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ASSOCIATION OF SUBJECTIVE AND OBJECTIVE MEASURES OF HEALTH AND FUNCTIONAL CAPACITY WITH INSTITUTIONALIZATION AND MORTALITY

A Follow-up Study of Community-Dwelling Older People

Anna Viljanen

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To the memory of Leena, Unto, Maila, and Sulho

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ABSTRACT

The ageing population poses increasing challenges on health and social services. There is a need for tools to identify older people at higher risk of institutional care and death to better target interventions.

The aim of this thesis was to identify tools feasible to use in primary care to identify persons at a higher risk of institutionalization or death. In addition, the aim was to describe the successful agers still living at home after a 20-year follow-up.

The study participants were aged 64 years or over and living in the municipality of Lieto at time of the baseline examination in 1998–1999 (n=1260). The baseline examination included measures of functional capacity, a physical examination and a review of the participants' medical records. Data on institutionalization were gathered from the electronic patient record system and data on mortality from the official national records during the follow-up periods of 10 and 18 years. The re-examination mirrored the baseline examination after a 20-year follow-up (n=138).

The studied variables were frailty (by three frailty tools), self-rated health, self-reported walking ability, comprehensive subjective health, objective health based on chronic conditions, and multimorbidity. Frailty, self-rated health, self-reported walking ability, dementia, neurological disorders, mood disorders and multimorbidity were associated with institutionalization. Frailty, subjective and objective health were associated with mortality. Subjective health had an additive effect on objective health in predicting mortality.

Successful agers still living at home without daily care at the age of 84 years or over had a lower biological than chronological age, and were satisfied with their lives both at baseline and at re-examination.

Self-rated health, self-reported walking ability, certain chronic conditions and multimorbidity could be used to screen for older people at higher risk of institutionalization. Frailty tools could be used in identifying older adults at higher risk of institutionalization and mortality. Successful agers were satisfied with life despite hardships and had a lower biological than chronological age. Further research is needed to evaluate possible causality.

KEYWORDS: Frailty, multimorbidity, personal biological age, satisfaction with life, self-rated health, self-reported walking ability, subjective health

TURUN YLIOPISTO
Lääketieteellinen tiedekunta
Kliininen laitos
Geriatria
ANNA VILJANEN: Subjektiivisen ja objektiivisen terveyden ja toimintakyvyn mittareiden yhteys pitkäaikaishoitoon joutumiseen ja kuolemaan
– seurantatutkimus kotona-asuvista iäkkäistä
Väitöskirja, 179 s.
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TIIVISTELMÄ

Ikääntyvä väestö tulee lisäämään terveydenhuollon ja sosiaalipalveluiden haasteita. Palveluiden kohdentamista varten tarvitaan seulontatyökaluja tunnistamaan ne iäkkäät, jotka ovat suuremmassa riskissä joutua pitkäaikaishoitoon tai kuolla.

Väitöskirjatutkimuksen tavoitteena oli löytää perusterveydenhuoltoon soveltuvia työkaluja sellaisten iäkkäiden tunnistamiseen, joilla on suurentunut riski joutua pitkäaikaishoitoon tai kuolla. Lisäksi tavoitteena oli kuvata ne onnistuneesti ikääntyneet tutkittavat, jotka edelleen asuivat kotonaan 20 vuoden seuranta-ajan jälkeen.

Tutkimusväestö koostui iältään 64-vuotiaista tai vanhemmista tutkittavista, jotka lähtötilanteessa vuosina 1998–1999 asuivat Liedon kunnassa (n=1260). Lähtötilanteessa arvioitiin toimintakykyä, tehtiin kliininen tutkimus sekä tarkasteltiin potilasasiakirjoja. Pitkäaikaishoitoon joutuminen selvitettiin potilastietojärjestelmästä ja kuolemat kansallisesta rekisteristä 10 ja 18 vuoden seuranta-ajoilta. Uudelleentutkimus 20 vuoden seuranta-ajan jälkeen vastasi lähtötilanteen tutkimusta (n=138).

Tutkitut muuttujat olivat gerastenia (kolme työkalua), itsearvioitu terveys, itsearvioitu kävelykyky, kattava subjektiivinen terveys, pitkäaikaissairauksiin perustuva objektiivinen terveys ja monisairastavuus. Gerastenia, itsearvioitu terveys, itsearvioitu kävelykyky, muistisairaus, neurologiset sairaudet, mielialasairaudet ja monisairastavuus olivat yhteydessä pitkäaikaishoitoon joutumiseen. Gerastenia sekä subjektiivinen ja objektiivinen terveys olivat yhteydessä kuolleisuuteen. Subjektiivisella terveydellä oli lisävaikutus objektiiviseen terveyteen kuolemaa ennustettaessa.

Onnistuneesti ikääntyneet, jotka 84 vuoden tai korkeammassa iässä asuivat kotona ilman päivittäistä apua, olivat biologisesti kronologista ikäänsä nuorempia ja tyytyväisiä elämäänsä sekä lähtötilanteessa, että seurantatutkimuksessa.

Itsearvioitu terveys, itsearvioitu kävelykyky, tietyt krooniset sairaudet ja monisairastavuus voisivat toimia seulontatyökaluina tunnistettaessa iäkkäitä, joilla on suurempi riski joutua pitkäaikaishoitoon. Gerasteniatyökaluilla voitaisiin tunnistaa iäkkäät, joilla on suurempi riski joutua pitkäaikaishoitoon ja kuolla. Onnistuneesti ikääntyneet olivat tyytyväisiä elämäänsä haasteista huolimatta ja biologiselta iältään kronologista nuorempia. Mahdollinen syy-yhteys vaatii lisätutkimuksia.

AVAINSANAT: Biologinen ikä, gerastenia, itsearvioitu kävelykyky, itsearvioitu terveys, monisairastavuus, subjektiivinen terveys, tyytyväisyys elämään

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Abbreviations

AD	Alzheimer's disease
AP	Attributable proportion due to interaction
BMI	Body mass index
CA	Chronological age
CFS	Clinical Frailty Scale
CGA	Comprehensive Geriatric Assessment
CI	Confidence interval
CSRH	Comparative Self-Rated Health
CVD	Cardiovascular diseases
EFS	Edmonton Frailty Scale
FI	Frailty Index
FS	FRAIL Scale
GSRH	Global Self-Rated Health
HALE	Healthy life expectancy
HIC	High-income countries
HR	Hazard ratio
ICD-10	10^{th} Revision of International Statistical Classification of Diseases and Related Health Problems
LE	Life expectancy
LMIC	Low- and middle-income countries
LTC	Long-term care
MMSE	Mini-Mental State Examination
O	Objectively healthy but subjectively unhealthy
OR	Odds ratio
PBA	Personal biological age
PRH	Physician-Rated Health
RERI	Relative excess risk due to interaction
S	Subjectively healthy but objectively unhealthy
S_y	Synergy Index
SA	Successful ageing
SDS	Zung Self-Rating Depression Scale

SO	Subjectively and objectively healthy
SOC	Sense of coherence
SPPB	Short Physical Performance Battery
SRH	Self-Rated Health
TFI	Tilburg Frailty Indicator
UH	Subjectively and objectively unhealthy
WHO	World Health Organization

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Salminen M, Viljanen A, Eloranta S, Viikari P, Wuorela M, Vahlberg T, Isoaho R, Kivelä SL, Korhonen P, Irjala K, Löppönen M, Viikari L. Frailty and mortality: an 18-year follow-up study among Finnish community-dwelling older people. *Aging Clinical and Experimental Research*, 2020 Oct;32(10):2013-2019. doi: 10.1007/s40520-019-01383-4.

II Viljanen A, Salminen M, Irjala K, Korhonen P, Wuorela M, Isoaho R, Kivelä SL, Vahlberg T, Viitanen M, Löppönen M, Viikari L. Frailty, walking ability and self-rated health in predicting institutionalization: an 18-year follow-up study among Finnish community-dwelling older people. *Aging Clinical and Experimental Research*, 2021 Mar;33(3):547-554. doi: 10.1007/s40520-020-01551-x.

III Viljanen A, Salminen M, Irjala K, Heikkilä E, Isoaho R, Kivelä SL, Korhonen P, Vahlberg T, Viitanen M, Wuorela M, Löppönen M, Viikari L. Subjective and objective health predicting mortality and institutionalization: an 18-year population-based follow-up study among community-dwelling Finnish older adults. *BMC Geriatrics*, 2021 Jun 10;21(1):358. doi: 10.1186/s12877-021-02311-w.

IV Viljanen A, Salminen M, Irjala K, Heikkilä E, Isoaho R, Kivelä SL, Korhonen P, Vahlberg T, Viitanen M, Wuorela M, Löppönen M, Viikari L. Chronic conditions and multimorbidity associated with institutionalization among Finnish community-dwelling older people: an 18-year population-based follow-up study. *European Geriatric Medicine*, 2021 Jul 14. doi: 10.1007/s41999-021-00535-y.

V Viljanen A, Salminen M, Irjala K, Korhonen P, Vahlberg T, Viitanen M, Löppönen M, Viikari L. Re-examination of successful agers with lower biological than chronological age still after a 20-year follow-up period. *Manuscript.*

1 Introduction

The population is ageing globally. The proportion of inhabitants aged 65 years or older is growing in Finland (Official Statistics of Finland, 2021). The increase in aged inhabitants leads to increase in morbidity and disability (Christensen et al., 2009) leading to increasing demands on health care and older people's services in the future. Organizers of these services need additional information to predict the need for future institutional care in order to plan and better organize the health and social services in the future. Also, identifying individuals with a higher risk of future adverse effects and targeting them with interventions to prevent or delay institutionalization or death is of course beneficial for the individual in question.

Frailty, self-rated health (SRH), walking ability and objective health measures have been shown to predict institutionalization (Bravell et al., 2009; Gutman et al., 2001; Jung et al., 2018; Rockwood et al., 2006; Rothman et al., 2008) and mortality (Clegg et al., 2013; DeSalvo et al., 2005; Huntley et al., 2012; Studenski et al., 2011) among community-dwelling older people. These predictors of adverse effects could be useful in predicting also the future need of health and social services in addition to the benefit for the individual persons.

Frailty in older adults is a clinical syndrome defined as the loss of resources in several organ systems leading to the inability to respond adequately to physical or psychosocial stressors, thus making the individual vulnerable (Clegg et al., 2013; Fried et al., 2001). Frailty can be defined as a phenotype (Fried et al., 2001) and as the accumulation of deficits (Mitnitski et al., 2001), and has been shown to predict institutionalization (Gonzalez-Colaço Harmand et al., 2017; Rockwood et al., 2006) and mortality (Clegg et al., 2013; Rockwood et al., 2006; Sirola et al., 2011) in older people.

Slowness is part of the classic phenotype definition of frailty (Fried et al., 2001), and is often measured as gait speed. Slow gait speed is associated with an increased risk of institutionalization and death (Jung et al., 2018; Rothman et al., 2008; Studenski et al., 2011). Slow gait-speed has been shown to predict the inability to walk 400 meters (Chang et al., 2004). Self-reported walking ability coincides well with the controlled ability to walk 400 meters (Sayers et al., 2004). Thus, the self-

reported ability to walk 400 meters could also predict the risk of institutionalization and death.

SRH is an individual's own perception of their health, and as such, a subjective assessment (Jylhä, 2009) affected also by cultural believes (Vuorisalmi et al., 2008). However, it still has been shown to predict institutionalization at an older age (Gutman et al., 2001), and mortality in different age groups and ethnicities (DeSalvo et al., 2005; Hirve et al., 2012; Jylhä, 2009; Santiago et al., 2010).

The World Health Organization's (WHO) definition of health is: "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (World Health Organization, 1948). In this thesis, subjective health was defined accordingly as having a good SRH, being able to walk 400 meters and being satisfied with life. Objective health was defined as the absence of illness.

Different chronic conditions are associated with a different risk of death. Multimorbidity, the co-existence of multiple chronic conditions, is often defined by disease counts (Carey et al., 2013; Halonen et al., 2019; Koller et al., 2014) or weighed comorbidity indices (Charlson et al., 1987), and has been shown to predict institutionalization (Halonen et al., 2019; Koller et al., 2014; Salminen et al., 2020) and mortality (Carey et al., 2013; Soh et al., 2020). Multimorbidity is often defined as having two or more chronic conditions, but also the approach of testing the study population for the number of chronic conditions that best identify the individuals at higher risk of adverse effects has been suggested (Johnston et al., 2018).

This thesis was conducted to investigate the abovementioned associations among community-dwelling Finnish older people: the association of frailty, SRH and self-rated walking-ability with institutionalization; the association of frailty with mortality; the association of subjective and objective health with institutionalization and mortality; and the association of chronic conditions and multimorbidity with institutionalization. The aim was to identify feasible tools for use in the primary care clinical setting to detect older people at higher risk of institutionalization and death, in order to target interventions correctly and timely, and also if used systematically, the information could be beneficial in planning the future health and older people's care services.

In addition to searching for feasible tools to identify older persons at higher risk of adverse effects, we also wanted to examine the opposite, namely the features that might lead to successful ageing (SA). SA has been defined in many different ways in research and thus, no feasible operationalization of the construct exists (Cosco et al., 2014). In this thesis, successful ageing was considered as the ability to live at home without daily care at the age of 84 years or older. We describe the still community-dwelling participants who attended a second physical examination after a twenty-year follow-up.

2 Review of the Literature

2.1 Ageing Population

In Finland, as in other Western countries, the population is ageing and the proportion of inhabitants who are 65 years or older is growing (Official Statistics of Finland, 2021). The increasing number of aged inhabitants leads to increase in morbidity and disability (Christensen et al., 2009). This poses increasing challenges on health and older people's services in the future, as it has been proposed that the growing life expectancy brings with it more years with disease and disability (Crimmins & Beltrán-Sánchez, 2011).

Healthy life expectancy (HALE), the number of years a person at a given age is expected to live in good health when accounting for age-specific mortality, morbidity and functional health status, might not be increasing as rapidly as life expectancy (LE), and varies substantially between countries (Salomon et al., 2012). As LE increases, HALE may fall behind and the difference increases with age, especially in women (Salomon et al., 2012).

However, disability-free life expectancy (DFLE) has been found to increase despite of the increased number of chronic conditions in a English population cohort aged 65 years in 1991 and 2011, with the exception of people with cognitive impairment (Bennett et al., 2022). For people with lower education, the gains in DFLE were smaller than for the ones with higher education in a Swedish population aged 77 years or older (Sundberg et al., 2021). Despite these encouraging findings, a systematic review in trends in health expectancies found that the expansion of disability in later life is evident in a number of high-income countries (HICs), with a clear exception of Swedish women, where the compression of disability signals progress in achieving healthier longer lives (Storeng et al., 2022).

In Finland, the LE at birth in the year 2019 was 82 years and the HALE 71 years, 86.6% of the LE (World Health Organization, 2020). In the year 2000, the LE at birth was 78 years and the HALE 68 years, 87.2% of the LE. However, when observing the LE and HALE at the age of 60, in the year 2019 the LE was 24 years and the HALE was 18 years, 75.0% of the LE, and in the year 2000, the LE was 22 years, and the HALE was 17 years, 77.2% of the LE (World Health Organization, 2020). The proportion of healthy years compared to all the years still left living may

be decreasing. This is of course only one country and also a high-income country, the population ages differently in low- and middle-income countries (LMICs). Also, other theories, such as the compression of morbidity to the latest years of life, have been proposed (Fries, 1980; Fries et al., 2011), and the recent findings concerning DFLE in Swedish women might support this (Storeng et al., 2022).

It is expected that the proportion of Finnish municipalities with over 20% of inhabitants being 75 years or older is going to increase from 0.6% in 2015 to 36.6% in 2030 (Sosiaali- ja terveysministeriö, 2017b). This leads to a substantially increased need for health and older people's services. In the municipality of Lieto, the proportion of inhabitants 65 years or older is predicted to be 23.9% by the year 2030 and 26.9% by the year 2040 (Kuntaliitto, 2019). There is a marked increase of 21.3% and 36.6%, respectively, when compared to the year 2020 when the proportion was 19.7% (Kuntaliitto, 2019). The growing number of very old people with chronic conditions will lead to an increased demand of care, especially institutional care nationwide (Aaltonen et al., 2019; Salminen et al., 2018).

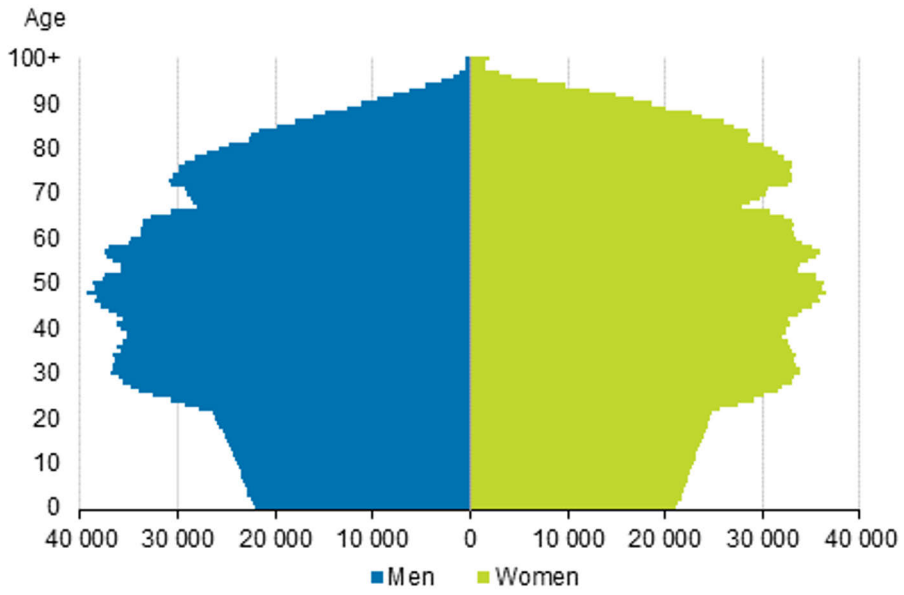

Figure 1. Population by age and gender 2040, projection 2019. Source: Official Statistics of Finland (OSF): Population projection [e-publication]. ISSN=1798-5153. 2019, Appendix figure 5. Helsinki: Statistics Finland [referred: 19.10.2021]. Access method: *http://www.stat.fi/til/vaenn/2019/vaenn_2019_2019-09-30_kuv_005_en.html* Reprinted according to the Creative Commons Attribution 4.0 International License.

2.2 Morbidity

The compression of morbidity –theory has also been studied (Fries, 1980; Fries et al., 2011). A recent study found an increase in the age at first hospital admission (admission for two or more days) in both men (from 67.8 years [95% CI 67.7–67.9] to 69.5 years [95% CI 69.4–69.6]) and women (from 69.1 years [95% CI 69.1–69.2] to 70.5 years [95% CI 70.4–70.6]) during a 27-year follow-up (from 1987 to 2014) in Denmark (Seaman et al., 2020). They also found an increase in the variation of the age at first hospital admission; the coefficient of variation increased from 9.1% (95% CI 9.0–9.1) to 9.9% (95% CI 9.8–10.0) among men, and from 10.3% (95% CI 10.2–10.4) to 10.6% (95% CI 10.5–10.6) among women (Seaman et al., 2020). The findings of Seaman et al. (2020) indicate possible compression of morbidity but more importantly, increasing heterogeneity among older people. This is a more challenging future to prepare for. This study only accounted for hospital admissions (Seaman et al., 2020). However, in Denmark, as well as in Finland, many diseases are diagnosed and treated in primary care and that data was not included in the study.

