previous results from the HBS cohort indicated that poor SRH in clinically healthy midlife was related to frailty during old age (Huohvanainen et al. 2016). Yates et al. (2008) showed that the SRH was significantly higher at a mean age of 72 among those who survived to the age of 90. However, in the present study (*Study III*), there was no difference in SRH between those who did or did not reach 90 years of age in the HBS cohort with a 44-year follow-up. This may be due to the fact that SRH has been found to have a better prognostic value in shorter follow-ups when an individual has more accurate information about one's health and condition (Strandberg et al. 2015). A previous cross-sectional study of HBS cohort showed that less than 5% of men reached the criteria of AHA, and these men had also higher scores in SRH and less frailty (Rantanen et al. 2015).

6.4.4 Successful aging and chronic diseases

Longitudinal studies of the relation of successful aging and chronic diseases are scarce. Our study population consisted of men certified as clinically healthy at baseline, but morbidity increased during follow-up. Advanced treatment and a cure of diseases can allow an individual to age "successfully" and maintain functionality in old age. However, studies suggest that the absence of diseases is not the main component of successful aging, and more focus should be on psychological and social factors (Nosraty et al. 2015, Baltes & Baltes 1990).

Some concern has been expressed that Rowe and Kahn's model, with its binary interpretation, may not be the most appropriate model for assessing the

successful aging of people with chronic diseases (Calasanti 2016). The successful aging model by Young et al. (2009) takes into account adaptive psychological and social mechanisms to compensate for limitations on physiological health. Manierre (2018) tested the validity of the Young et al. (2009) model and demonstrated that it provides a more holistic perspective on successful aging, especially among those with chronic diseases. The AHA criteria used in the HBS cohort covered the physical, psychological, and social components of successful aging defined by Rowe and Kahn (1997, 1987). However, the AHA criteria also included a question of happiness that could describe the dimension of emotional vitality proposed by Young et al. (2009). *Study II* showed that meeting the criteria of psychological and social dimensions was not dependent on the absence of diseases. The concept of healthy aging has raised much debate, as longevity has increased and different definitions of successful aging have been introduced (Kleineman et al. 2018, Cosco et 2014, Depp & Jeste 2006). Successful aging has generally highlighted a very long, healthy, and active life (Young et al. 2009, Fries 1980). An important aspect of this paradigm is "the compression of morbidity" that explains that disabilities and illnesses can be packed into a minimum period during later years and thus extend a healthy life span (Fries 1980). The results of this study also support that theory.

A main focus in successful aging is how to expand healthy and active years in old age. The previous cross-sectional study of the HBS cohort showed that about 5% of men met all AHA criteria, which may conclude the strictness of the assessment (Rantanen et al. 2015). In the present longitudinal study, 4.7% of the whole study population and 10% of survivors in 2010 met all AHA criteria and can be defined as active and healthy agers. The proportion of successful agers has varied widely in studies. In the review of Depp and Jeste (2006), the mean proportion was 36%. In any case, active and healthy aging is not a common phenomenon. The results, in which the AHA is strictly defined, demonstrated the importance of midlife factors for longevity and functional aging.

The life expectancy of the same birth cohort as our study group had a mean of only 50.2 years at birth, while men's life expectancy in Finland is 78.7 years (Statistics Finland 2017). The cohort survivors were at a mean age of 82 years old in 2010, which already exceeds the average life expectancy, even among the highest socioeconomic group (Human Mortality Database 2018).

The proportion of people who reach 90 years of age has increased over the past century (Newman & Murabito 2013). During past decades, the life expectancy has increased especially for the people who already have entered old age (Newman & Murabito 2013). The results of this study are in line with

Wilhelmsen et al. (2011) who showed that a high socioeconomic status and good functional capacity were associated with the survival to the age of 90 years. A high socioeconomic status provides a wide range of resources for maintaining and promoting health. The highly educated have better information capacity, and also their economic opportunities to manage health are better.