A study on Finnish age cohorts from aged 75 to 95 years in 1989 and 2009 showed that there were no longer improments in disability and there was an increase in comorbities despite favourable trends in mortality (Karppinen et al., 2017). However, when the latest wave of this study was added to the data, participants aged 75 to 85 years had improvements in functional abilities and a decreasing trend in comorbities (Öhman et al., 2022). These positive trends in health and functioning, as well as a reduction in mortality, might be due to more active preventive health care, early diagnostics and improved secondary prevention as well as improved care of acute events (Jousilahti et al., 2016).

The most common prescription medicine group in Finland (assessed by the number of prescriptions per physician) in the year 2019 were the agents acting on the renin-angiotensin system (7.8%) followed by analgesics (6.7%), beta blocking agents (6.1%), lipid modifying agents (5.8%), antidepressants (4.8%) and antiasthmatics (inhalants) (4.8%) (Social Insurance Institution of Finland, 2020). This indicates that cardiovascular diseases (CVD) are very common in Finland. The prevalence of CVD increases with age. As the ageing population is growing, the number of people with cardiovascular disease and other morbidities is growing as well.

2.3 Mortality

In Finland, all deaths are recorded by the diagnoses on the death certificate to the official national register of deaths (Official Statistics of Finland, 2019). This register is a comprehensive source for precice data on causes of death.

The most common causes of death in Finland are CVD, cancer and dementia (Official Statistics of Finland, 2019). The prevalence of dementia increases as the population ages and the age-standardized mortality rate for dementia as the cause of death has increased during recent years (an increase of 34.7% from 2009 to 2019) and dementia represented 19% of all deaths in the year 2019 (Official Statistics of Finland, 2019). CVD and cancer represented 34% and 25%, of all deaths, respectively. However, in the older population, among persons over 75 years of age, the proportion of dementia-caused deaths was higher (27%), as was the proportion of CVD related deaths (38%), and the proportion of cancer as a cause of death was lower (19%) (Official Statistics of Finland, 2019).

2.4 Institutionalization

The definition of institutionalization or long-term care (LTC) varies somewhat between countries. The Organization for Economic Co-operation and Development defines LTC as the need for day-to-day help with activities such as washing and dressing, or help with household activities such as cleaning and cooking along with some types of medical care (Organization for Economic Co-operation and Development, 2021). Unlike in many countries, in Finland, home care is not included in the definition of LTC (Sosiaali- ja terveysministeriö, 2017a). LTC in Finland includes the decreasing number of LTC provided by primary care long-term units and by nursing homes, and the increasing number of LTC provided by 24/7 assisted living units (Forma et al., 2017).

Traditionally, 24/7 assisted living has been the lightest form of LTC and the older people needing special care have been housed in primary care long-term units (Forma et al., 2017). In Finland, health care center wards nowadays provide foremost acute care and rehabilitation, and LTC is provided mostly by 24/7 assisted living units, even for older people with increasing medical care needs (Sosiaali- ja terveysministeriö, 2017b). In Finland, 11.9% of inhabitants aged 75 years or older were in need of institutional care in the year 2014 (Sosiaali- ja terveysministeriö, 2017a).

Institutional care and institutionalization is hereafter defined as a permanent entry into a primary care long-term unit, nursing home or 24/7 assisted living unit, the choice of which is strongly affected by the time of institutionalization as the two former LTC options were more prevalent earlier, and the latter is the most prevalent nowadays (Forma et al., 2017), and these are not separately assessed in the analyses.

2.4.1 Future Prospects of Institutionalization

Most of older adults prefer to "age in place", at home, in familiar surroundings (de Jong et al., 2022; Wiles et al., 2011). The proportion of older people institutionalized during their life time varies between countries, municipalities and communities, and depends on multiple demographic, epidemiological and socioeconomic factors, including possibilities for home care and informal care, in addition to national and/or municipal policies (CORDIS EU, 2013). However, the percentage increase in the number of institutional care users is projected to be higher than the percentage increase in the number of formal home care users (CORDIS EU, 2013).

The timing, extent and speed of population ageing varies between countries (CORDIS EU, 2013). In Finland, the population is ageing fast with the number and proportion of inhabitants 70 years or older growing constantly. Therefore, many municipalities will need to urgently assess their future need for institutional care.

The goal of policy in Finland is to decrease institutionalization and increase home care to enable older people to live at home longer (Sosiaali- ja terveysministeriö, 2017b). This is a political, and also an economical issue as institutional care is the smallest, but most expensive part of older people's care in Finland (Sosiaali- ja terveysministeriö, 2017b) and is mostly paid for and provided by municipalities. However, a Finnish study on the care profiles of older people during the last two years of life found that while majority of older people lived at home until the very last months of life, there was an increase in the need of institutional care (Aaltonen et al., 2017). This occurred during the time of the policy change from institutional based care to home based care (Aaltonen et al., 2017).

In the Netherlands, were the admission into institutional care is nowadays needs-based, somewhat similarly as in Finland, the use of formal or informal home care has increased while the use of institutional care has decreased (Alders et al., 2017; Alders & Schut, 2019). They found no difference in the needs of care for those age cohorts, but found the change to likely be due to the combined effects of changes in policy, technological advances and changes in the social norms (Alders et al., 2017). They still project an increasing need of institutional care because of the rapidly ageing population, as while the care needs of most older people can be met at home while ageing in place, the more advanced needs of some older people are met only by institutional care (Alders & Schut, 2019).

Also, people with dementia are often in need of informal or formal care and eventually institutional care. However, it is often not considered that the care of a home-dwelling person with severe dementia could infact be more expensive than institutional care (Pitkälä et al., 2020).

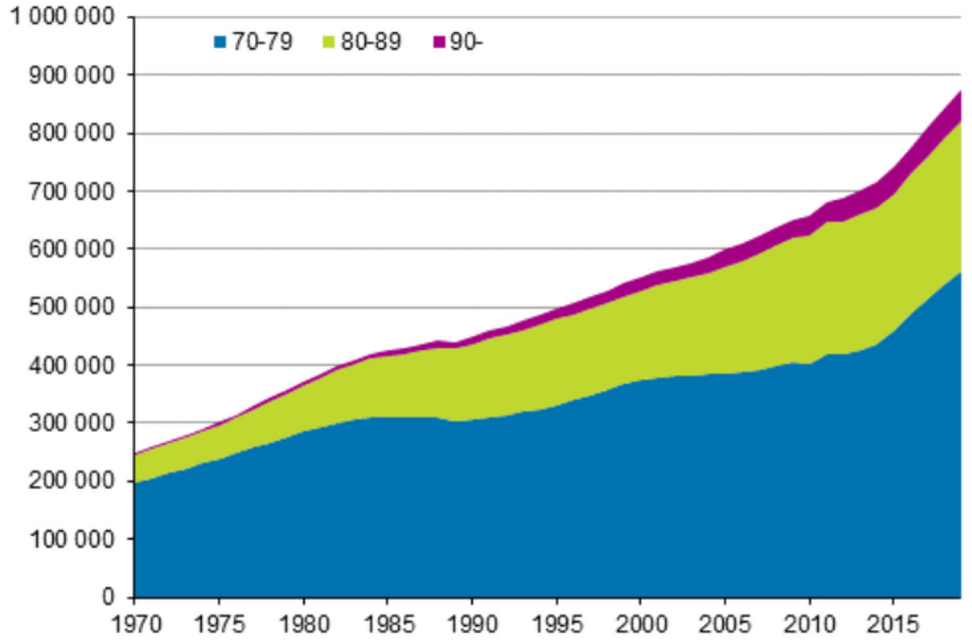

Figure 2. Number of persons aged 70 or over in Finland in 1970 to 2019. Source: Official Statistics of Finland (OSF): Population structure [e-publication]. ISSN=1797-5395. 2019. Helsinki: Statistics Finland [referred: 25.10.2021]. Access method: http://www.stat.fi/til/vaerak/2019/vaerak_2019_2020-03-24_tie_001_en.html Reprinted according to the Creative Commons Attribution 4.0 International License.

2.4.2 Factors Associated with Increased Risk of Institutionalization

Earlier research has shown that higher age, living alone, low socioeconomic status, use of home care, low number of specialist visits, frailty, low SRH, low body mass index (BMI), dementia and cognitive decline, functional impairment including walking difficulties and falls, several chronic conditions and multimorbidity are associated with an increased risk of institutionalization in older people (Andel et al., 2007; Bravell et al., 2009; Gonzalez-Colaço Harmand et al., 2017; Hajek et al., 2015; Koller et al., 2014; Luppa et al., 2012; Luppa, Luck, Weyerer, et al., 2010; Rockwood et al., 2004, 2006; Salminen et al., 2020, 2017).

Dementia, neurological disorders, mood disorders, stroke, diabetes and hip fracture have been associated with an increased risk of institutionalization (Koller et al., 2014; Nihtilä et al., 2008). Dementia naturally increases the risk of inability to live at home and has been found to increase the risk of institutionalization in older people in many studies (Hajek et al., 2015; Halonen et al., 2019; Koller et al., 2014; Luppa, Luck, Weyerer, et al., 2010; Salminen et al., 2020). In people with dementia,

the advanced stage of the disease, behavioral symptoms and many social factors have been associated with an increased risk of institutionalization (Luppa et al., 2008). In people without dementia, functional disabilities such as slow gait speed, the inability to walk 400 meters; the effects of stroke and cardiac infarction; and low SRH have been found to increase the risk of institutionalization (Andel et al., 2007; Luppa, Luck, Matschinger, et al., 2010).

2.5 Frailty

Frailty in older adults is a complex and much studied entity. It has been described as a phenotype including weight loss, exhaustion, low physical activity, slowness and weakness (Fried et al., 2001), as well as the accumulation of deficits related to ageing (Mitnitski et al., 2002; Rockwood & Mitnitski, 2007). Frailty researchers are divided by these two lines of research. The current consensus on the definition of frailty is that "frailty is a clinical state in which there is an increase in an individual's vulnerability for developing an increased dependency and/or mortality when exposed to a stressor" (Rodríguez-Mañas et al., 2013). This can be applied to both the phenotype version (Fried et al., 2001) and tools based on that (Morley et al., 2012), and to the accumulation of deficits version (Mitnitski et al., 2002; Rockwood & Mitnitski, 2007) and tools based on that (Blodgett et al., 2016; Burn et al., 2018; Searle et al., 2008). Guidelines for the screening and management of frailty have recently been described (Dent, Morley, et al., 2019). The clinical characteristics include anorexia, sarcopenia, osteoporosis, fatigue, risk of falls, and poor physical health (Strandberg & Pitkälä, 2007).

Frailty is linked to ageing but cannot be determined simply by age. In ageing, a gradual decline in physiological reserves occurs, but in frailty, this is accelerated and the decline occurs in multiple organ systems (Clegg et al., 2013). Chronic inflammation has been suggested as the potential mechanism (Chen et al., 2014).

Frailty overlaps with disability and comorbidity (Fried et al., 2004). Having multiple chronic conditions does not necessarily mean the individual is frail or disabled as the mere presence of chronic conditions does not always lead to frailty or disability. However, if left untreated and/or if the individual develops multiple conditions, they may develop frailty and/or disability. It is important to evaluate all of these separate entities (frailty, disability and comorbidity) as each of them requires a different intervention (Fried et al., 2004).

2.5.1 Prevalence of Frailty

The prevalence of frailty by three systematic reviews is shown in Table 1. The prevalence is affected by the minimal age chosen for the inclusion criteria, the setting

of the study (community-based or non-community-based) and the frailty tools used (Collard et al., 2012; O'Caoimh et al., 2018, 2021). The prevalence of frailty increases with age (O'Caoimh et al., 2021). The accumulation of deficits –definition yields often higher prevalence than the phenotype-based definition (Koivukangas et al., 2021; O'Caoimh et al., 2018, 2021; Perttilä et al., 2017).

When analyzing a global younger study population (aged 50 years or over, 62 countries, altogether 1,731,107 individuals), the prevalence of frailty by the phenotype definition was highest in Africa 22% (95% CI 10–37%) and by accumulation of deficits in Oceania 31% (95% CI 20–42%) (O'Caoimh et al., 2021). The lowest prevalence using both measures was in Europe (8%; 95% CI 7–10% and 19%; 95% CI 16–21%, respectively), reflecting probably the differences in prevalence between HICs and LMICs (O'Caoimh et al., 2021).

Also, there seems to be an increase in the prevalence of frailty in more recent cohorts than in earlier cohorts of people aged 65 or older, even when accounting for period, gender, marital status, education, socioeconomic status, lifestyle and social factors (Yu et al., 2018). Another study comparing a more recent (2010) and and an earlier (2002) cohort of people aged over 70 years found also that there is no evidence for improvement in levels of frailty across cohorts (Marshall et al., 2015). More recent age cohorts of over 70 years had higher levels of frailty compared with earlier cohorts and it was apparent particularly for the poorest group of people (Marshall et al., 2015). This may reflect the improvement in prevention and health care that enables longer survival even for the frail individuals (Marshall et al., 2015). A Finnish study, however, found that the prevalence of frailty was higher in an earlier birth cohort (born in 1935) in comparison to a more recent birth cohort (born in 1945) when assessed at the age of 70 years (Koivukangas et al., 2021).

Frailty is more prevalent in women than in men (Clegg et al., 2013; O'Caoimh et al., 2018; Song et al., 2010). However, regarding the risk of adverse effects related to frailty, women seem to tolerate frailty better (Gordon et al., 2017; Song et al., 2010). A systematic review and meta-analysis found that for any age group, the mean degree of frailty by Frailty Index (FI) was greater in women than in men (Gordon et al., 2017). It also showed that men had an increased mortality rate compared with women at each level of the FI indicating that women tolerate frailty better when regarding survival. Frailty prevalence is also higher in persons with lower education, low socioeconomic status and in persons from ethnic minority groups (Feng et al., 2017).

Table 1. The prevalence of frailty according to systematic reviews.

Author, year	Region	Number of countries	Community or non-community	Number of studies/datasets reviewed	Number of participants	Age of the participants, years	Frailty assessed by	Prevalence (95% CI)	Remarks
Collard et al. 2012	Global	18	community-based	21 studies	61,500	≥65	any definition	10.7% (10.5–10.9%)	
			community-based	15 studies	44,894	≥45	phenotype-based definitions	9.9% (9.6–10.2%)	
			community-based	8 studies	24,072	≥45	broad definition of the phenotype	13.6% (13.2–14.0%)	
O'Caoimh et al. 2018	Europe	22	community- and non-community-based	62 studies / 68 datasets	77,400	≥65	any definition	18% (15–21%)	number of participants counted from the prevalence data
			community-based	53 studies	90,175	≥45	any definition	12% (10–15%)	number of participants counted from the prevalence data
			non-community-based	15 studies	6,913	≥60	any definition	45% (27–63%)	number of participants counted from the prevalence data
			community-based	45 studies	49,682	≥45	phenotype-based definitions	12% (10–14%)	number of participants counted from metadata
			community-based	8 studies	10,688	≥50	other than phenotype-based definitions	16% (7–29%)	number of participants counted from metadata

Author, year	Region	Number of countries	Community or non-community	Number of studies/datasets reviewed	Number of participants	Age of the participants, years	Frailty assessed by	Prevalence (95% CI)	Remarks
O'Caoimh et al. 2021	Global	62	community-based	240 studies / 253 datasets	1,731,107	≥50	any definitions	17% (16–18%)	
			community-based	178 studies	360,438	≥50	physical frailty	12% (11–13%)	
			community-based	71 studies	1,334,964	≥50	accumulation of deficits	24% (22–26%)	

2.5.2 Incidence of Frailty

The global incidence of frailty among community-dwelling older adults aged 60 years or over was investigated in a systematic review and meta-analysis (Ofori-Asenso et al., 2019). They found twenty studies that reported the incidence of frailty among 17,523 people who were robust and 19,613 people who were pre-frail at baseline and who survived over a median follow-up of 3.0 years. During the follow-up, 4.6% of robust individuals and 18.5% of pre-frail individuals developed frailty. Ten studies compared the frailty incidence between 11,959 men and 13,870 women who survived a median follow-up of 4.0 years and found that 9.2% of men and 15.6% of women developed frailty. The incidence of pre-frailty was investigated in 21 studies among 32,268 community-dwelling older adults who were robust at baseline and survived a median follow-up of 2.5 years, and 30.9% of them became pre-frail during the follow-up (Ofori-Asenso et al., 2019).

In this systemic review and meta-analysis (Ofori-Asenso et al., 2019), they found that the incidence was higher when using the physical phenotype than when using other methods, in contrast to the finding on prevalence (Collard et al., 2012). HICs were associated with a lower incidence of frailty than LMICs (Ofori-Asenso et al., 2019), which combined with the knowledge of the trajectory of frailty in recent age cohorts compared with earlier cohorts especially in the poorer individuals (Marshall et al., 2015), paints a grim picture for the future at least for the lower socioeconomic group.

2.5.3 Clinical Implications of Frailty

Frailty is associated with a higher risk of death (Clegg et al., 2013; Fried et al., 2001; Rockwood & Mitnitski, 2007), but it is not recorded as an official cause of death in Finland, even if it were present at time of death. Frailty is also associated with increased risk of falls, hospitalization, institutionalization and morbidity in older adults (Clegg et al., 2013; Fried et al., 2001; Hajek et al., 2015; Kojima, 2018a; Rockwood et al., 2006).

Therefore, frailty should be screened for to identify older individuals at higher risk of adverse effects (Kojima, 2018a). The task force of the International Conference of Frailty and Sarcopenia Research have prepared the international clinical practice guidelines for identification and management of physical frailty and they recommend that all adults aged 65 years or older should be offered screening for frailty using a simple, validated frailty instrument suitable to the specific setting or context (Dent, Morley, et al., 2019). Primary care was seen as the logical place for screening, particularly in the early stages of frailty when it is more likely to respond to interventions.

The recommended screening tools (Dent, Morley, et al., 2019) include the Clinical Frailty Scale (CFS) (Rockwood et al., 2005), the FRAIL Scale (FS) (Morley et al., 2012) and the Edmonton Frailty Scale (EFS) (Rolfson et al., 2006). The EFS includes

also tests on cognition and functional performance (Rolfson et al., 2006) making it more time-consuming than the CFS (Rockwood et al., 2005), a clinical assessment done by the professional using a nine-point pictorial scale paired with corresponding text describing classifications of frailty, and the FS (Morley et al., 2012), that includes five self-reported items and is thus fast and feasible to use in the clinical setting. CFS is however, a subjective measure done by professionals using the pictorial scale for reference (Rockwood et al., 2005). However, a new app has been created to help standardize the professional's assessments (*Clinical Frailty Scale App*, 2020).

Although the task force recommends screening for frailty in older adults, they acknowledge that there is no evidence-base for the fact that frailty screening would lead to improved management of older people with frailty, or that it would be cost-effective (Dent, Morley, et al., 2019). When screening for frailty, the task force recommends that all individuals screened positive for frailty or pre-frailty would be subjected to a Comprehensive Geriatric Assessment (CGA) and an individual comprehensive management plan should follow (Dent, Morley, et al., 2019). This plan should include the treatment of sarcopenia, polypharmacy, present and underlying chronic conditions, and treatable causes of undernutrition (Dent, Morley, et al., 2019). Also frail older adults should be offered a multi-component physical activity program that should include a progressive resistance-training component (Dent, Morley, et al., 2019). Exercice to preserve and increase muscle mass and strength and appropriate nutrition are first-line treatments of frailty (Strandberg & Pitkälä, 2007). The goal of the interventions is to delay or reverse the cascade of frailty, which is possible because it is a dynamic state (Figure 3) (Dent, Morley, et al., 2019).

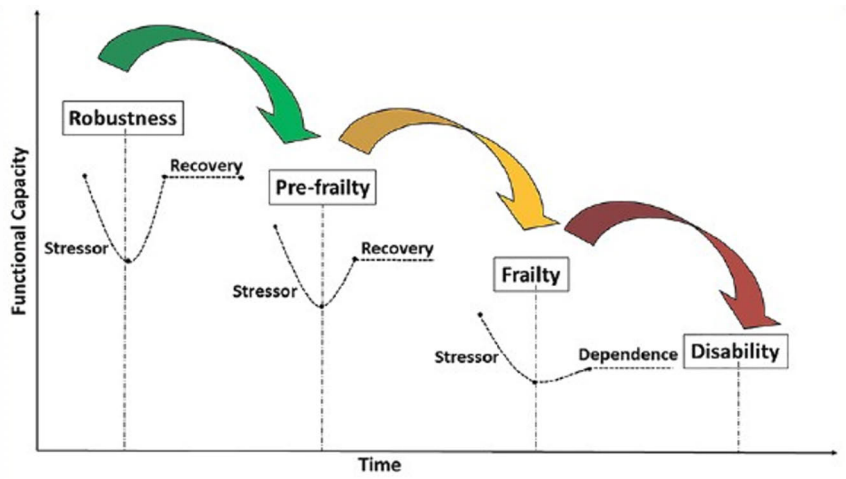

Figure 3. The cascade of functional decline in older adults from independence, through to frailty and disability (in the absence of intervention). Reprinted from (Dent, Morley, et al., 2019). Copyright © The Authors. Distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/).

A scoping review on frailty interventions (Puts et al., 2017) including 14 studies examining the effects of interventions on frailty found that nine of the intervention studies were effective in preventing or reducing frailty using the level of frailty as the intervention target. The effective interventions included exercise, nutrition, cognitive training, geriatric assessment and management, and prehabilitation (Puts et al., 2017). Of these interventions, the ones with exercise (varied programs) were the most significant, with mixed results for geriatric assessment (Puts et al., 2017). The intervention programs were feasible with adherence rates around 70% (Puts et al., 2017). Mean ages of the participants were in the seventies and eighties (Puts et al., 2017). However, despite encouraging results in studies examining interventions, the evidence-based knowledge of the quality of the intervention and their effects is still low (Dent, Martin, et al., 2019).

A Finnish study showed that CGA based individually targeted multifactorial interventions were effective in maintaining the ability to walk 400 meters among pre-frail and frail community-dwelling older adults when comparing them to a control group without the interventions (Tikkanen et al., 2015). The SPRINTT study showed that a multicomponent intervention was associated with a reduction in the incidence of mobility disability in frail older adults (Bernabei et al., 2022). A randomized clinical trial of 12-month home-based physical exercice in comparison to usual care in frail and pre-frail older Finnish adults resulted in a reduction of the severity of frailty (Suikkanen et al., 2022).

Frailty is a dynamic state and transitions between robust, pre-frail and frail occur (Gill et al., 2006). During follow-up periods from baseline to 18 months, from 18 months to 36 months, and from 36 months to 54 months, most of the participants categorized as robust at baseline still remained robust or transitioned back to robust (51.5%, 54.8% and 47.5%, respectively) (Gill et al., 2006). Most of the pre-frail also remained in or transitioned back to the original category (58.3%, 55.1% and 57.7%, respectively) (Gill et al., 2006). A substantial proportion of robust individuals transitioned to pre-frail (40.1%, 37.3% and 43.3%, respectively), and pre-frail individuals to frail during the follow-up periods (24.9%, 25.0% and 26.1%, respectively) (Gill et al., 2006). The majority of frail individuals remained in or transitioned back to the original category (63.9%, 66.0% and 66.1%, respectively), and an increasing proportion of them died during the follow-up periods (13.1%, 16.0% and 20.1%, respectively) (Gill et al., 2006). There were also transitions to the other direction during the follow-up periods: from pre-frail to robust (11.9%, 16.5% and 9.5%, respectively), and from frail to pre-frail (23.0%, 17.9% and 12.9%, respectively) (Gill et al., 2006) suggesting that interventions could truly make a difference.

2.5.4 Implications of Frailty for the Health Care System

Frailty is associated with increased use and cost of health-care services (Hoogendijk et al., 2019). Higher frailty was associated with higher health-care use, both outpatient and in-hospital (Hoogendijk et al., 2019). Frailty was associated with increased total, outpatient, in-hospital and postoperative health-care costs (Hoogendijk et al., 2019). The implications for LMICs are especially difficult as their population is ageing faster and the health-care system would need to adapt quickly and the resources for that might be more scarce than in HICs (Hoogendijk et al., 2019). In addition to health care costs, frailty is associated with a substantial increase in social care costs (Nikolova et al., 2022).

Primary care is the natural place for identifying frailty (Strandberg & Pitkälä, 2007). Also, the possible interventions should be based in the primary care sector in order to be as feasible as possible. These goals require resources.

Identifying frail older adults is also crucial in acute care as frailty has a notable impact on the patient's manifestation of illnesses and also on their reaction to treatments and on outcomes. However, a recent Finnish study found no benefits when a CGA was performed on frail and pre-frail patients in the emergency department (Alakare et al., 2021). There is earlier evidence on CGA increasing the likelihood of still living at home 3 to 12 months after a hospital stay when performed in geriatric wards or by mobile teams after acute admission to hospital (Ellis et al., 2017). Frailty should also be taken into account when planning specialist or surgical care to better determine who can benefit from the available treatments and who instead could suffer harm from them (Hoogendijk et al., 2019).

2.5.5 Identifying Frailty – Frailty Tools

The ability to predict adverse outcomes is the critical determinant of a frailty tool's effectiveness (Gonzalez-Colaço Harmand et al., 2017). FS is a recommended (Dent, Morley, et al., 2019; Morley et al., 2013) frailty screening tool, simple to use and can also be obtained from data included in a CGA (Lopez et al., 2012; Morley et al., 2012; Woo et al., 2012). PRISMA-7 (Raîche et al., 2007) is also a feasible frailty screening tool with high sensitivity and moderate specificity in identifying frailty in community-dwelling older people (Apóstolo et al., 2017). The FI is a broadly validated frailty tool with good predictive capability (Mitnitski et al., 2005; Rockwood & Mitnitski, 2007; Song et al., 2010). The FI has low to moderate sensitivity, but good specificity to frailty (Apóstolo et al., 2017). These three tools are used in this thesis.

The visual CFS (Rockwood et al., 2005) and the classic Fried phenotype of frailty (Fried et al., 2001) can also be used to identify frailty. Also, an electronic FI

derived directly from electronic patient record system has been described (Clegg et al., 2016).

2.5.5.1 FRAIL Scale

FS includes 5 items (Morley et al., 2012): fatigue, resistance (ability to climb one flight of stairs), ambulation (ability to walk 100 meters), illnesses (more than five) and loss of weight (>5%). The items are scored 1 point for each component and an individual is categorized as robust (0 points), pre-frail (1–2 points), or frail (3–5 points) (Morley et al., 2012).

A systematic review on modifications of the phenotype criteria (Theou et al., 2015) found that modifying the components affects the precision, especially the specificity, of the frailty tool but it is still able to identify persons at higher risk of adverse effects. Modifications, such as replacing measurable criteria with self-report criteria, are often used in population based research, as they are more feasible in the clinical setting. The same systematic review (Theou et al., 2015) touched on the modifications made to the cut-off points of the original phenotype and found that many researchers consider the original cut-off points as the golden standard but also some researchers choose to adjust the cut-off points according to the study population, and this might increase the prevalence of frailty found by the tool.

FS has been validated in different populations (Lopez et al., 2012; Morley et al., 2012; Thompson et al., 2020) and predicts mortality, functional decline and disability (Dent et al., 2016; Lopez et al., 2012; Morley et al., 2012; Thompson et al., 2020), although it doesn't identify all the same individuals as frail as other frailty tools (Theou et al., 2013) and the diagnostic test accuracy can depend on the cut-off used (Thompson et al., 2020).

2.5.5.2 PRISMA-7

PRISMA-7 was originally intended to screen for disability (Raîche et al., 2007) but has since been used also as a frailty screening tool, and frailty and disability have been shown to overlap (Fried et al., 2001). PRISMA-7 has also been validated as a frailty tool in different populations (Yaman & Ünal, 2018).

PRISMA-7 contains seven simple self-reported items to identify frailty: older than 85 years, male, health problems that limit activities, support of another person needed, health problems requiring staying at home, social support, and use of a cane/walker/wheelchair. For every "yes" answer the individual gets one point and a total score of three or more points is deemed frailty (Raîche et al., 2007). PRISMA-7 has good accuracy in identifying frailty in community-dwelling older people but tends to over-screen (Dent et al., 2016).

2.5.5.3 Frailty Index

FI is based on the theory of accumulation of deficits (Mitnitski et al., 2001). It is widely validated (Mitnitski et al., 2005) and has been shown to predict mortality and institutionalization (Mitnitski et al., 2005; Rockwood & Mitnitski, 2007; Song et al., 2010). It is considered a comprehensive, multidimensional frailty tool with good predictive ability, with the drawback being that it tends to be time-consuming and thus not feasible for screening in the busy clinical setting (Dent et al., 2016).

A standard procedure for creating a frailty index has been described (Searle et al., 2008). Briefly, a frailty index should include 30 to 40 variables, and the more variables are included, the more precise estimates become, but also the use of the tool becomes more infeasible (Searle et al., 2008). The variables chosen should be associated with health status, their prevalence should increase with age but not saturate too early, and all the variables must cover a range of organ systems (Searle et al., 2008). The index is expressed as a ratio of deficits present in the individual to the total number of deficits considered and cut-off points of robust (FI≤0.08), pre-frail (FI 0.09–0.24) and frail (FI ≥0.25) are most commonly used (Song et al., 2010). The rate of deficit accumulation per year has been suggested to be 0.03 (Mitnitski et al., 2001, 2005; Rockwood & Mitnitski, 2007), and the estimate for the age-invariant limit to the FI has been suggested to be ~0.67 beyond which the individual is not likely to survive (Mitnitski et al., 2005; Rockwood & Mitnitski, 2007).

FI is widely used in research for its good predictive capability (Apóstolo et al., 2017; Dent et al., 2016), although it can be too time consuming in the clinical setting, if not readily available from CGA data (Burn et al., 2018), or directly electronically calculated from patient record data (Clegg et al., 2016).

The FI has also been regarded as a proxy measure of ageing, a measure of the individual's biological age (Mitnitski et al., 2002). A personal biological age (PBA) can be calculated from the FI by assessing the mean results of the FI at any given age among a population and then allocating a PBA for each person by comparing their FI score with the mean scores of the population at different ages (Mitnitski et al., 2002). PBA is a stronger correlate to mortality than chronological age (CA) (Mitnitski et al., 2002). However, the same approach in a Chinese population yielded different results: they found the CA a better predictor of mortality than the PBA (Goggins et al., 2005).

2.6 Subjective Health Measures

Subjective health measures include self-evaluated and self-reported measures. It is personal what the individual includes in their evaluation of subjective health (Jylhä, 2009). For research purposes, it is useful to define subjective health measures in order to get comparable answers (DeSalvo et al., 2005).

2.6.1 Self-Rated Health

SRH is an individual's own perception of their health and as such, a subjective assessment (Jylhä, 2009). How the individual perceives their health is of course unique (Jylhä, 2009). Two persons with the same chronic conditions causing the same amount of disability can perceive their SRH differently. However, SRH has been associated with all-cause mortality in older adults (Mossey & Shapiro, 1982). Poor SRH as been shown to associate with certain biomarkers, such as lower hemoglobin and higher white cell count, describing perhaps the biological connection for the association with mortality (Jylhä et al., 2006).

SRH is often evaluated by a question on the respondents global SRH (GSRH), for example "How would you describe your current state of health?" but also comparative SRH (CSRH) can be used, for example "How would you describe your current state of health compared to others of the same age?" (DeSalvo et al., 2005).

The association of SRH with mortality persists in different age groups (DeSalvo et al., 2005), even in the very old (> 90 years) population (Tiainen et al., 2013). There are cultural differences as to how individuals perceive their health (Jylhä et al., 1998; Vuorisalmi et al., 2008), but poor SRH has been associated with a higher risk of death also in different ethnicities (Hirve et al., 2012; Santiago et al., 2010). People with poor SRH had a two-fold all-cause mortality risk than persons with excellent SRH, and the responses to a simple GSRH question maintained a strong association with mortality even after adjustments for key covariates (DeSalvo et al., 2005). Poor SRH has also been associated with cardiovascular mortality in populations with and without prior cardiovascular disease (Mavaddat et al., 2014).

In people with mild Alzheimer's disease (AD), poor SRH was not associated with increased mortality (Nielsen et al., 2016). This was thought to be due to loss of insight associated with AD (Nielsen et al., 2016). There was a similar finding when studying people with subjective memory complaints (Nielsen et al., 2014).

The association of poor SRH with increased mortality has been identified in both genders (DeSalvo et al., 2005; Ferraro & Wilkinson, 2015), with some differences between genders found in previous studies (Reile et al., 2016; Szybalska et al., 2018; Vuorisalmi et al., 2005). Reile et al. (2016) found SRH to be a better predictor of mortality in older men than in older women. Szybalska et al. (2018), however, found SRH a better predictor of mortality in women than in men aged 65 years or older, when accounting for important covariates. In the very old population (>90 years) the association of poor SRH with mortality was stronger in women than in men, although it has to be considered that there were substantially less men in that age group (Tiainen et al., 2013). Vuorisalmi et al. (2005) found that both GSRH and CSRH were better predictors of mortality during a 5-year follow-up in older men than in women, and that they worked better in women only after a 10-year follow-up. However, only a few women died during the 5-year follow-up and that of course

affected these results (Vuorisalmi et al., 2005). Despite these differences, the association of poor SRH and increased mortality is clear in both genders.

Also, poor SRH has been associated with institutionalization in both genders (Gutman et al., 2001; Luppa, Luck, Weyerer, et al., 2010; Saevareid et al., 2007). SRH has been also associated with health-care expenditure: it predicted expenses as well as a more comprehensive evaluation of health or diagnosis-based risk assessment (DeSalvo et al., 2009).

A person's sense of coherence (SOC) has been regarded as the ability to find and utilize resources more efficiently, even when they are scarce (Suominen et al., 2001). Individuals with strong SOC perceive their life as comprehensible, manageable and meaningful, even when facing difficulties. The individual's SOC has been found to influence also their future subjective health (Suominen et al., 2001).

The concordance and differences in predictive abilities of SRH and physician rated health (PRH) have also been studied. A study comparing the concordance of SRH and PRH (based on registered illnesses) found SRH a better predictor of institutionalization (Thygesen et al., 2009). Having the combination of poor SRH and poor PRH has been associated with a higher risk of death than the combinations of poor SRH but good PRH or good SRH but poor PRH (Giltay et al., 2012). PRH, although based on registered illnesses, is however, a subjective assessment made by the professional and thus cannot be considered purely as an objective health measure.

2.6.2 Self-Reported Walking Ability

Slowness is part of the classic phenotype definition of frailty (Fried et al., 2001) and can be assessed by gait speed. Gait speed is associated with frailty status and declines with age (Clegg et al., 2015; Jung et al., 2018). Also slow gait speed on its own has been associated with an increased risk of death and institutionalization (Apóstolo et al., 2017; Jung et al., 2018; Rothman et al., 2008; Studenski et al., 2011).

Also other means for assessing walking ability and their association with adverse effects have been studied. The Short Physical Performance Battery (SPPB) has been shown to predict short-term mortality and institutionalization (Guralnik et al., 1994). However, the SPPB is not a feasible screening test as it requires a professional to evaluate it. The SPPB also includes gait speed evaluation and because gait speed alone has been shown to predict mortality and institutionalization in older people (Jung et al., 2018; Rothman et al., 2008; Studenski et al., 2011), the additional tests included in the SPPB are surplus in regarding predictions of adverse effects. The Timed Up and Go test (Podsiadlo & Richardson, 1991) has been shown a strong and independent predictor of short-term mortality in a community-dwelling population of older people (Chua et al., 2020), but it also requires a professional to evaluate it thus impeding it's feasibility in screening.

Slow gait speed is associated with the inability to walk 400 meters (Chang et al., 2004) and the self-reported ability to walk 400 meters coincides well with the controlled walking ability (Sayers et al., 2004). Also, self-reported walking ability has been shown a very good indicator of mobility performance in community-dwelling older adults (Alexander et al., 2000). Hence, the use of self-reported data on walking ability could be utilized instead of physical measures (Alexander et al., 2000).

2.6.3 Satisfaction with Life

Satisfaction with life is also a subjective assessment. Socioeconomic factors, perceived health and social relationships are associated with satisfaction with life (Barger et al., 2009). A study on near-centenarians and centenarians found SRH and basic functional abilities predictors of satisfaction with life despite the decline in objective health (Jopp et al., 2016). The adaptation to declining health while maintaining good satisfaction with life could be the key in ageing successfully (Jopp et al., 2016).

High satisfaction with life compared to low satisfaction is associated with reduced mortality and better SRH (Kim et al., 2021). Also, frailty is associated with satisfaction with life, particularly satisfaction with one's health (St John et al., 2013).

2.7 Objective Health Measures

Objective health can be measured by disease counts, using weighed indices or using the definition of multiple chronic conditions, i.e. multimorbidity.

2.7.1 Multimorbidity

Multimorbidity is generally based on disease counts as it is most often defined as having two or more chronic conditions, but could also be defined by testing the number of conditions which best identify individuals at higher risk of adverse effects in the study population (Johnston et al., 2018). Multimorbidity can also be assessed using weighed comorbidity indices, such as the Charlson Comorbidity Index (Charlson et al., 1987), or a simpler comorbidity index for use in the primary care setting (Carey et al., 2013). Comorbidity is not, however, the same as multimorbidity. Comorbidity means additional chronic conditions that are somehow associated with the index condition (Valderas et al., 2009), whereas multimorbidity can include any conditions, associated with others within the individual, or not.

Multimorbidity is also a risk factor for frailty but they are two distinct concepts. They can, however, contribute to each other. A systematic review and meta-analysis

(Vetrano et al., 2019) found that the prevalence of frailty among individuals with multimorbidity (definitions in different studies ranging from two or more chronic conditions being the most common, to even six or more chronic conditions) was 16% (95% CI 12–21%), and the prevalence of multimorbidity among frail individuals was 72% (95% CI 63–81%). Most of the studies included in the meta-analysis used the phenotype definition of frailty, but some used the FI, which often already includes chronic conditions or even multimorbidity as one item (Vetrano et al., 2019). Multimorbidity increased the likelihood of being frail almost two-fold, but only a small proportion of individuals with multimorbidity had developed frailty (Vetrano et al., 2019).

The prevalence of multimorbidity has increased in primary care (Uijen & van de Lisdonk, 2009). Uijen & van de Lisdonk (2009) discovered that among people aged 65 or older, the prevalence of only one chronic condition had remained the same when the prevalence of having two or three chronic conditions had increased in a 20-year follow-up. The prevalence of having four or more chronic conditions had tripled during the follow-up period (Uijen & van de Lisdonk, 2009). A systematic review found greatest variance in multimorbidity prevalence at the age of 75 years (Fortin et al., 2012).