In *Study III*, the physical health summary score at mean age of 73 years was higher among those businessmen who reached 90 years of age. Also, at the mean age of 73, those who deceased before 90 years of age had more disability and morbidity than survivors. Prevention and advanced treatment of chronic diseases enable an individual to maintain functionality and age "successfully" (Grande et al. 2020, Artaud et al. 2016). Cardiovascular risk factors are well known, and their treatments have evolved in recent decades (Flegal et al. 2013), however, the intensity of treatment varies between different risk factors despite effective treatments for conditions such as hypertension and dyslipidemia. The obesity epidemic, in turn, still lacks effective treatments (Flegal et al. 2013). However, in order to achieve exceptional longevity, the results of this study highlight the cumulative effects of common risk factors, which should be considered in practice and in health promotion.

6.5 Interpretation of the results

Life expectancy as well as the number of healthy years of life have increased over the past decades. Due to the longevity of life and a low birth rate in Finland, the Finnish population is among the oldest in the world and currently ranked fourth (Statista 2022). In the coming decades, an increasing amount of people will reach an advantaged age, and the number of people aged 85 or over will almost triple by year 2050 in Finland (Rotkirch 2021). Therefore, successful aging is an important goal in Finland and in other aging societies.

In order to achieve successful aging, the results of this study highlight the importance of health promotion. The results show that the burden of midlife cardiovascular risk factors is associated with the survival to advanced ages, and the results suggest that having a healthy lifestyle during midlife, especially by avoiding smoking and obesity, may improve the probability of reaching active and healthy aging with exceptional longevity. This requires health policy procedures by the government and health information and support for individuals. Values influence health behavior, and the findings of this study give a novel insight of the long-term aspects of personal values. Understanding

the midlife predictors of successful aging can be used for health policies and for increasing health and well-being in aging populations in different societies.

At the societal level, promoting successful aging requires decisions that promote health and well-being. The focus should be on preventive health care services and on the identification of those who are at risk of cardiovascular diseases. Health check-ups should be available also for people who do not have occupational health care. At the individual level, successful aging refers to a long and healthy life as well as a sufficient functional capacity. For the individual, successful aging is, above all, a subjective experience. As the results of this study showed, aging can also be good and successful despite illnesses, and it is possible to compensate for the impairment of functional capacity in some areas with other strengths.

The theoretical framework presented in the literature review support the results of this study. The results of this study highlight the importance of considering all the dimensions of successful aging when studying and implementing the concept.

7 CONCLUSIONS

The present study investigated successful aging and related midlife factors among a socioeconomically homogenous Helsinki Businessmen Study (HBS) cohort.

The following conclusions can be drawn from the sub studies:

1. Personal value priorities (PVP) in midlife had long-term associations with health outcomes in later life. PVP were associated with HRQoL and frailty in old age, and they also predicted mortality. Valuing health in midlife was positively associated with RAND-36 domains of Physical functioning and Vitality and had a lower risk of frailty in old age. Valuing an enjoyable and varying life in midlife predicted higher mortality risk.

2. Lower levels of cardiovascular risk factors and good SRH in midlife were associated with active and healthy aging. Midlife non-smoking, lower BMI, lower total cholesterol levels, and a higher SRH predicted AHA without chronic diseases. Non-smoking, a lower BMI and alcohol consumption, and higher SRH in midlife predicted AHA with the possibility of one or more chronic diseases. SRF was not a significant predictor of AHA in these analyses, although there was a linear trend between the AHA groups.

3. The burden of major cardiovascular risk factors prevented reaching 90 years of age. Of those having none of cardiovascular risk factors, 51% survived until 90 years of age, whereas among those with five cardiovascular risk factors, only 7% reached that age. Smoking, a higher BMI, and higher levels of glucose and cholesterol were significant predictors for mortality and prevented survival to the age of 90. Survivors had less chronic diseases at the mean age of 73 years, and their physical health summary score was higher than among non-survivors. MHO was associated with lesser odds of reaching 90 years of age than MHN.

4. Men with a MHO at baseline had consistently worse physical components of quality of life at 73 years and 80 years of age compared to men with MHN. MHO reduces odds for successful aging. These results suggest that survival prognosis is driven by metabolic health, but odds for successful aging are driven by being overweight/obese in midlife.