As multimorbidity increases, it is the most common condition managed in primary care (Bierman & Tinetti, 2016). This increase is probably due to both the ageing population and the improved diagnostics. However, the evidence-based guidelines to managing patients with comorbidities have been vague (Lugtenberg et al., 2011). In this systematic analysis of evidence-based guidelines, Lugtenberg et al. (2011) found that the current guidelines have only limited applicability to patients with comorbid conditions and suggested that more patients with comorbidities should be included in future clinical trials to gather information on the most prevalent combinations of chronic conditions. This systematic analysis considered comorbidity, not multimorbidity, but managing multimorbidity faces the same problem.

Just recently, the National Institute for Health and Care Excellence in the United Kingdom published a guideline for the clinical assessment and management of multimorbidity (National Institute for Health and Care Excellence, 2016) where they also highlight the assessment of frailty in multimorbid older adults to better target the treatments and care with a person-centered vision. Also in Finland, the Finnish Medical Society Duodecim published the Current Care Guideline for Multimorbidity in which they highlight the need for identifying high risk multimorbid patients, and focusing their care towards better acknowledgement of functional ability and quality of life (Working group set up by the Finnish Medical Society Duodecim and the Finnish General Medicine Society, 2021).

The awareness for identifying and caring for multimorbid older adults is increasing, which is a positive trend as multimorbidity has been shown to predict mortality (Carey et al., 2013; Halonen et al., 2019; Huntley et al., 2012; Soh et al., 2020) and institutionalization (Halonen et al., 2019; Koller et al., 2014; Salminen et al., 2020). An increased risk of institutionalization has been associated with multimorbidity defined by two or more (Salminen et al., 2020), and three or more chronic conditions (Halonen et al., 2019; Koller et al., 2014). A systematic review of prevalence studies on multimorbidity (Fortin et al., 2012) suggested that in addition to the multimorbidity definition of two or more chronic conditions, at least the definition of three or more chronic conditions should be used in order to better identify those at higher risk of adverse effects.

2.8 Successful Ageing

SA is the term widely used in research for depicting extraordinary or exceptional ageing in contrast to usual ageing. According to the classic concept by Rowe and Kahn, SA is defined as avoiding disease and disability, having high cognitive and physical function, and being actively engaged with life (Rowe & Kahn, 1997). The term SA has, however, been deemed a little controversial as it implies that usual ageing would be somehow unsuccessful and thus the concept of SA would be stigmatizing to those not categorized as successful agers (Cosco et al., 2014; Rolfson, 2018).

SA in research has been defined in various ways and thus, comparing or combining the results of different studies is difficult (Cosco et al., 2014). This review by Cosco et al. (2014) highlighted that this vast heterogeneity will require this concept to be framed multidimensional instead of unidimensional. According to this review, 92.4% of the reviewed operational definitions included physiological constructs (physical functioning, cognitive function, illness/disease presence, health status, longevity, mental health), 49.5% engagement constructs (active life/social engagement, support system), 48.6% well-being constructs (satisfaction with life/well-being, affective status), 25.7% personal resources (resilience, independence/autonomy), and 5.7% extrinsic factors (finances, environment) (Figure 4) (Cosco et al., 2014). The number of constructs included varied from one to five (mean 2.2, median 2, SD 1.1) (Cosco et al., 2014).

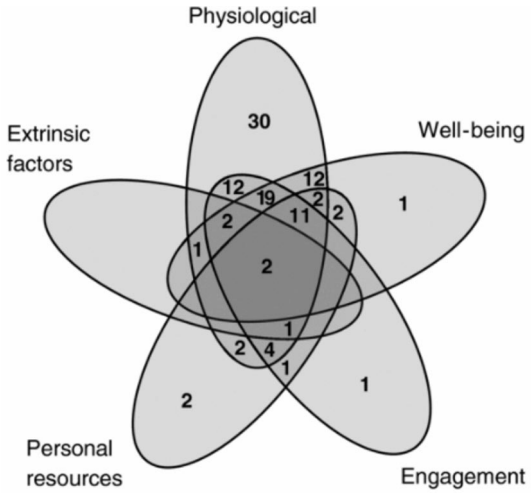

Figure 4. Frequency of studies identifying SA constructs: a Venn diagram. Modified from (Cosco et al., 2014) with permission from Cambridge University Press. Copyright © International Psychogeriatric Association 2013.

There was a marked difference in prevalence of SA when using researcher defined SA (26.0%; 95% CI 22.1–29.9%) and participant defined self-rated SA (71.3% ; 95% CI 56.4–86.2%) (Cosco et al., 2014). The definitions in these different studies had commonalities as well: SA is considered vastly more complex than mere survival and cannot be defined simply by absence of illness/disease (Cosco et al., 2014). Different definitions of SA and its history are also well explained in a recent review: the evolvement of the concept has led to inclusion of psychosocial factors in addition to physical factors, and the acknowledgement of also the older adults' values, what they themselves regard as a success in ageing (Martin et al., 2015).

A Finnish review on successful ageing depicted the concept as including both subjective and objective measures of biomedical (health and functional ability) and psychosocial factors (adaptation to ageing and engagement in life) (Urtamo et al., 2019). These factors lead to healthy, active and productive ageing and thus to ageing successfully (Urtamo et al., 2019). Also, the will-to-live has been associated with survival in community-dwelling older adults irrespective of age, gender and comorbidities (Karppinen et al., 2012).

SA has also been investigated as the possible opposite of frailty and the two have similarities that could imply a continuum: both are considered to have biomedical explanations and multidimensional characteristics; and both have similar strategies of operationalization including biomarkers, physical phenotypes, performance-based measures and multidimensional models that also include psychosocial aspects (Rolfson, 2018). In this systematic review, Rolfson (2018) describes four original articles that used explicit criteria for both frailty and successful ageing. Frailty was

assessed by the phenotype criteria (Fried et al., 2001) and the SA measures were a blend of functional independence, quality of life, cognition and SRH (Rolfson, 2018). The phenotype definition for frailty doesn't capture the multidimensional aspects such as cognition or mood, but using the same definition makes comparisons between studies possible. However, for SA, there was heterogeneity in the measures used thus making comparisons challenging (Rolfson, 2018). This depicts the lack of consensus on the definition of SA. The prevalence of frailty and SA varied between the studies and this could be due to different populations, different measurements used and also due to different age-categories used (frailty prevalence from 11.8% to 44.0%, and SA prevalence from 10.4% to 47.2%) (Rolfson, 2018). There were overlaps of the SA groups and the pre-frail and frail groups, and in some studies, they were quite significant (Rolfson, 2018). If frailty and SA were at the opposite end of a continuum, no overlap of this magnitude should exist. Rolfson (2018) explains that the continuum view seems to be supported by biomedical factors, while the differences become more apparent as psychosocial elements are included. Rolfson (2018) concludes that there are marked differences in how frailty researchers and SA researchers see those concepts and collaboration would be in order.

2.8.1 Resilience

Psychological resilience is defined by the American Psychological Association as "the process of adapting well in the face of adversity, trauma, tragedy, threats, or significant sources of stress" (American Psychological Association, 2020). High resilience in older adults has been associated with better quality of life, better mental health, wellbeing and satisfaction with life, and also longevity (MacLeod et al., 2016). Physical resilience has been defined as "a characteristic at the whole person level which determines an individual's ability to resist functional decline or recover physical health following a stressor" and is linked to psychosocial, genetic and environmental factors (Whitson et al., 2016). Psychological resilience refers to the person's ability to adapt in the face of sources of stress and physical resilience to the maintenance or recovery of function after the challenge (Whitson et al., 2018). Hence, they are distinct concepts. In addition, although sometimes referred to as the opposite of frailty (robust) in studies, physical resilience encompasses more than that. It has been suggested that if robustness describes the plenty of physiological potential the individual has to react to stressors, physical resilience would describe the ability to actualize that potential (Whitson et al., 2016).

Do the words of Sir Winston Churchill, "Success consists of going from failure to failure without loss of enthusiasm" apply in ageing successfully? The meaning of ageing in place has been related to a sense of identity both through independence and autonomy, and through caring relationships and roles in the community (Wiles

et al., 2011). Also, social networks and familiarity of the surroundings were considered important resources for ageing well in place (Wiles et al., 2011).

2.8.2 Exceptional Longevity

Studying the modifiable risk factors for exceptional longevity in a cohort of older men revealed no surprises: abstinence from smoking, managing weight, controlling blood pressure and exercising regularly during early older years were associated with longevity and also good health and function during older years (Yates et al., 2008).

One study investigating near-centenarians and centenarians found that 78% of them were women, 75% widowed, and an unexpectedly large proportion of them were still community-dwelling (74%) (Jopp et al., 2016). They had on average five illnesses and most had difficulties with instrumental activities, but 67% reported good or excellent SRH (Jopp et al., 2016). Also, mental health was good and few had cognitive restrictions (Jopp et al., 2016). Satisfaction with life was moderate, 66% reported moderate to excellent satisfaction with life (Jopp et al., 2016). There was a positive correlation with life satisfaction and number of living children, personal activities of daily living and SRH, which correlated negatively with number of illnesses (Jopp et al., 2016). The main finding was that in contrast to their poor objective health, their subjective health was good, although many of them had limitations in their social activities, suggesting these survivors have high resilience (Jopp et al., 2016).

A study on Finnish nonagenarians found that SA by a concept constructed with physical, psychological and social components was associated with increased survival even in this very old population (Nosraty et al., 2015). Not only the physical health, but also the psychological and social components were associated with survival (Nosraty et al., 2015). In this same population of nonagenareans, poor SRH has also been associated with increased mortality (Tiainen et al., 2013).

2.8.3 Chronological and Biological Age

The person's CA is naturally a risk factor for certain illnesses, death and institutionalization, but chronological age doesn't take into consideration the vast heterogeneity of the older people (Rockwood et al., 1994). At the same CA their functional and cognitive abilities can be very different (Rockwood et al., 1994).

Frailty has been proposed as the proxy measure of ageing (Mitnitski et al., 2001), and the concept of biological age based on the FI has been proposed (Mitnitski et al., 2002). Frailty is better at predicting adverse effects than CA, making it a true proxy of biological age (Clegg et al., 2013). Also biomarkers have been studied as the measure of biological age (Mitnitski et al., 2015). However, a recent review found

that frailty is a clinically and research-relevant proxy for biological ageing and biomarkers can be used to supplement that, but currently are not feasible on their own (Diebel & Rockwood, 2021).

A PBA can be calculated from the FI by assessing the mean results of the FI at any given age among a population and then allocating a PBA for each person by comparing their FI score with the mean scores of the population at different ages (Mitnitski et al., 2002). The difference between the individual's CA and PBA has been proposed as relative fitness (if PBA younger than CA) and relative frailty (if PBA older than CA) (Mitnitski et al., 2002). The calculations are somewhat population specific and comparisons of PBAs (counted from the FI) across different populations should be made cautiously (Mitnitski et al., 2002).

2.8.4 "Eyeball Test"

Traditionally, the risks and benefits of major surgeries have been assessed clinically by the operator using the "eyeball test". Essentially, this has been an assessment of the patient's frailty status and with that, the risks and benefits of surgery. However, the "eyeball test" has been shown to be unreliable in assessing frailty and thus, the higher risks related to operating on an frail older person (Jain et al., 2014). This study compared different clinicians' assessments of frailty ("eyeball tests") with each other and found them inconsistent. Also, they found poor correlation between the "eyeball test" and a validated frailty tool (Jain et al., 2014).

Nowadays, more emphasis is given to validated frailty tools when planning care for an older person (Yanagawa et al., 2019). The CFS is one suggested tool to use instead of the traditional eyeball test (Yanagawa et al., 2019). It is easy to use and with the helpful images and texts, could be considered as an upgraded "eyeball test" (Afilalo, 2017).

3 Aims

This thesis aimed to investigate the association of frailty by three frailty tools (FS, PRISMA-7 and FI), SRH, self-reported walking ability, subjective and objective health, chronic conditions and multimorbidity, with institutionalization and mortality among a community-dwelling Finnish population of older people; and to describe the possible factors leading to successful ageing in the same population.

The specific aims were:

1. To assess the association of frailty with institutionalization and mortality, and the association of SRH and self-reported walking ability with institutionalization (Studies I and II).
2. To assess the association of subjective and objective health with institutionalization and mortality (Study III), and the association of chronic conditions and multimorbidity with institutionalization (Study IV).
3. To describe the still community-dwelling participants after a 20 year follow-up and the possible factors leading to their successful ageing (Study V).

4 Materials and Methods

4.1 Study Population

This study is part of the longitudinal Lieto study, a clinical, epidemiological study of subjects aged 64 years or older. It was carried out in Lieto, a semi-industrialized rural municipality in South-Western Finland.

All residents born in the year 1933 or earlier living in Lieto on February 16th of 1998 (n=1596; 666 men and 930 women, 12% of the population) were invited, in a random order, to participate in the study at baseline. Of those eligible, 63 died before the baseline examination, 190 refused, 69 did not respond, 4 had moved elsewhere and 10 could not be traced (Figure 5). The refusal rate was 15%, 22%, and 27% in subjects aged 64–74, 75–84, and 85 years or older, respectively. The most common reason for declining was ill health (44/190). Altogether 1260 subjects participated in the baseline examination, 533 men and 727 women (Löppönen et al., 2003). The participation rate was 82%. An outlier, institutionalized at the age of 17 years in year 1930 was excluded from all analyses in this thesis.

In this thesis, cross-sectional data collected between March 1998 and September 1999 were used as baseline information. In addition, data on the participants' acquired chronic conditions, institutionalization and mortality were collected from the electronic patient record system and official national records up till January 2017, providing a follow-up-period of 18 years.

Additionally, for Study V, the data on chronic conditions, institutionalization and mortality were gathered from the electronic patient record system up till June of 2018, when the still community-dwelling participants were invited for re-examination that took place 20 years after the baseline examination.

For Study V we invited the original study participants still living at home in the municipality of Lieto in June of 2018 (n=221) for re-examination that took place between September and November of 2018. Before the re-examination, five were deceased and three were institutionalized. Seventy-five subjects did not participate, leaving 138 participants for the re-examination. Participants needing daily formal or informal care were excluded from the statistical analyses leaving 112 participants for Study V. There were in addition 53 admissible possible participants who declined to participate. Of those, 44 (83%) answered by mail.

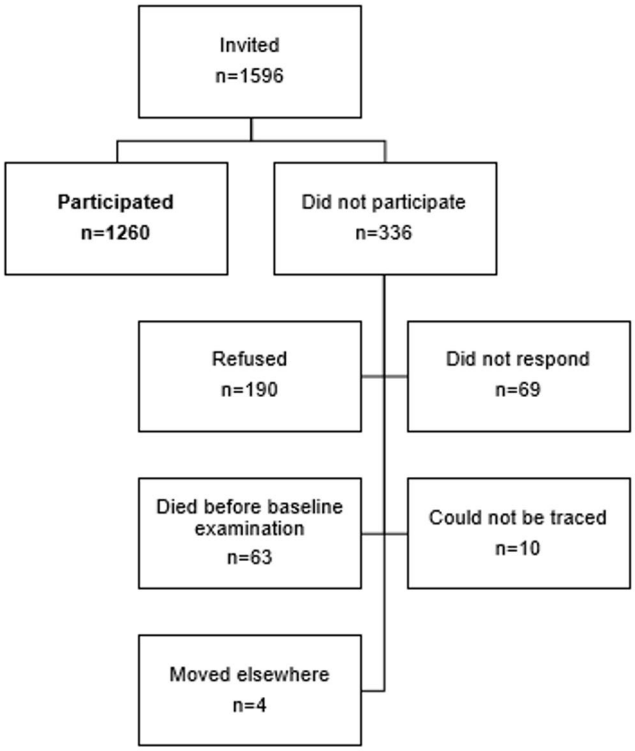

Figure 5. Flow chart of the original Lieto study

4.2 Methods

4.2.1 Baseline Examination

Baseline examination took place between March 1998 and September 1999. The study protocol (Löppönen et al., 2003) consisted of an extensive interview performed by the study nurse (n=1260) on sociodemographic factors, health behavior, functional ability, sense of well-being, quality of life and medication; measurements of weight, height, blood pressure, pulse, vision and hearing; the Mini-Mental State Examination (MMSE) (Folstein et al., 1975) and the Zung Self-Rating Depression Scale (SDS) (Zung, 1965). The participants were examined by the research physician and their medical records were reviewed (n=1252). In this comprehensive examination of participants and their health history, their former diagnoses were recorded and new diagnoses were set when appropriate (Löppönen et al., 2003). The participants were referred to additional examinations and treatments if necessary.

4.2.2 Frailty Tools

The frailty tools used in this thesis were FS, PRISMA-7 and FI. The tools were chosen because of their known properties in predicting adverse effects in older people (Dent et al., 2016), and also because the information needed to use these tools was available in the baseline data.

4.2.2.1 FRAIL Scale

The FS includes five components: fatigue, resistance (ability to climb one flight of stairs), ambulation (ability to walk 100 meters), illnesses (more than five) and loss of weight (>5%). One point is assigned for each component and respondents are classified as robust (0 points), pre-frail (1–2 points) or frail (≥3 points) (Morley et al., 2012).

In this thesis, a modified version of the FS was used as all of the exact information on the five components was not available in the baseline data. In addition, the information on illnesses was gathered from the participants' medical records and not as self-report data.

The five components used in this thesis were assessed by: *fatigue* by SDS (Zung, 1965) question "I get tired for no reason" and scored positive if answered "good part of the time" or "most of the time"; *resistance* by self-reportedly being unable to climb stairs; *ambulation* by self-reportedly being unable to walk 400 meters; *illnesses* by reviewing the participant's medical records for five or more of the selected illnesses (high blood pressure, diabetes, cancer, chronic lung disease, myocardial infarction, congestive heart failure, angina, arthritis, stroke and kidney disease); and *loss of weight* by the SDS (Zung, 1965) question "I notice that I am losing weight" and scored positive if answered "good part of the time" or "most of the time". Participants with missing data were excluded from the analyses (n=44). Each of the components were assigned 1 point and the original cut-off points were used: robust (0 points), pre-frail (1–2 points), or frail (3–5 points) (Morley et al., 2012).

4.2.2.2 PRISMA-7

PRISMA-7 includes seven self-reported components: age over 85 years, male gender, health problems which limit activities, support of another person needed, health problems requiring staying at home, social support, and use of a walking aid or a wheelchair. One point is assigned for each "yes" response and respondents are classified as robust (0–2 points) or frail (≥3 points) (Raîche et al., 2007).

In this thesis, a modified version of the PRISMA-7 was used as all of the exact information on the seven components was not available in the baseline data. The information on age and gender was available and the other components were

assessed as follows: *health problems which limit activities* was substituted with rather poor or poor self-rated health which was assessed by the question "How would you describe your current state of health?" with answer options of "very good", "good", "average", "rather poor" and "poor"; *support of another person needed* was assessed by needing help with taking care of personal hygiene and/or with taking care of finances, on which the information was gathered from the extensive interview performed by the study nurse; *health problems requiring staying at home* was assessed by self-reportedly being unable to move outdoors; *social support* was assessed by self-reportedly having someone close to count on in case of need for help; and *use of a walking aid or a wheelchair* was specified as use of a stick, walker/rollator or wheelchair. Participants with missing data were excluded from the analyses (n=91). Each of the components were assigned 1 point and the original cut-off points were used (Raîche et al., 2007).

4.2.2.3 Frailty Index

FI originally included 92 items from which the index was calculated (Mitnitski et al., 2001). Since then, a standard procedure for creating a frailty index has been proposed (Searle et al., 2008). This suggests that the FI is constructed with at least 30 to 40 variables. More variables are also possible but using more impedes the feasibility. When creating the standard procedure, it was found that the results of the FI are insensitive to the precise composition of the index and the variables can therefore be selected quite freely at random (Searle et al., 2008). However, the variables chosen must satisfy the following criteria: must be associated with health status, the deficit's prevalence must increase with age, the deficit must not saturate too early in life, the chosen variables must cover a range of systems as a group and if the FI is to be used serially on the same people, the items in it must stay the same. The items can be symptoms, signs, disabilities, diseases or laboratory measurements (Searle et al., 2008).

In this thesis, the FI was constructed using 36 deficits (Table 2). The information on the chosen variables was gathered from the baseline data including the extensive interview by the study nurse and physical examination and review of the medical records by the study physician. The index was calculated as the ratio of deficits present in the individual to the total number of deficits considered. Missing of two items was permitted and the index was calculated accordingly, i.e. the total number of deficits considered was 34 to 36 per participant. Participants with more items missing were excluded from the analyses (n=76). Previously described cut-off points were used: robust ≤0.08, pre-frail 0.09–0.24 and frail ≥0.25 (Song et al., 2010).

The deficits used were selected by the previously described criteria (Searle et al., 2008) and included self-report data, clinical assessments and data discovered by reviewing the participant's medical records.

Table 2. Frailty Index items.

Assessed by interview	Assessed clinically	Assessed by reviewing medical records
Needs help for toileting	Suffers from the effects of stroke	Arthritis or rheumatism
Needs help for dressing and undressing	Hearing problem	High blood pressure
Needs help for preparing meals	Speech problem	Heart disease[j]
Needs help for house work		Chronic bronchitis or emphysema
Needs help for heavy household chores		Diabetes mellitus
Needs help for personal care		Cancer
Needs help for moving about inside house		Stomach or intestinal ulcers
Difficulties carrying or lifting light loads		Hip or femoral fracture
Mobility problem[a]		Other medical problems[k]
Limited activities[b]		Five or more medications
No regular physical exercise		
Bodily pain[c]		
Memory problem[d]		
Vision problem[e]		
Urinary incontinence		
Stool incontinence		
Shortness of breath		
Angina pectoris		
Resting tremor		
Feeling hopeless[f]		
Emotional problem[g]		
Weight loss[h]		
Feeling tired all the time[i]		

[a]Scored positive if needing any walking aid or the help or another
[b]Scored positive if has four or less activities out of 11
[c]Assessed by the question "Have you had pain in the last 4 weeks?" and scored positive if answered "mild", "average", "hard" or "very hard" with the other options being "not at all" and "very mild"
[d]Assessed by the question "Do you consider your memory to be inferior to others of the same age on average?" and scored positive if answered anything other than "no"
[e]Assessed by the question "Can you see enough to ambulate in foreign surroundings?" and scored positive if answered "no"
[f]Assessed by the SDS[l] question "I feel that others would be better off if I were dead" and scored positive if answered "some of the time", "good part of the time" or "most of the time"
[g]Assessed by the SDS[l] question "I feel down hearted and blue" and scored positive if answered "good part of the time" or "most of the time"
[h]Assessed by the SDS[l] question "I notice that I am losing weight" and scored positive if answered "good part of the time" or "most of the time"
[i]Assessed by the question "Have you felt tired or listless for at least two weeks?" and scored positive if answered "yes"
[j]Known heart disease (ICD-10[m]: I20–I25, I48, I49)
[k]Other disease (ICD-10[m]: E03, E05, G20, G35, J44–J46, M15–M17, M47)
[l]Zung Self-Rating Depression Scale
[m]10[th] Revision of the International Statistical Classification of Diseases and Related Health Problems

4.2.3 Self-Rated Health

SRH was assessed by the question “How would you rate your current state of health?” with the answer options of “very good”, “good”, “moderate”, “poor” and “very poor”. For the analyses, the options were collapsed into three categories: “very good” and “good” were collapsed into “good”, and “poor” and “very poor” were collapsed into “poor”, with “moderate” staying the same.

4.2.4 Self-Reported Walking Ability

Self-reported walking ability was assessed by the question “Are you able to walk at least 400 meters?” with the answer options of “no”, “if someone helps”, “with difficulty, but without help” and “without difficulty”. For the analyses, the options were collapsed into two categories: “no” including the answer options of “no” and “if someone helps”, and “yes” including the answer options of “with difficulty, but without help” and “without difficulty”.

4.2.5 Satisfaction with Life

Satisfaction with life was assessed by the question “How would you rate your current satisfaction with life?” with the answer options of “very satisfied”, “satisfied”, “moderately satisfied”, “unsatisfied” and “very unsatisfied”. For the analyses in Study V, the answer options were collapsed into three categories: “very satisfied” and “satisfied” were considered as good satisfaction with life, and “unsatisfied” and “very unsatisfied” were considered as poor satisfaction with life, with “moderate” staying the same.

4.2.6 Subjective Health

In Study III, we used a broader definition of subjective health instead of the simple SRH. Subjective health was defined in line with the WHO’s definition: “Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity” (World Health Organization, 1948). Participants were categorized as subjectively healthy if they met all the following criteria: SRH very good or good, self-reported satisfaction with life very good or good, and self-reportedly able to walk 400 meters independently, with or without difficulties.

The data were gathered at the baseline examination by the questions: “How would you rate your current state of health?” with the answer options of “very good”, “good”, “moderate”, “poor” and “very poor”; “How would you rate your current satisfaction with life?” with the answer options of “very satisfied”, “satisfied”, “moderately satisfied”, “unsatisfied” and “very unsatisfied”; and “Are you able to

walk at least 400 meters?" with the answer options of "no", "if someone helps", "with difficulty, but without help" and "without difficulty".

4.2.7 Objective Health

In Study III, we used an objective health measure to combine and compare with the subjective health measure. Objective health was defined by the baseline data of the participant's registered illnesses gathered from the patient records and clinical examination. The illnesses were classified according to the 10th International Statistical Classification of Diseases and Related Health Problems (ICD–10) (World Health Organization, 2019) and the illnesses considered are shown in Table 3.

Participants were considered objectively healthy if they didn't have any of the illnesses. The cut-off point for objectively healthy was chosen to best identify subjectively and objectively healthy, the "super healthy" participants. That is also why we chose so many illnesses to consider in Study III. These illnesses were selected by assessing which illnesses could affect a person's objective health. At this point, no consideration for the prevalence of these illnesses in the study population was made. The selection was deliberately broad to find those truly objectively healthy.

Table 3. Registered illnesses used in defining objective health.

ICD-10[a]	Registered illness
C0–C97 (except C44.01, C44.11, C44.21, C44.31, C44.41, C44.51, C44.61, C44.71, C44.81, C44.91)	Malignant neoplasms (except basal cell carcinomas)
E10–E14	Diabetes mellitus
F00–F03	Dementia
F10	Alcohol induced disorders
F19	Drug use induced disorders
F30–F39	Mood disorders
G10–G26	Systemic atrophies, extrapyramidal and movement disorders
G30	Alzheimer's disease
G35	Multiple Sclerosis
G45	Transient cerebral ischaemic attack
G62	Other polyneuropathies
I11	Hypertensive heart disease
I20–I25	Ischaemic heart disease
I34–I37	Valve disorders
I48	Atrial fibrillation
I60–I69	Cerebrovascular disorders
I70	Atherosclerosis
I73.9	Peripheral vascular disease, unspecified
J40–J47	Chronic lower respiratory diseases
M05–M06	Rheumatoid arthritis
M45	Ankylosing spondylitis
N17–N19	Renal failure

[a]10th Revision of the International Statistical Classification of Diseases and Related Health Problems

4.2.8 Combined Health Information

In Study III, the subjective and objective health measures were combined into four categories: subjectively and objectively healthy (SO), subjectively healthy but objectively unhealthy (S), subjectively unhealthy, but objectively healthy (O), and subjectively and objectively unhealthy (UH). The associations of combined health information with institutionalization and mortality were investigated.

4.2.9 Acquired Conditions

For Study IV, we wanted to consider chronic conditions' or illnesses' association with institutionalization. In addition to the baseline information on the participants' chronic conditions, we gathered the information on the acquired conditions during the follow-up period of 18 years. We only included participants institutionalized or deceased during the follow-up period of 18 years to ascertain that we had gathered all the chronic conditions acquired during the participants' lifetime, and also to ascertain that the participants weren't institutionalized at a later date.

The data were gathered from the official Finnish Care Register for Health Care including the Register of Primary Health Care Visits, where they are coded by ICD-10 (World Health Organization, 2019), and from the municipality's electronic patient record system by individually reviewing the participants' patient records. Coding the ICD-10 codes for every visit has not earlier been the norm for the physicians working in Lieto Health Care Center, and that is why we also needed to review the patient records to ascertain that we included all diagnoses of the considered chronic conditions as they were not always coded by ICD-10, and thus were not included in the official national records.

We considered 17 chronic conditions or groups of conditions in Study IV: malignant neoplasms (except basal cell carcinomas), iron deficiency anaemia, B12-vitamin anaemia, hypothyroidism, diabetes mellitus, hypercholesterolemia, dementia, mood disorders, neurological disorders (systemic atrophies, extrapyramidal and movement disorders, referred to hereafter as neurological disorders), hypertension, ischaemic heart disease, atrial fibrillation, intracranial haemorrhage, stroke, atherosclerosis, chronic lower respiratory diseases, and renal failure.

For Study IV, we selected the conditions on the basis of the distribution of the conditions in the study population during the follow-up period. This decreased the amount of conditions considered when compared to Study III. Also some conditions were added on the basis of previous research into factors associated with institutionalization. In Study III the emphasis was finding the truly objectively healthy participants. In Study IV the emphasis was investigating the conditions that were prevalent in the study population and were previously known to be associated

with institutionalization. Also, the definition of multimorbidity was desired to be based on conditions prevalent in the study population.

4.2.10 Multimorbidity

For Study IV, we used the data on participants' acquired conditions during the follow-up period of 18 years to define multimorbidity and examine its association with institutionalization. Multimorbidity was defined various ways to define the best cut-off for multimorbidity in this study population: two or more chronic conditions (multimorbidity2+), three or more chronic conditions (multimorbidity3+), four or more chronic conditions (multimorbidity4+), five or more chronic conditions (multimorbidity5+), and six or more chronic conditions (multimorbidity6+).

For the purpose of analyzing the association of chronic conditions and multimorbidity with institutionalization in participants without dementia, we excluded the participants with dementia.

4.2.11 Institutionalization

Institutionalization was defined as a permanent entry into a nursing home, a primary care long-term unit or a 24/7 assisted living unit. Data on institutionalization were gathered from the electronic patient record system by individually investigating the participants' patient records, and coded by month and year of entry. By investigating the patient records, we also excluded the participants who had moved to another municipality during the follow-up-period (n=86) as institutionalization could not be ascertained on their part. We also excluded the participants already living in institutional care at baseline (n=67). Exclusions left us with 1106 participants for the institutionalization analyses.

Also, for Study V, which included a re-examination after the original follow-up period, the data on institutionalization were gathered from the electronic patient record system before the re-examination.

4.2.12 Mortality

Data from all participants who died before January 2017 were obtained from the official Finnish Cause of Death Registry using unique personal identification numbers.

Also, for Study V, which included a re-examination after the original follow-up period, the data on mortality were gathered from the electronic patient record system before the re-examination.

4.2.13 Re-examination

In Study V, we wanted to explore the factors that could be related to ageing successfully. We invited all original participants still living at home in the municipality of Lieto to participate in the re-examination. Flow-chart of the re-examination is shown in Figure 6.

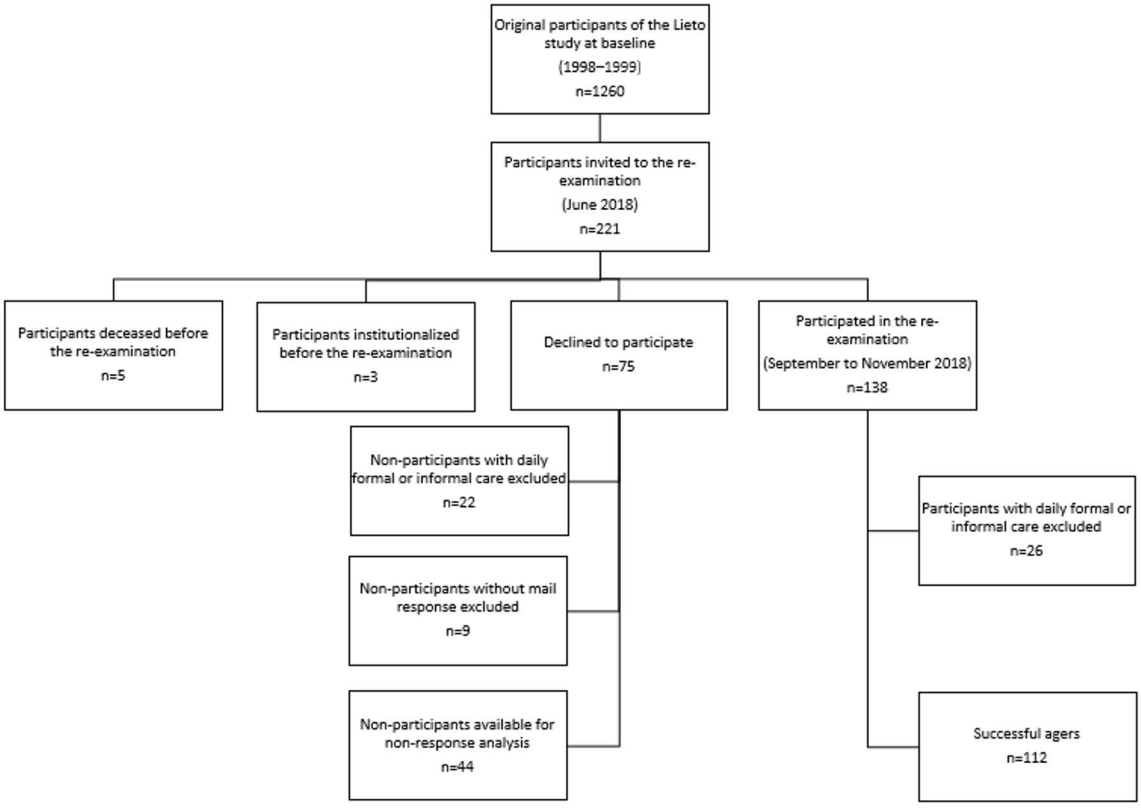

Figure 6. Flow chart of the re-examination. Reprinted from Study V (Viljanen et al., 2023). Submitted.

The re-examination was performed in collaboration with the study nurse and the study physician at the participants' home or at the Lieto Health Care Center. It included an extensive interview on socioeconomic factors, health behavior, functional ability, sense of well-being and quality of life. Also measurements of weight, height, blood pressure, pulse, vision and hearing were performed. The study nurse performed the MMSE (Folstein et al., 1975) and the SDS (Zung, 1965).

In this re-examination, more attention was paid on the functional ability of the participants and in addition to self-reported data on walking ability, gait speed and

grip strength were measured. SRH and satisfaction with life were recorded as well as the overall subjective health as described in Study III, and chronic conditions as described in Study IV. The need of daily formal or informal care was gathered from the electronic patient record system.

The physical examination was performed by the study physician, a specialist in general practice with years of experience in primary care caring for mostly older adults. In addition to the physical examination, a review of the participants' medical records including all medications used was performed. Former diagnoses were recorded and new ones were set when appropriate. The participants were referred to additional examinations if necessary.

Frailty was assessed using FS, PRISMA-7 and the FI, and a PBA was counted from the FI both at baseline and at re-examination. A PBA can be calculated from the FI by assessing the mean results of the FI at any given age among a population and then allocating a PBA for each person by comparing their FI score with the mean scores of the population at different ages (Mitnitski et al., 2002). The study physician also made a clinical judgment as to whether the participants seemed younger than their chronological age, the same, or older than their chronological age. This judgement was based on the clinical appearance of the participant at time of re-examination, the "eyeball test". PBA was compared to the CA, and the difference between the CA and the PBA was categorized in three categories: PBA lower than CA, PBA the same as CA and PBA higher than CA. The PBA was considered the same as the CA if they were within a year of each other. This difference was then compared to the physician's clinical assessment as to whether the participant seemed younger than, the same as, or older than their chronological age.

The data acquired in the re-examination were combined with the data of the baseline examination to compare the baseline and re-examination results within the individuals. In Study V, we wanted to investigate the successful agers. We defined SA as the ability to live at home without daily formal or informal care at the age of 84 years or over. We excluded the participants with a need for daily care leaving 112 participants for the statistical analyses, although we re-examined all of the 138 participants. We also analyzed the available data on the 44 non-participants that declined but responded by mail. Also, the successful agers' responses on satisfaction with life were compared to the responses of the re-examined participants with daily formal or informal care and the non-participants with daily formal or informal care.

The participants were all offered an extensive medical management plan and also the opportunity to discuss this plan and their own expectations for their future medical care with a nurse at the Lieto Health Care Center.

4.2.14 Statistical Analyses

Descriptive statistics are shown as the number of subjects, as proportions with percentages for categorical variables, and as means with standard deviations (SD) for normally distributed continuous variables. Differences in baseline categorical characteristics were tested using the Chi squared test (Studies I-IV). Differences in baseline continuous variables were compared with two-sample t-test (Studies I, II, IV), or with one-way analysis of variance using Tukey-s method in pairwise comparisons between four groups (Study III). The follow-up periods were calculated from the baseline measurements to the end of the follow-up period of 10 and 18 years, or to the institutionalization or death of the individual. Death was used as a competitive factor in the institutionalization analyses (Studies II-IV). The follow-up period for Study V was 20 years.

Hazard rations (HR) and their 95% confidence intervals (CI) were calculated using Cox proportional hazard models (Studies I-IV). P values less than 0.05 were considered statistically significant. All statistical analyses were performed using SAS System for Windows, version 9.4 (SAS Institute Inc., Cary, NC, USA).

In Study I, the association of frailty (characterized using three commonly used approaches: FS, PRISMA-7 and FI) with mortality was investigated by Cox proportional hazard models. First, unadjusted Cox regression analyses were conducted for the association of the three frailty tools with mortality. Second, Cox regression analyses for FS and FI were adjusted for age and gender, which are items of PRISMA-7. The interaction between gender and frailty indices were included in the Cox regression models. The follow-up periods were calculated from baseline measurements to the end of the follow-period of 10 and 18 years or to the death of the individual.

In Study II, the association of frailty by three frailty tools (FS, PRISMA-7 and FI), SRH, and self-reported walking ability with institutionalization were investigated by Cox proportional hazard models. First, unadjusted Cox regression analyses were conducted for the three frailty tools, SRH and self-reported walking ability. Second, Cox regression analyses for FS, FI, SRH and self-reported walking ability were adjusted for age and gender, which are items of PRISMA-7. The interactions between gender and all explanatory variables were included in the Cox regression models. The follow-up periods were calculated from baseline measurements to the end of the follow-period of 10 and 18 years or to the institutionalization of the individual. Death was used as a competing factor in the analyses.