8 IMPLICATIONS FOR CLINICAL PRACTICE AND FUTURE STUDIES

Results of this study show that health status, personal values, and lifestyle during midlife have a long-term influence on health and function. Therefore, it is recommended to give strong recommendations for a healthier lifestyle during middle age to reduce the risk factors for CVD and to predict successful aging. Successful aging has many benefits both at the population and at the individual level.

The HBS cohort is a life-course study, which has been followed up from early midlife to old age, and it continues until the end of the life span of the cohort. This cohort has experienced war time, and a reconstruction time after the war, which would not influence the later cohorts in a same way. Every birth cohort lives a different life that is reflected by the situation in the society and the world at the time. Today's middle-aged people will be elderly in the 2050s–2060s. Their current state of health will also determine their health and functional capacity in the coming years. Of the current 65–74-year-olds, many are active, late-middle-aged individuals and in better health and condition than previous generations at the same age. The future elderly population will be better educated than the previous generations with lifelong learning as well as having a longer employment period.

However, the COVID-19 pandemic might have caused a decrease in functional capacity in the 70+ birth cohort. Due to the pandemic, the 70+ birth cohort may have a higher burden of disease, and the good development of the healthier younger birth cohorts might be getting worse. In addition, being overweight is more common today than it was during the middle-age years of the HBS cohort. The obesity epidemic is a major challenge in developed countries and can prevent achieving successful aging.

The longitudinal studies on successful aging should be repeated among younger cohorts, and it would be interesting to study the cohort trends between the birth cohorts and also among women. Qualitative data would provide valuable additional information on the factors affecting successful aging. Overall, the main interest in the concept of successful aging is how to expand good health and disability-free years during the life span with a reduction of morbidity (Fries 1980, Fries 1990), which should be studied more in the future.

Furthermore, the concept of successful aging has been under a lot of debate, and especially the term "successful" has provoked criticism. In a world where people always have to do better, it is not easy if people should also age very successfully. Alternative terms could be "rewarding aging" and "optimal aging." However, successful aging is a multidimensional concept, and it has many aspects. From the older peoples' point of view, various dimensions may be highlighted individually and people themselves are the best experts in their own sufficiently good aging.

It also matters who you grow old with. With the increase in life expectancy, families have several generations alive and up to two generations retired at the same time. Close interpersonal relationships are an integral part of well-being. In particular, meaningful interactions create cohesion and the experience of being heard and understood. Loneliness and social exclusion are threats to the ability to function. The dimensions of successful aging include the experience of inclusion and necessity. Active seniors need meaningful tasks and roles in which they can participate. Volunteering, communality, and identifying strengths support inclusion as well as mental well-being and successful aging.

Recently, sustainability has been linked also to good aging (van Gils et al. 2021, United Nations General Assembly 2021). Enabling a good life in a sustainable way requires taking into account many different factors. Successful and sustainable old age includes not only health, but also social interaction and inclusion, a perceived purpose of life, a sense of security, and a relationship with the environment (van Gils et al. 2021). The concept of successful and sustainable old age also takes into account future generations (van Gils et al. 2021). Future studies of successful aging should take into account aspects of sustainability.

The World Health Organization (WHO 2022) has declared this decade to be the United Nations Decade of Healthy Aging (2021–2030). Globally, the future challenges of aging include pandemics, issues of sustainable development, the climate crisis, and increasing inequality. Healthy and successful aging is promoted throughout life by investing in health-promotion measures, education, and the prevention of exclusion. Aging is not a period that suddenly separates from life, but a change and continuum that occurs throughout life. Societal decisions decide the future of aging well and can provide opportunities for dignified and successful aging.

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APPENDICES

Appendix 1. Questions of personal value priorities (PVP) in 1974 (in Finnish).

Appendix 2. Rand-36/ SF-36 questionnaire (Aalto et al. 1999).

Appendix 1.

Questions of personal value priorities (PVP) in 1974 (in Finnish).