In Study III, the association of subjective and objective health with institutionalization and mortality were investigated by Cox proportional hazard models. First, unadjusted Cox regression analyses were conducted for the association of combined health information (subjective and objective health) with

institutionalization and mortality. Second, Cox regression analyses were adjusted for age, BMI, MMSE scores and education. Also, relative excess risk due to interaction (RERI), attributable proportion due to interaction (AP) and the Synergy Index (S_y) were calculated for subjective and objective health (Andersson et al., 2005). The follow-up periods for mortality analyses were calculated from the baseline measurements to the end of the follow-up period of 10 and 18 years or to the death of the individual. In institutionalization analyses, the follow-up periods were calculated from the baseline measurements to the end of the follow-period of 10 and 18 years or to the institutionalization of the individual. Death was used as a competing factor in the institutionalization analyses.

In Study IV, the association of chronic conditions and multimorbidity with institutionalization were investigated by Cox proportional hazard models. Multimorbidity was defined different ways to best identify the cut-off for the association with institutionalization. The different cut-offs analyzed were multimorbidity2+, multimorbidity3+, multimorbidity4+, multimorbidity5+ and multimorbidity6+. First, unadjusted Cox regression analyses were conducted for the association of chronic conditions and multimorbidity with institutionalization. Second, Cox regression analyses were adjusted for age, gender, living situation and MMSE scores. Third, unadjusted and adjusted multivariable analyses featuring variables found significantly associated with an increased or decreased risk of institutionalization were conducted. Fourth, unadjusted Cox regression analyses were conducted for the association of chronic conditions and multimorbidity with institutionalization in participants without dementia and then adjusted for age, gender, living situation and MMSE scores. The follow-up periods were calculated from the baseline measurements to the end of the follow-up period of 18 years or to the institutionalization of the individual. Death was used as a competing factor in the analyses.

In Study V, we combined the baseline data and re-examination data of the successful agers to investigate the possible factors associated with their SA. Differences between the variables at baseline and re-examination were examined with binary logistic regression for dictotomous variables and ordinal logistic regression for ordinal variables. Generalized estimating equations with exchangeable correlation structure for dichotomous variables and independent correlation structure for ordinal variables were used to account for the correlation between the repeated measurements. Results are shown as odds ratios (OR) with 95% CI. Sensitivity, specificity, positive predictive value and negative predictive value for the clinician's "eyeball test" to identify participants with a PBA younger than their CA was calculated. Differences in categorical variables between the successful agers and the non-participants, and between the successful agers and the re-examined participants with daily formal or informal care and the mail-responders

with daily formal or informal care, were examined with the Chi squared test. Difference in mean age was examined with the two-sample t-test.

4.2.15 Ethical Issues

Studies included in this thesis were conducted according to the guidelines of the Declaration of Helsinki. The Ethics Committee of the Hospital District of Southwest Finland approved the study protocol. Participants provided written informed consent for the study.

5 Results

5.1 Characteristics of the Participants

The mean age of the participants (n=1259) at baseline (1998–1999) was 73.5 years (SD 6.8, range 64–100). There were 532 (42%) men and 727 (58%) women. Education level was low, only 12% had more than a basic education (basic defined as six years of elementary school). Most of the participants had MMSE scores equal to or higher than 26 points (72%). Most were living with someone, only 30% were living alone at baseline.

5.2 Prevalence of Frailty (Study I)

The prevalence for frailty by the FI was highest, 24%. PRISMA-7 categorized 17% of the participants as frail and the FS only 2%. The prevalence of pre-frailty by FI and FS were 57 and 32 percent, respectively. Frailty and pre-frailty were more common in women by FI and FS, and in men by PRISMA-7.

Altogether 1083 participants were assessed for frailty by all three frailty tools used: FI, FS, and PRISMA-7. The overlap by different frailty tools used is shown in Table 4. Only 20% of the participants were categorized as frail or robust identically according to all three tools (2% frail, 18% robust).

Table 4. Overlaps of FRAIL Scale, Frailty Index and PRISMA-7.

	Frailty Index (n = 1118)				PRISMA-7 (n = 1110)		
FRAIL Scale	**Robust**	**Pre-frail**	**Frail**	**P-value**	**Robust**	**Frail**	**P-value**
			n (%)				
Robust	199 (92)	468 (74)	74 (28)	<.001	684 (74)	62 (33)	<.001
Pre-frail	18 (8)	168 (26)	166 (63)		234 (25)	111 (58)	
Frail	0 (0)	0 (0)	25 (9)		2 (0)	17 (9)	
Frailty Index					(n = 1090)		
Robust					212 (24)	4 (2)	<.001
Pre-frail					583 (65)	50 (27)	
Frail					107 (12)	134 (71)	

5.3 Prevalence of Institutionalization (Study II)

In Study II, we excluded participants already living in institutional care at baseline (n=67) and participants no longer living in the municipality of Lieto (n=86) as it was not possible to ascertain whether they were still living at home or institutionalized in another municipality, leaving 1106 participants for the analyses. During the 10- and 18-year follow-ups, 162 (15%) and 328 (30%) of the participants had been institutionalized, respectively.

When counting the prevalence of institutionalization in the study population, we excluded the participants still alive at the end of the follow-up period as institutionalization was still possible in the future for them. The prevalence of institutionalization was 41%. There was a higher prevalence in women (49%) than in men (30%). The mean age at time of institutionalization and mean time spent living in an institution before death are shown in Table 5 for both genders, and men and women separately, for three time-periods: before baseline, from baseline to January 2008, and from January 2008 to January 2017. The overall mean age at time of institutionalization was 84.6 years (SD 6.3), and mean time spent living in an institution 3.1 years, (SD 2.9).

Table 5. Age of study participants at time of institutionalization and mean time spent living in an institution.

	Mean age in years at time of institutionalization (SD)			Mean time in years spent living in an institution (SD)		
	Before baseline	Baseline – January 2008	January 2008 – January 2017	Before baseline	Baseline – January 2008	January 2008 – January 2017
Both [n]	81.6 (7.0) [67]	83.9 (5.9) [160]	87.4 (5.3) [112]	5.2 (3.8)	3.2 (2.7)	1.7 (1.5)
Men [n]	81.1 (6.6) [18]	82.3 (5.6) [54]	85.4 (5.0) [37]	4.5 (3.6)	2.7 (2.6)	1.5 (1.4)
Women [n]	81.8 (7.1) [49]	84.7 (5.9) [106]	88.4 (5.1) [75]	5.4 (3.9)	3.5 (2.8)	1.9 (1.5)

5.4 Association of Frailty with Institutionalization (Study II)

The associations of frailty by different frailty tools with institutionalization for the 10-year follow-up are shown in Table 6, and for the 18-year follow-up in Table 7. Being frail or pre-frail according to FS and FI were associated with a higher risk of institutionalization in unadjusted analyses during the 10-year follow-up. After age- and gender-adjustments, the associations persisted for FI and for pre-frailty according to FS. Frailty according to PRISMA-7 was associated with a higher risk of institutionalization during the 10- and 18-year follow-ups. During the 18-year follow-up, being pre-frail according to FS and pre-frail or frail according to FI were associated with a higher risk of institutionalization in the unadjusted analyses. After adjustments, the association persisted in being frail according to FI.

Table 6. The associations of frailty by three frailty tools for institutionalization during the 10-year follow-up.

	Community-dwelling n (%)	Institutionalized n (%)	Deceased n (%)	Unadjusted HR (95% CI)	P-value	Adjusted[a] HR (95% CI)	P-value
FRAIL Scale (n = 1087)							
Robust (n = 710)	496 (70)	74 (10)	140 (20)	1		1	
Pre-frail (n = 350)	158 (45)	75 (21)	117 (33)	2.25 (1.63–3.10)	<.001	1.48 (1.04–2.10)	0.030
Frail (n = 27)	1 (4)	8 (30)	18 (67)	3.32 (1.57–7.00)	0.002	1.33 (0.57–3.11)	0.505
Frailty Index (n = 1061)							
Robust (n = 197)	164 (83)	8 (4)	25 (13)	1		1	
Pre-frail (n = 596)	402 (67)	64 (11)	130 (22)	2.74 (1.32–5.69)	0.007	2.32 (1.12–4.79)	0.023
Frail (n = 268)	76 (28)	79 (29)	113 (42)	8.82 (4.28–18.20)	<.001	4.50 (2.11–9.63)	<.001
PRISMA-7 (n = 1055)							
Robust (n = 860)	613 (71)	85 (10)	162 (19)	1			
Frail (n = 195)	42 (22)	63 (32)	90 (46)	3.95 (2.85–5.49)	<.001		

HR = Hazard Ratio
CI = Confidence Interval
[a]Values are adjusted for age and gender, which are items of PRISMA-7

Table 7. The associations of frailty by three frailty tools for institutionalization during the 18-year follow-up.

	Community-dwelling n (%)	Institutionalized n (%)	Deceased n (%)	Unadjusted HR (95% CI)	P-value	Adjusted[a] HR (95% CI)	P-value
FRAIL Scale (n = 1087)							
Robust (n = 710)	221 (31)	185 (26)	304 (43)	1		1	
Pre-frail (n = 350)	61 (17)	126 (36)	163 (47)	1.56 (1.24–1.96)	<.001	1.22 (0.96–1.55)	0.110
Frail (n = 27)	0 (0)	9 (33)	18 (67)	1.50 (0.72–3.09)	0.278	0.82 (0.37–1.81)	0.629
Frailty Index (n = 1061)							
Robust (n = 197)	73 (37)	36 (18)	88 (45)	1		1	
Pre-frail (n = 596)	192 (32)	159 (27)	245 (41)	1.56 (1.10–2.21)	0.013	1.38 (0.98–1.97)	0.068
Frail (n = 268)	11 (4)	114 (43)	143 (53)	3.08 (2.13–4.46)	<.001	2.00 (1.34–2.97)	<.001
PRISMA-7 (n = 1055)							
Robust (n = 860)	278 (32)	228 (27)	354 (41)	1			
Frail (n = 195)	6 (3)	82 (42)	107 (55)	2.03 (1.55–2.66)	<.001		

HR =Hazard Ratio
CI = Confidence Interval
[a]Values are adjusted for age and gender, which are items of PRISMA-7

5.5 Association of Frailty with Mortality (Study I)

In Study I, participants living in institutional care at baseline (n=65) or in sheltered housing (n=18) or with missing data for frailty indices were excluded leaving 1152 participants for the analyses. During the 10- and 18-year follow-ups, altogether 382 (33%), and 776 (67%) participants were deceased, respectively.

Frailty and pre-frailty according to both FI and FS were associated with a higher risk of death during both follow-ups in unadjusted, and age- and gender-adjusted analyses (items of PRISMA-7) (Table 8). Frailty according to the binary PRISMA-7 was associated with a higher risk of death. The association of frailty, by any of the tools used, did not differ significantly between men and women in either follow-up. The Kaplan-Meier –curves for survival, age- and gender-adjusted for FS and FI, and unadjusted for PRISMA-7 are shown in Figure 7.

Table 8. The association of frailty according to FRAIL Scale, Frailty Index and PRISMA-7 with mortality during 10- and 18-year follow-ups.

		10-year follow-up				18-year follow-up			
		Unadjusted		Adjusted[a]		Unadjusted		Adjusted[a]	
	n (%)	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
FRAIL Scale n=1152									
Robust	763 (66)	1		1		1		1	
Pre-frail	364 (32)	2.19 (1.78–2.69)	<.001	1.69 (1.36–2.10)	<.001	1.69 (1.46–1.96)	<.001	1.35 (1.15–1.57)	<.001
Frail	25 (2)	7.96 (5.10–12.41)	<.001	4.91 (3.10–7.80)	<.001	6.32 (4.17–9.57)	<.001	3.92 (2.55–6.01)	<.001
Frailty Index n=1126									
Robust	217 (19)	1		1		1		1	
Pre-frail	642 (57)	1.81 (1.25–2.62)	0.002	1.75 (1.21–2.54)	0.003	1.31 (1.07–1.61)	0.011	1.27 (1.03–1.56)	0.026
Frail	267 (24)	5.97 (4.13–8.64)	<.001	4.05 (2.75–5.97)	<.001	3.95 (3.16–4.94)	<.001	2.85 (2.25–3.63)	<.001
PRISMA-7 n=1124									
Robust	928 (83)	1				1			
Frail	196 (17)	4.41 (3.55–5.48)	<.001			3.78 (3.19–4.49)	<.001		

HR = Hazard Ratio
CI = Confidence Interval
[a]Adjusted for age and gender, which are items of PRISMA-7

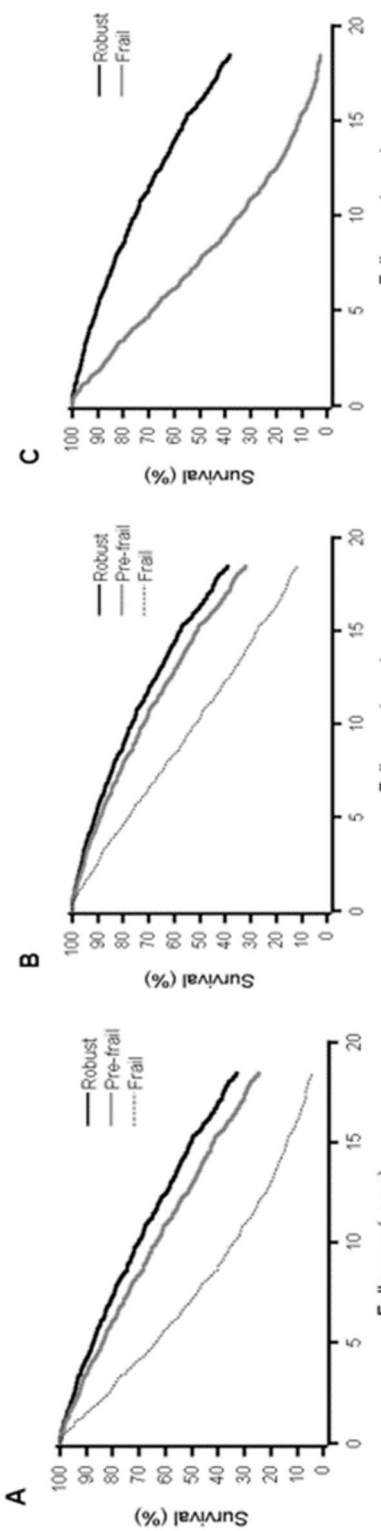

Figure 7. Age- and gender-adjusted survival curves by FRAIL Scale (A) and Frailty Index (B) and unadjusted survival curves by PRISMA-7 (C). The median follow-ups were 14.2 (A), 14.3 (B), and 14.5(C) years. Reprinted from Study I (Salminen et al., 2019). Copyright © The Authors. Published by Springer. Distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/).

5.6 Self-Rated Health and Self-Reported Walking Ability (Study II)

The numbers and proportions of community-dwelling, institutionalized and deceased participants at the end of the follow-up by their SRH and self-reported walking ability are shown in Table 9.

Table 9. The numbers and proportions of community-dwelling, institutionalized and deceased participants at the end of the follow-up period of 18 years by their self-rated health and self-reported walking ability.

	Community-dwelling n (%)	Institutionalized n (%)	Deceased n (%)
Self-reported walking ability (n = 1101)			
Yes (n = 1011)	284 (28)	285 (28)	442 (44)
No (n = 90)	0 (0)	42 (47)	48 (53)
Self-rated health (n=1105)			
Good (n=446)	143 (32)	128 (29)	175 (39)
Moderate (n=500)	133 (27)	136 (27)	231 (46)
Poor (n=159)	10 (6)	64 (40)	85 (53)

5.6.1 Association of Self-Rated Health and Self-Reported Walking Ability with Institutionalization

Poor SRH and the inability to self-reportedly walk 400 meters were significantly associated with an increased risk of institutionalization in the unadjusted analyses during the 10- and 18-year follow-ups, and in the age- and gender-adjusted analyses during the 10-year follow-up (Table 10).

Table 10. The association of self-rated health and self-reported walking ability with institutionalization during the 10- and 18-year follow-ups.

	10-year follow-up				18-year follow-up			
	Unadjusted HR (95% CI)	P value	Adjusted[a] HR (95% CI)	P value	Unadjusted HR (95% CI)	P value	Adjusted[a] HR (95% CI)	P value
Self-reported walking ability (n = 1101)								
Yes (n = 1011)	1		1		1		1	
No (n = 90)	4.82 (3.29–7.05)	<.001	2.06 (1.25–3.41)	0.005	2.31 (1.59–3.36)	<.001	1.28 (0.82–2.01)	0.305
Self-rated health (n=1105)								
Good (n=446)	1		1		1		1	
Moderate (n=500)	1.18 (0.82–1.69)	0.380	1.07 (0.74–1.54)	0.73	0.96 (0.76–1.22)	0.75	0.91 (0.72–1.16)	0.461
Poor (n=159)	2.51 (1.67–3.77)	<.001	1.59 (1.00–2.53)	0.05	1.65 (1.21–2.25)	0.002	1.29 (0.92–1.81)	0.137

HR = Hazard Ratio
CI = Confidence Interval
[a]Values are adjusted for age and gender

5.7 Subjective and Objective Health (Study III)

The participants were categorized according to their combined health information: subjectively and objectively healthy (SO) (n=150), subjectively healthy but objectively unhealthy (S) (n=270), subjectively unhealthy but objectively healthy (O) (n=160), and subjectively and objectively unhealthy (UH) (n=679). For the institutionalization analyses, the exclusions changed the composition of the groups as follows: SO group n=138, S group n=251, O group n=138 and UH group n=579.

Table 11 shows the baseline characteristics of the four combined health information groups. The participants in the SO group were statistically significantly younger than the UH group. Also, more of them had more than basic education, higher MMSE scores, and higher BMI than the UH group. For BMI and education, there was also a difference between the SO and O group.

Table 11. Baseline characteristics of the participants according to the combined health information (n=1259).

	Subjectively and objectively healthy (SO) (n=150)	Subjectively healthy[c] (S) (n=270)	Objectively healthy[d] (O) (n=160)	Unhealthy[e] (UH) (n=679)	P value
Age, years[a]	70.5 (5.1) [64–85]	72.1 (5.8) [64–92]	71.5 (6.0) [64–94]	75.1 (7.3) [64–100]	<.001*
	n (%)	**n (%)**	**n (%)**	**n (%)**	
Age, years					<.001*
64–74	121 (81)	193 (71)	117 (73)	363 (53)	
75–84	25 (17)	69 (26)	37 (23)	229 (34)	
≥85	4 (3)	8 (3)	6 (4)	87 (13)	
Gender					0.802
Men	65 (43)	116 (43)	72 (45)	279 (41)	
Women	85 (57)	154 (57)	88 (55)	400 (59)	
MMSE					<.001*
≥26	133 (89)	217 (80)	122 (76)	431 (63)	
<26	17 (11)	53 (20)	38 (24)	248 (37)	
BMI (n=1255)					<.001**
< 20	2 (1)	7 (3)	4 (3)	61 (9)	
20–24.9	42 (28)	68 (25)	45 (28)	189 (28)	
25–29.9	83 (55)	136 (50)	65 (41)	259 (38)	
30–34.9	15 (10)	49 (18)	35 (22)	130 (19)	
≥35	8 (5)	10 (4)	11 (7)	36 (5)	
Education					<.001***
Basic[b] or less than basic	116 (77)	222 (82)	142 (89)	633 (93)	
More than basic	34 (23)	48 (18)	18 (11)	46 (7)	
Living situation					0.259
Alone	37 (25)	77 (29)	44 (28)	217 (32)	
With someone	113 (75)	193 (71)	116 (73)	462 (68)	

[a]Values are mean (standard deviation) [range]
[b]Six years of elementary school
[c]Subjectively healthy and objectively unhealthy
[d]Subjectively unhealthy and objectively healthy
[e]Subjectively and objectively unhealthy
*SO vs UH, p<.001
**SO vs O, p=0.025; SO vs UH, p<.001
***SO vs O, p=0.007; SO vs UH, p<.001

5.7.1 Association of Subjective and Objective Health with Institutionalization

Being in the UH group was associated with an increased risk of institutionalization during the 10- and 18-year follow-ups in the unadjusted analyses when compared to the SO group (HR 2.85 [95% CI 1.50–5.41], p 0.001; HR 1.81 [95% CI 1.23–2.67], p 0.003, respectively), but after adjusting for age, BMI, MMSE scores and education, the associations were no longer significant. During the 18-year follow-up, also being in the S group was associated with an increased risk of institutionalization in the unadjusted analyses when compared to the SO group (HR 1.59 [95% CI 1.04–2.42], p 0.032). The association did not persist after the adjustments.

The institutionalization rate per 1000 person-years was 7.7 in the SO group and 26.2 in the UH group during the 10-year follow-up. For S group the rate was 13.2 and for O group 10.4. During the 18-year follow-up, the rates were 14.2, 23.4, 19.6, and 33.2 for SO, S, O, and UH groups, respectively.

5.7.2 Association of Subjective and Objective Health with Mortality

Being in the UH or S groups were associated with an increased risk of death during the 10-year follow-up in the unadjusted analyses when compared to the SO group (HR 4.40 [95% CI 2.89–6.72], p<.001; HR 1.69 [95% 1.05–2.72], p 0.030, respectively). After adjusting for age, BMI, MMSE scores and education, the association persisted in the UH group (HR 2.57 [95% CI 1.66–3.96], p<.001). During the 18-year follow-up, being in the UH group was associated with a higher risk of death compared to the SO group in both unadjusted, and adjusted analyses (HR 2.32 [95% CI 1.85–2.92], p<.001; HR 1.59 [95% CI 1.12–2.01], p<.001, respectively).

The mortality rate per 1000 person-years during the 10-year follow-up was 69.1 in the UH and 16.0 in the SO group. The S and the O groups had quite similar mortality rates to each other, 26.9 and 24.5, respectively. During the 18-year follow-up, the mortality rates per 1000 person-years were 37.7, 44.0, 38.6, and 79.9 for SO, S, O, and UH groups, respectively. The Kaplan-Meier curves for survival and institutionalization by combined health information are shown in Figure 8.

Additional analyses including only participants followed-up for over 5 years showed a continuous higher mortality rate for the UH group even after 5 years (Figure 9).

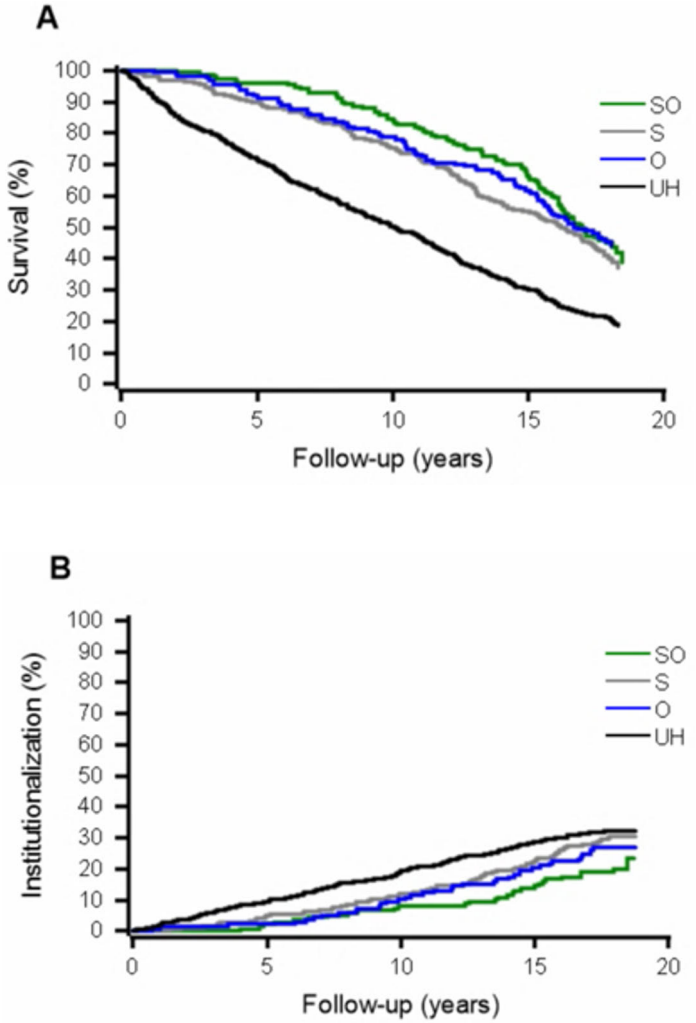

Figure 8. Rates of survival (A) and institutionalization (B) by combined health information (self-reported [subjective] health and registered illnesses [objective health]) during the 18-year follow-up. SO = good subjective and objective health, S = good subjective and poor objective health, O = poor subjective and good objective health and UH = unhealthy, poor subjective and objective health. Modified from Study III (Viljanen et al., 2021b).

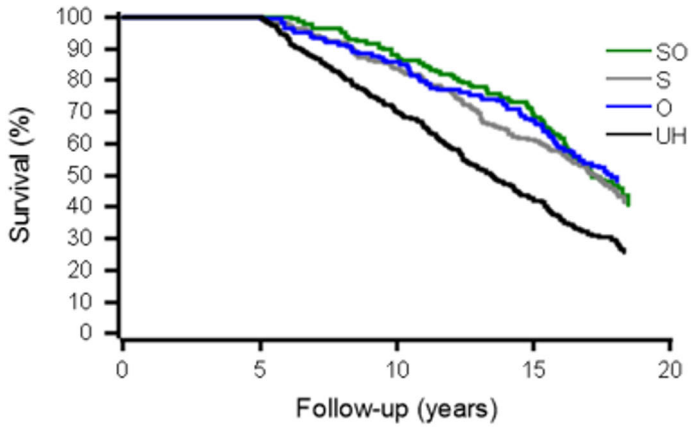

Figure 9. Rates of survival by combined health information (self-reported [subjective] health and registered illnesses [objective health]) for participants followed-up for more than 5 years, during the 18-year follow-up. SO = good subjective and objective health, S = good subjective and poor objective health, O = poor subjective and good objective health and UH = unhealthy, poor subjective and objective health. Modified from Study III (Viljanen et al., 2021b). Copyright © The Authors. Published by BioMed Central Limited, part of Springer Nature. Distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/).

5.7.3 Measures of Biological Interaction

The RERI (Relative excess risk due to interaction) for mortality was found significant in the unadjusted, and adjusted analyses for both follow-ups (Table 12). No statistical significance for RERI was found for institutionalization.

The AP (Attributable proportion due to interaction) for mortality was found significant in the unadjusted, and adjusted analyses for both follow-ups. No statistical significance for AP was found for institutionalization.

The S_y (Synergy index) was only significant in the unadjusted analysis for mortality during the 10-year follow-up. For the adjusted analysis during the 18-year follow-up, the confidence interval for the S_y was not possible to count. No statistical significance for S_y was found for institutionalization.

Table 12. Measures of biological interaction in the association of subjective and objective health with mortality.

	10-year follow-up		18-year follow-up	
	Unadjusted	**Adjusted[a]**	**Unadjusted**	**Adjusted[a]**
RERI[b] (95% CI)	2.17 (1.24–3.11)	0.93 (0.32–1.54)	1.10 (0.76–1.45)	0.64 (0.34–0.94)
AP[c] (95% CI)	0.49 (0.31–0.68)	0.36 (0.09–0.63)	0.48 (0.32–0.63)	0.40 (0.19–0.62)
S_y[d] (95% CI)	2.76 (1.28–5.97)	2.47 (0.64–9.43)	0.51 (0.16–1.63)	-10.65

[a]Values are adjusted for age, BMI, MMSE scores and education
[b]Relative excess risk due to interaction
[c]Attributable proportion due to interaction
[d]Synergy index

5.8 Chronic Conditions and Multimorbidity (Study IV)

In Study IV, we only took into account the participants who had been institutionalized or deceased while living at home during the follow-up period of 18 years to ascertain that we didn't categorize someone as community-dwelling when they could have been institutionalized at a later date. This left us with 820 participants for the analyses in Study IV. The baseline characteristics of the participants are shown in Table 13. The excluded participants (n=286) were still living at home at the end of the follow-up period and were younger, more often women, more often living with someone than alone, had higher MMSE scores and were less multimorbid than the study population (n=820) (data not shown).

For the purpose of analyzing the association of chronic conditions and multimorbidity with institutionalization in participants without dementia, we excluded the participants with dementia (n=334) leaving 486 participants for these analyses.

Table 13. Baseline characteristics of study participants according to institutionalization (n=820).

	Community-dwelling (n=492)	Institutionalized (n=328)	P value
Age, years[a]	74.2 (6.9) [64–97]	75.3 (6.5) [64–95]	0.008
	n (%)	**n (%)**	
Age, years			0.073
64–74	284 (58)	163 (50)	
75–84	166 (34)	134 (41)	
≥85	42 (9)	31 (9)	
Gender			<.001
Men	252 (51)	105 (32)	
Women	240 (49)	223 (68)	
Living			0.001
Alone	153 (31)	140 (43)	
With someone	339 (69)	188 (57)	
MMSE			0.002
≥26	413 (84)	247 (75)	
<26	79 (16)	81 (25)	

[a]Values are mean (standard deviation) [range]

Figure 10 shows the distribution of the number of chronic conditions by community-dwelling and institutionalized participants. The most common number of chronic conditions was four, with 24% or the participants in this category. Only 5 participants (1%) had none of the chosen chronic conditions. Ten (2%) had nine or more conditions. If the usual definition of multimorbidity, two or more chronic conditions, would have been used in this population, the prevalence of multimorbidity would have been 96%. When using the multimorbidity4+ and multimorbidity5+, the prevalence was 70% and 46%, respectively.

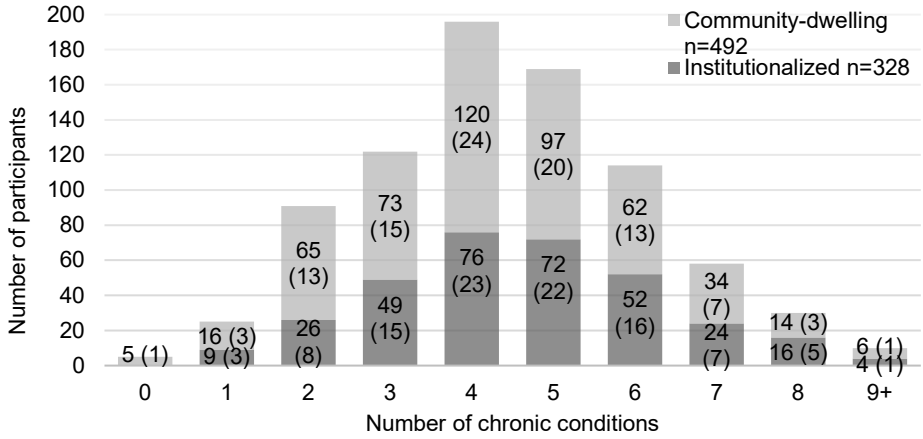

Figure 10. Participants (community-dwelling and institutionalized) according to their number of chronic conditions (n=820). Percentages of participants with each number of chronic conditions in either category (community-dwelling [n=492] or institutionalized [n=328]) are shown in parentheses. Reprinted from Study IV (Viljanen et al., 2021a). Copyright © The Authors. Published by Springer. Distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/).

5.8.1 Association of Chronic Conditions and Multimorbidity with Institutionalization

A significantly larger proportion of institutionalized participants had dementia, mood disorders, neurological disorders, and hypothyroidism than those not institutionalized (Table 14). A significantly smaller proportion of institutionalized participants had malignant neoplasms, ischaemic heart disease, atrial fibrillation, atherosclerosis, chronic lower respiratory diseases and renal failure than those not institutionalized. A significantly larger proportion of institutionalized participants had multimorbidity3+, multimorbidity4+, and multimorbidity5+ than those not institutionalized.

Table 14. Participants according to chronic conditions, multimorbidity and institutionalization.

Chronic conditions	Community-dwelling (n=492) n (%)	Institutionalized (n=328) n (%)	P value
Malignant neoplasms (except basal cell carcinomas)	212 (43)	74 (23)	<.001
Iron deficiency anaemia	57 (12)	39 (12)	0.894
B12-vitamin anaemia	40 (8)	23 (7)	0.556
Hypothyroidism	48 (10)	47 (14)	0.045
Diabetes mellitus	125 (25)	78 (24)	0.597
Hypercholesterolaemia	174 (35)	114 (35)	0.858
Dementia	104 (21)	230 (70)	<.001
Mood disorders	104 (21)	150 (46)	<.001
Systemic atrophies, extrapyramidal and movement disorders[a]	30 (6)	40 (12)	0.002
Hypertension	290 (59)	198 (60)	0.684
Ischaemic heart disease	302 (61)	169 (52)	0.005
Atrial fibrillation	184 (37)	98 (30)	0.026
Intracranial haemorrhage	23 (5)	17 (5)	0.740
Stroke	159 (32)	124 (38)	0.105
Atherosclerosis	54 (11)	23 (7)	0.057
Chronic lower respiratory diseases	124 (25)	62 (19)	0.035
Renal failure	77 (16)	33 (10)	0.021
Multimorbidity3+[b]	406 (83)	293 (89)	0.007
Multimorbidity4+[b]	333 (68)	244 (74)	0.039
Multimorbidity5+[b]	213 (43)	168 (51)	0.026
Multimorbidity6+[b]	116 (26)	96 (29)	0.068

[a]Referred to as neurological disorders in the main text
[b]The number signifies the number of chronic conditions used as a cut-off for multimorbidity; multimorbidity3+ denotes 3 or more chronic conditions, multimorbidity4+ denotes 4 or more chronic conditions, multimorbidity5+ denotes 5 or more chronic conditions and multimorbidity6+ denotes 6 or more chronic conditions.

Seventy percent (n=230) of the institutionalized participants had dementia. There was a significantly larger proportion of malignant neoplasms among the institutionalized participants without dementia, than among the ones with dementia (Table 15). The proportions of participants with mood disorders were high in both groups. The proportion of neurological disorders was higher among institutionalized participants without dementia than in those with dementia, but the difference was

not statistically significant. Multimorbidity defined all different ways was more common among the institutionalized participants with dementia than those without dementia.

Dementia, mood disorders, neurological disorders, and multimorbidity5+ were associated with a higher risk of institutionalization during the 18-year follow-up both in the unadjusted, and adjusted analyses (Table 16). Malignant neoplasms, ischaemic heart disease, atrial fibrillation and renal failure were associated with a lower risk of institutionalization both in the unadjusted, and adjusted analyses. In participants without dementia, mood disorders and neurological disorders were associated with an increased risk of institutionalization. Malignant neoplasms and ischaemic heart disease were again associated with a decreased risk of institutionalization.

When analyzing multiple variables (dementia, mood disorders, neurological disorders, malignant neoplasms, ischaemic heart disease, atrial fibrillation, renal failure, and multimorbidity5+) in the same model, dementia, mood disorders and neurological disorders were associated with a higher risk, and malignant neoplasms with a lower risk of institutionalization (data not shown).

Table 15. Institutionalized participants according to dementia and other chronic conditions (n=328).

Chronic condition	With dementia (n=230) n (%)	Without dementia (n=98) n (%)	P value
Malignant neoplasms (except basal cell carcinomas)	42 (18)	32 (33)	0.004
Iron deficiency anaemia	24 (10)	15 (15)	0.212
B12-vitamin anaemia	14 (6)	9 (9)	0.315
Hypothyroidism	37 (16)	10 (10)	0.164
Diabetes mellitus	50 (22)	28 (29)	0.183
Hypercholesterolaemia	86 (37)	28 (29)	0.125
Mood disorders	105 (46)	45 (46)	0.965
Systemic atrophies, extrapyramidal and movement disorders[a]	23 (10)	17 (17)	0.063
Hypertension	136 (59)	62 (63)	0.484
Ischemic heart disease	120 (52)	49 (50)	0.718
Atrial fibrillation	66 (29)	32 (33)	0.474
Intracranial haemorrhage	10 (4)	7 (7)	0.296
Stroke	86 (37)	38 (39)	0.813
Atherosclerosis	13 (6)	10 (10)	0.140
Chronic lower respiratory diseases	41 (18)	21 (21)	0.446
Renal failure	23 (10)	10 (10)	0.955
Multimorbidity3+[b]	212 (92)	81 (83)	0.011
Multimorbidity4+[b]	178 (77)	66 (67)	0.018
Multimorbidity5+[b]	128 (56)	40 (41)	0.005
Multimorbidity6+[b]	76 (33)	20 (20)	0.007

[a]Referred to as neurological disorders in the main text
[b]The number signifies the number of chronic conditions used as a cut-off for multimorbidity; multimorbidity3+ denotes 3 or more chronic conditions, multimorbidity4+ denotes 4 or more chronic conditions, multimorbidity5+ denotes 5 or more chronic conditions and multimorbidity6+ denotes 6 or more chronic conditions.
Modified from Study IV (Viljanen et al., 2021a).

Table 16. Association of chronic conditions and multimorbidity with institutionalization during the 18-year follow-up.

	All participants (n=820)				Participants without dementia (n=486)			
Chronic conditions	Unadjusted HR (95% CI)	P value	Adjusted[a] HR (95% CI)	P value	Unadjusted HR (95% CI)	P value	Adjusted[a] HR (95% CI)	P value
Malignant neoplasms (except basal cell carcinomas)	0.46 (0.36–0.60)	<.001	0.51 (0.40–0.67)	<.001	0.58 (0.38–0.89)	0.013	0.62 (0.40–0.95)	0.029
Dementia	4.84 (3.80–6.16)	<.001	4.73 (3.69–6.05)	<.001				
Mood disorders	2.31 (1.86–2.87)	<.001	2.00 (1.58–2.52)	<.001	2.92 (1.97–4.34)	<.001	2.69 (1.77–4.10)	<.001
Systemic atrophies, extrapyramidal and movement disorders[b]	1.71 (1.24–2.37)	0.001	1.97 (1.41–2.77)	<.001	2.74 (1.59–4.72)	<.001	3.31 (1.85–5.91)	<.001
Ischaemic heart disease	0.75 (0.61–0.93)	0.010	0.73 (0.58–0.91)	0.005	0.65 (0.44–0.96)	0.032	0.63 (0.43–0.94)	0.025
Atrial fibrillation	0.75 (0.59–0.95)	0.015	0.77 (0.60–0.98)	0.030	0.76 (0.50–1.16)	0.205	0.75 (0.49–1.14)	0.181
Renal failure	0.65 (0.45–0.92)	0.015	0.67 (0.47–0.96)	0.028	0.58 (0.31–1.11)	0.101	0.56 (0.29–1.08)	0.084
Multimorbidity3+[c]	1.50 (1.04–2.16)	0.032	1.31 (0.90–1.91)	0.165	1.11 (0.65–1.90)	0.713	0.96 (0.55–1.66)	0.879
Multimorbidity4+[c]	1.25 (0.97–1.60)	0.087	1.14 (0.87–1.48)	0.340	1.08 (0.71–1.65)	0.728	0.98 (0.64–1.51)	0.917
Multimorbidity5+[c]	1.26 (1.01–1.56)	0.037	1.25 (1.00–1.56)	0.0498	1.05 (0.70–1.57)	0.802	1.05 (0.70–1.58)	0.799
Multimorbidity6+[c]	1.20 (0.95–1.52)	0.120	1.19 (0.93–1.52)	0.159	0.91 (0.56–1.47)	0.685	0.90 (0.54–1.47)	0.662

HR = Hazard ratio
CI = Confidence interval
[a]Adjusted for age, gender, living situation and MMSE score
[b]Referred to as neurological disorders in the main text
[c]The number signifies the number of chronic conditions used as a cut-off for multimorbidity; multimorbidity3+ denotes 3 or more chronic conditions, multimorbidity4+ denotes 4 or more chronic conditions, multimorbidity5+ denotes 5 or more chronic conditions and multimorbidity6+ denotes 6 or more chronic conditions.