47. Mihin tärkeysasteeseen sijoittuvat Teidän henkilökohtaisessa arvojärjestelmässänne seuraavat hyvinvointiin liittyvät tavoitteet:

	Vähän tärkeä	Suotava	Tärkeä	Erittäin tärkeä	Välttämätön
Viihtyisä työympäristö	1	2	3	4	5
Viihtyisä asuinympäristö	1	2	3	4	5
Kykyjä vastaava työ	1	2	3	4	5
Tehokkaat terveyspalvelut	1	2	3	4	5
Laaja ystäväpiiri	1	2	3	4	5
Liikunta	1	2	3	4	5
Hyvät matkustamismahdollisuudet	1	2	3	4	5
Vaihteleva elämä	1	2	3	4	5
Hyvä terveydentila	1	2	3	4	5
Tehokas ympäristönsuojelu	1	2	3	4	5
Pitkä ikä	1	2	3	4	5
Mahdollisuus viettää loma-aikaa maalla	1	2	3	4	5

Appendix 2.

Rand-36/ SF-36 questionnaire (Aalto et al. 1999).

Liite 3

RAND 36-ITEM HEALTH SURVEY 1.0 (RAND-36)

Suomenkielinen versio

STAKES/KTL

1. **Onko terveytenne yleisesti ottaen ...**
(ympyröikää yksi numero)

1 erinomainen
2 varsin hyvä
3 hyvä
4 tyydyttävä
5 huono

2. **Jos vertaatte nykyistä terveydentilaanne vuoden takaiseen, onko terveytenne yleisesti ottaen ...**
(ympyröikää yksi numero)

1 tällä hetkellä paljon parempi kuin vuosi sitten
2 tällä hetkellä jonkin verran parempi kuin vuosi sitten
3 suunnilleen samanlainen
4 tällä hetkellä jonkin verran huonompi kuin vuosi sitten
5 tällä hetkellä paljon huonompi kuin vuosi sitten

Seuraavassa luetellaan erilaisia päivittäisiä toimintoja. Rajoittaako terveydentilanne nykyisin suoriutumistanne seuraavista päivittäisistä toiminnoista? Jos rajoittaa, kuinka paljon?
(ympyröikää yksi numero joka riviltä)

		kyllä, rajoittaa paljon	kyllä, rajoittaa hiukan	ei rajoita lainkaan
3.	huomattavia ponnistuksia vaativat toiminnat (esimerkiksi juokseminen, raskaiden tavaroiden nostelu, rasittava urheilu)	1	2	3
4.	kohtuullisia ponnistuksia vaativat toiminnat, kuten pöydän siirtäminen, imurointi, keilailu	1	2	3
5.	ruokakassien nostaminen tai kantaminen	1	2	3
6.	nouseminen portaita useita kerroksia	1	2	3
7.	nouseminen portaita yhden kerroksen	1	2	3
8.	vartalon taivuttaminen, polvistuminen, kumartuminen	1	2	3
9.	noin kahden kilometrin matkan kävely	1	2	3
10.	noin puolen kilometrin matkan kävely	1	2	3
11.	noin 100 metrin matkan kävely	1	2	3
12.	kylpeminen tai pukeutuminen	1	2	3

Onko teillä viimeisen 4 viikon aikana ollut RUUMIILLISEN TERVEYDENTILANNE TAKIA alla mainittuja ongelmia työssänne tai muissa tavanomaisissa päivittäisissä tehtävissänne?
(ympyröikää yksi numero joka riviltä)

		kyllä	ei
13.	Vähensitte työhön tai muihin tehtäviin käyttämäänne aikaa	1	2
14.	Saitte aikaiseksi vähemmän kuin halusitte	1	2
15.	Terveydentilanne asetti teille rajoituksia joissakin työ- tai muissa tehtävissä	1	2
16.	Töistänne tai tehtävistänne suoriutuminen tuotti vaikeuksia (olette joutunut esim. ponnistelemaan tavallista enemmän)	1	2

Onko teillä viimeisen 4 viikon aikana ollut TUNNE-ELÄMÄÄN LIITTYVIEN vaikeuksien (esim. masentuneisuus tai ahdistuneisuus) takia alla mainittuja ongelmia työssänne tai muissa tavanomaisissa päivittäisissä tehtävissänne?
(ympyröikää yksi numero joka riviltä)

		Kyllä	ei
17.	Vähensitte työhön tai muihin tehtäviin käyttämäänne aikaa	1	2
18.	Saitte aikaiseksi vähemmän kuin halusitte	1	2
19.	Ette suorittanut töitänne tai muita tehtäviänne yhtä huolellisesti kuin tavallisesti	1	2

20. **MISSÄ MÄÄRIN ruumiillinen terveydentilanne tai tunne-elämän vaikeudet ovat viimeisen 4 viikon aikana häirinneet tavanomaista (sosiaalista) toimintaanne perheen, ystävien, naapureiden tai muiden ihmisten parissa?**
(ympyröikää yksi numero)

1 ei lainkaan
2 hieman
3 kohtalaisesti
4 melko paljon
5 erittäin paljon

21. **Kuinka voimakkaita ruumiillisia kipuja teillä on ollut viimeisen 4 viikon aikana?**
(ympyröikää yksi numero)

1 ei lainkaan
2 hyvin lieviä
3 lieviä
4 kohtalaisia
5 voimakkaita
6 erittäin voimakkaita

22. **Kuinka paljon kipu on häirinnyt tavanomaista työtänne (kotona tai kodin ulkopuolella) viimeisen 4 viikon aikana?**
(ympyröikää yksi numero)

1 ei lainkaan
2 hieman
3 kohtalaisesti
4 melko paljon
5 erittäin paljon

Seuraavat kysymykset koskevat sitä, miltä teistä on tuntunut viimeisen 4 viikon aikana. Merkitkää kunkin kysymyksen kohdalla se numero, joka parhaiten kuvaa tuntemuksianne.
(ympyröikää yksi numero joka riviltä)

Kuinka suuren osan ajasta olette viimeisen 4 viikon aikana ...	koko ajan	suurimman osan aikaa	huomattavan osan aikaa	jonkin aikaa	vähän aikaa	en lainkaan
23. tuntenut olevanne täynnä elinvoimaa	1	2	3	4	5	6
24. ollut hyvin hermostunut	1	2	3	4	5	6
25. tuntenut mielialanne niin matalaksi, ettei mikään ole voinut teitä piristää	1	2	3	4	5	6
26. tuntenut itsenne tyyneksi ja rauhalliseksi	1	2	3	4	5	6
27. ollut täynnä tarmoa	1	2	3	4	5	6
28. tuntenut itsenne alakuloiseksi ja apeaksi	1	2	3	4	5	6
29. tuntenut itsenne “loppuunkuluneeksi”	1	2	3	4	5	6
30. ollut onnellinen	1	2	3	4	5	6
31. tuntenut itsenne väsyneeksi	1	2	3	4	5	6

32. **Kuinka suuren osan ajasta ruumiillinen terveydentilanne tai tunne-elämän vaikeudet ovat viimeisen 4 viikon aikana häirinneet tavanomaista sosiaalista toimintaanne (ystävien, sukulaisten, muiden ihmisten tapaaminen)?**
(ympyröikää yksi numero)

1 koko ajan
2 suurimman osan aikaa
3 jonkin aikaa
4 vähän aikaa
5 ei lainkaan

Kuinka hyvin seuraavat väittämät pitävät paikkansa teidän kohdallanne?
(ympyröikää yksi numero joka riviltä)

	pitää ehdotto-masti paikkansa	pitää enimmäk-seen paikkansa	en osaa sanoa	enimmäk-seen ei pidä paikkansa	ehdotto-masti ei pidä paikkansa
33. Minusta tuntuu, että sairastun jonkin verran helpommin kuin muut ihmiset	1	2	3	4	5
34. Olen vähintään yhtä terve kuin kaikki muutkin tuntemani ihmiset	1	2	3	4	5
35. Uskon, että terveyteni tulee heikkenemään	1	2	3	4	5
36. Terveyteni on erinomainen	1	2	3	4	5