5.9 Successful Agers (Study V)

Successful agers in this study were defined as being able to live at home at the age of 84 years or older without daily formal or informal care. Baseline characteristics of the successful agers are shown in Table 17 together with follow-up characteristics.

At baseline, the successful agers' mean age was 67.8 years (SD 2.5, range 64–77). Fifty-five percent were women and 16% lived alone. Only one percent used mobility aids, 93% exercised weekly and 91% were able to self-reportedly walk 400 meters. Ninety-six percent had MMSE scores of 26 or over and reported their SRH as at least moderate. Satisfaction with life was high with only three percent reporting poor satisfaction with life. Only one percent had five or more chronic conditions. In addition, only three and two percent were categorized as frail by PRISMA-7 and the FI, respectively, and no one by the FS.

At re-examination, the mean age was 87.6 (SD 2.5, range 84–96). Over half of them now lived alone. In all variables analyzed, there was a statistically significant change depicting poorer physical ability and subjective health at re-examination than at baseline.

The need for mobility aids had increased during the follow-up period. Still, 75% of the successful agers were self-reportedly able to walk 400 meters and almost as many exercised weekly. The results for gait speed and grip strength and their normative values are shown in Table 18.

Of the successful agers, 53% still had MMSE scores of 26 or higher, although the proportion with lower MMSE scores had significantly increased during the follow-up period. Twenty-one percent now had five or more chronic conditions.

Still, 80% of the successful agers assessed their SRH as at least moderate at re-examination. Only one person (1%) described their satisfaction with life as poor. Of the successful agers, 25% were categorized as subjectively healthy (must be self-reportedly able to walk 400 meters, have good SRH and good satisfaction with life) at re-examination, with 46% at baseline.

Most of the successful agers were categorized as robust by the FS and PRISMA-7, and as pre-frail by the FI at baseline. After a 20-year follow-up, most were categorized as frail by PRISMA-7, and as pre-frail by the FS and the FI. The FS still identified only 21% as frail, when PRISMA-7 categorized 75%, and the FI 46% as frail. Frailty measured by any of these three tools, had increased during the follow-up.

Table 17. Baseline and re-examination characteristics of the successful agers and the odds ratios for change in the categorical variables from baseline to re-examination (n=112).

	Baseline (1998–99)	**Re-examination (2018)**	**Re-examination vs. baseline (2018 vs. 1998–99)**	
Age, years	mean (SD) [range]			
	67.8 (2.5) [64–77]	87.6 (2.5) [84–96]		
	n (%)	**n (%)**	**OR (95% CI)**	**P-value**
Gender				
Men	50 (45)	50 (45)		
Women	62 (55)	62 (55)		
Living situation				
with someone	94 (84)	52 (46)	1	
alone	18 (16)	60 (54)	6.03 (3.69–9.83)	<.001
Mobility aid[a]	n=111			
no	110 (99)	52 (46)	1	
yes	1 (1)	60 (54)	124.81 (17.39–895.54)	<.001
Exercise	n=107			
weekly	99 (93)	81 (72)	1	
less than weekly/not at all	8 (7)	31 (28)	4.82 (2.20–10.55)	<.001
Self-reported walking ability	n=110			
yes	100 (91)	84 (75)	1	
no	10 (9)	28 (25)	3.25 (1.51–7.01)	0.003
MMSE[b]		n=111		
26–30	107 (96)	59 (53)	1	
≤25	5 (4)	52 (47)	18.68 (6.80–51.34)	<.001
Self-rated health[c]				
good	56 (50)	32 (29)	1	
moderate	51 (46)	57 (51)	1	
poor	5 (4)	23 (21)	2.93 (1.90–4.51)	<.001

	Baseline (1998–99)	Re-examination (2018)	Re-examination vs. baseline (2018 vs. 1998–99)	
Satisfaction with life[c]				
good	94 (84)	78 (70)	1	
moderate	15 (13)	33 (29)	1	
poor	3 (3)	1 (1)	2.28 (1.35–3.85)	0.002
Subjective health				
healthy	52 (46)	28 (25)	1	
not healthy	60 (54)	84 (75)	2.60 (1.61–4.20)	<.001
Number of chronic conditions				
0-2	100 (89)	41 (37)	1	
3-4	11 (10)	48 (43)	1	
≥5	1 (1)	23 (21)	14.87 (7.65–28.89)	<.001
FRAIL Scale[d]	n=109	n=109		
robust	90 (83)	44 (37)	1	
pre-frail	19 (17)	53 (49)	1	
frail	0 (0)	23 (21)	8.04 (4.75–13.50)	<.001
PRISMA-7	n=110	n=110		
robust	107 (97)	28 (25)	1	
frail	3 (3)	82 (75)	104.45 (31.94–341.61)	<.001
Frailty Index[d]	n=107	n=107		
robust	33 (30)	8 (7)	1	
pre-frail	73 (68)	50 (47)	1	
frail	2 (2)	49 (46)	12.88 (6.47–25.66)	<.001

OR = odds ratio
[a]Having any mobility aid was compared to not having a mobility aid
[b]Mini-Mental State Examination
[c]Poorer category was compared to better categories
[d]Being frail was compared to being pre-frail or robust
Modified from Study V (Viljanen et al., 2023) Submitted.

Table 18. The results of the re-examination for gait speed and grip strength and the normative values.

Results	Age, years	Men	Women	Normative values	Reference	Age, years	Men	Women	Remarks
		Mean (SD) [range]					Mean (SD)		
Gait speed, m/s		n=50	n=62		(Lusardi et al., 2003)	80–89	0.88 (0.24)	0.80 (0.20)	The number of participants in this age category was small
	≥84	1.06 (0.32) [0.36–2.00]	0.87 (0.30) [0.36–2.00]			≥90	0.72 (0.14)	0.71 (0.23)	The number of participants in this age category was small
					(Hollman et al., 2011)	80–85	1.12 (0.17)	1.01 (0.15)	Many common illnesses were considered as exclusion criteria in this study
						≥85	1.01 (0.22)		The number of participants in this age category was small and there were no women
Grip strength, kg		n=50	n=62		(Finnish Institute for Health and Welfare, 2018)	≥80	32 (95% CI 30–34)	20 (95% CI 19–21)	The number of participants in these age categories were 108 for men and 184 for women
	≥84	32.0 (8.5) [12–51]	19.8 (5.4) [10–31]		(Werle et al., 2009)	80–84	31 (9)	19 (5)	The minimum size for each age category was 28 participants
						≥85	22 (6)	17 (5)	

SD = standard deviation
CI = confidence interval
Modified from Study V (Viljanen et al., 2023). Submitted.

5.9.1 Personal Biological Age and "Eyeball Test"

The mean CA and PBA were 67.8 and 61.3 years at baseline, respectively (Table 19). At re-examination, the mean CA and PBA were 87.6 and 77.1 years, respectively. The difference between the CA and the PBA was greater at re-examination than at baseline. One of the successful agers had a FI score of zero, so their PBA was not possible to count.

The concordance of the "eyeball test" and the difference between the CA and the PBA of the successful agers is shown in Table 20. Of the successful agers, no one was clinically assessed as seeming older than their chronological age, when in fact there were 12 of them with a PBA higher than their CA. Among the successful agers with a PBA lower than their CA, the sensitivity and specificity of the "eyeball test" were 0.73 and 0.80, respectively, with a positive predictive value of 0.99 and negative predictive value of 0.14.

Table 19. Chronological and personal biological age of the successful agers at baseline and at re-examination, and their difference.

	Baseline (1998–99)	**Re-examination (2018)**
Chronological age, years	n=112	n=112
mean (SD) [range]	67.8 (2.5) [64–77]	87.6 (2.5) [84–96]
Personal biological age, years	n=105	n=111
mean (SD) [range]	61.3 (11.5) [35.7–81.5]	77.1 (11.5) [36.3–94.7]
Difference of chronological and personal biological age, years	n=105	n=111
mean (SD) [range]	6.44 (11.21) [-16.47–32.88]	10.48 (11.01) [-8.25–48.70]

Modified from Study V (Viljanen et al., 2023). Submitted.

Table 20. Concordance of personal biological age and clinical assessment, the "eyeball test".

	Clinical assessment, the "eyeball test" n=110[a]		
	Younger than their chronological age	Same as their chronological age	Older than their chronological age
Personal biological age in relation to chronological age n=110[a]		n	
Personal biological age younger than their chronological age	68	25	0
Personal biological age same as their chronological age[b]	1	4	0
Personal biological age older than their chronological age	3	9	0

P value for the table <.001.
[a]The clinical assessment was missing for one participant and in addition, for one participant, the personal biological age was not possible to count.
[b]Personal biological age was considered the same as chronological age if they were within a year of each other.
Modified from Study V (Viljanen et al., 2023). Submitted.

5.9.2 Additional Analyses

There were no significant differences in age, gender, living situation, self-reported walking ability, SRH or satisfaction with life between the successful agers and non-participants (Table 21). The use of a mobility aid was more common among the non-participants than the successful agers.

A larger proportion of the successful agers were satisfied with their lives on re-examination than the re-examined participants with daily informal or formal care or the non-participants with daily informal or formal care (Table 22).

Table 21. Differences between the non-participants and successful agers.

	Non-participants n=44	Successful agers n=112	P value
Age, years	**mean, (SD) [range]**		
	87.8 (2.6) [84–94]	87.6 (2.5) [84–96]	0.657
	n (%)		
Gender			0.346
Men	16 (36)	50 (46)	
Women	28 (64)	62 (55)	
Living situation	n=43		0.788
Alone	22 (51)	60 (54)	
With someone	21 (49)	52 (46)	
Mobility aid	n=43		0.008
Yes	33 (77)	60 (54)	
No	10 (39)	52 (46)	
Self-reported walking ability[a]			0.091
Yes	27 (61)	84 (75)	
No	17 (39)	28 (25)	
Self-rated health			0.220
Good	8 (18)	32 (29)	
Moderate	22 (50)	57 (51)	
Poor	14 (32)	23 (21)	
Satisfaction with life	n=43		0.051
Good	24 (56)	78 (70)	
Moderate	16 (20)	33 (29)	
Poor	3 (7)	1 (1)	

[a]Self-reported ability to walk 400 meters
Modified from Study V (Viljanen et al., 2023). Submitted.

Table 22. Satisfaction with life among successful agers, re-examined participants with daily formal or informal care and non-participants with daily formal or informal care.

	Successful agers n=112	Re-examined participants with daily care n=26	Non-participants with daily care n=11
		n (%)	
Satisfaction with life			
Good	78 (70)	13 (50)	4 (36)
Moderate	33 (30)	11 (42)	4 (36)
Poor	1 (1)	2 (8)	3 (27)

Successful agers compared to re-examined participants with daily care p=0.03
Successful agers compared to non-participants with daily care p<.001
Modified from Study V (Viljanen et al., 2023). Submitted.

6 Discussion

The main results of this thesis are that also the more feasible frailty tools, FS and PRISMA-7, as well as the more comprehensive FI, were good at predicting mortality during both the 10- and 18-year follow-ups in this study population. Frailty prevalence by FI and PRISMA-7 were similar to previous research (Collard et al., 2012; O'Caoimh et al., 2018, 2021), but possibly the modifications used in the FS led to a lower than expected prevalence by that tool.

Being frail according to PRISMA-7 and the FI were associated with an increased risk of institutionalization during both follow-ups. Also poor SRH and the inability to self-reportedly walk 400 meters were associated with an increased risk of institutionalization during the 10-year follow-up. These simple self-reported measures could be used instead of frailty tools to predict institutionalization in older adults.

Being subjectively and objectively unhealthy was associated with an increased risk of death when compared to being subjectively and objectively healthy, even after the long follow-up period of 18 years. Poor subjective health also had an additive effect on poor objective health in predicting mortality.

Dementia, mood disorders and neurological disorders were associated with an increased risk of institutionalization during the 18-year follow-up. In participants without dementia, mood disorders and neurological disorders were associated with an increased risk of institutionalization. Multimorbidity was very prevalent in the study population, with four being the most common number of chronic conditions (24%). Multimorbidity5+ was associated with an increased risk of institutionalization during the 18-year follow-up.

The successful agers had mostly good or moderate SRH, although their objective health had worsened during the follow-up period. Also, despite that both their objective and subjective health had worsened during the follow-up period, their satisfaction with life was still at least moderate. The prevalence of frailty had naturally increased as the participants aged. The successful agers' PBA was lower than their CA at both baseline and at re-examination and the difference between the CA and the PBA had increased during the follow-up. The "eyeball test" was not good at identifying participants with a PBA higher than their CA.

6.1 Study Population

The study population included a broad caption of the aged population at the time of the baseline examination in the years of 1998 and 1999 living in the semi-industrialized mid-size municipality of Lieto. At baseline, with 12 % of the population aged 65 years or older, the age structure was comparable to the whole country with 15 % of the population aged 65 years or older (Official Statistics of Finland, 2018). This enables generalizability to most of the municipalites in Finland.

The Compulsory School Attendance Act was ratified in the year 1921 in Finland. The duration of the compulsory education was six years. That was the basic education level for most of the participants. Only 12% of the participants had a higher than basic education which is common for these age cohorts (Official Statistics of Finland, 2007).

The participation rate for the baseline examination was high. The study population can be considered a good sample of the aged population at the time, and the follow-up period for adverse effects was long.

Also, from the participants invited for the re-examination, a notable proportion of 62% participated. There were no significant differences between the participants and non-participants in regarding age, gender, living situation, self-reported walking ability, SRH or satisfaction with life. However, the non-participants did have lower functional ability (more of them used a mobility aid) than the participants suggesting non-response bias (Banack et al., 2019; Kelfve et al., 2013), a common challenge in researching ageing populations (Hardy et al., 2009)

6.2 Methods

6.2.1 Baseline Examination

The baseline examination was extensive including the interview, physical examination and review of medical records. The baseline examination was thoroughly planned and executed giving an abundance of baseline data for the studies included in this thesis, although the baseline examination at the time focused more on respiratory and CVD, as well as dementia.

6.2.2 Frailty Tools

The frailty tools used in this thesis have been shown to predict adverse effects in older adults (Dent et al., 2016). They have all been validated in different populations (Lopez et al., 2012; Morley et al., 2012; Oviedo-Briones et al., 2021; Raîche et al., 2007; Song et al., 2010; Yaman & Ünal, 2018). The three frailty tools have been

shown to differentiate in the best intended usage and feasibility (Dent et al., 2016; Oviedo-Briones et al., 2021) and choosing the frailty tool according to the intended use has been suggested (Gonzalez-Colaço Harmand et al., 2017).

The FI is often used in research and has good specificity to frailty (Apóstolo et al., 2017) but is not as feasible in the clinical setting as the FS (Woo et al., 2012). PRISMA-7 is also a good tool for the screening of frailty, but the FI is more comprehensive (Apóstolo et al., 2017). A review on multiple frailty tools suggests that the FI is suitable for both clinical and population settings, but is time-consuming if not automatically calculated from the CGA (Dent et al., 2016). According to that review, the FI has been validated and is good at predicting adverse outcomes, whereas the FS and PRISMA-7, while also validated, would need more studies to explore their ability to predict adverse outcomes, and suggests that the PRISMA-7 be used in population-level screening only (Dent et al., 2016). Also FS was suggested for screening of frailty only and if positive for frailty or pre-frailty, CGA should be performed (Dent, Morley, et al., 2019).

However, another systematic review (Kojima, 2018b) including eight original studies examining the association of frailty defined by FS with mortality, concluded that the FS is a promising tool for use in the clinical setting. The FS effectively identified frailty and pre-frailty and quantified frailty status in a graded manner in relation to mortality risk (Kojima, 2018b). The meta-analysis included 9,273 middle-aged and older individuals and the pooled HR for mortality in pre-frail and frail participants when compared to robust individuals were 1.75 (95% CI 1.14–2.70) and 3.53 (95% CI 1.66–7.49), respectively (Kojima, 2018b).

Modifications had to be used as the information on all items of the FS and PRISMA-7 were not available as such in the baseline data. The modifications made to FS and PRISMA-7 could have had an impact on the results. However, although modifications to the FS have been shown to affect the specificity of the frailty tool, it still has been shown to be able to identify persons at higher risk of adverse effects (Theou et al., 2015). The FI can be calculated from almost any available data as long as the procedure for creating a frailty index is followed (Searle et al., 2008) as it was in this thesis.

6.2.3 Self-Rated Health

The SRH measure used in this thesis was the GSRH. This measure has been shown to predict mortality and other adverse effects (DeSalvo et al., 2005; Gutman et al., 2001; Mossey & Shapiro, 1982; Saevareid et al., 2007). The form of the question used in this thesis was in line with earlier research (DeSalvo et al., 2005).

6.2.4 Self-Reported Walking Ability

Self-reported walking ability has been found a good indicator of mobility performance in older adults (Alexander et al., 2000). Also, the self-reported ability to walk 400 meters has been shown to coincide well with the controlled ability to walk 400 meters (Sayers et al., 2004), and the inability to walk 400 meters has been shown to be associated with slow gait speed (Chang et al., 2004). Slow gait speed is part of the frailty phenotype (Fried et al., 2001) and has been shown also independently to predict the risk of death and institutionalization (Jung et al., 2018; Rothman et al., 2008; Studenski et al., 2011).

With this earlier research in mind, the choice of the self-reported walking ability as one of the studied variables in this thesis is justifiable. Gait speed was not measured at baseline and also, the aim was to explore variables that would be feasible for use in the primary care setting, and self-reported walking ability is much more feasible than the measuring of gait speed.

The question of self-reported walking ability is simple and easy to answer and in line with earlier research (Sayers et al., 2004).

6.2.5 Satisfaction with Life

Satisfaction with life was measured as a general question on life satisfaction. This is in line with previous research (Barger et al., 2009). High life satisfaction has been associated with reduced mortality (Martín-María et al., 2017) and with higher SRH (Kim et al., 2021), and thus a justifiable part of the subjective health measurement used in this thesis.

6.2.6 Subjective Health

Comprehensive subjective health in this thesis was defined more extensively than mere SRH. Subjective health was defined according to the WHO definition of health (World Health Organization, 1948), and is as such a justifiable definition. The definition of good subjective health was deliberately extensive, and as such somewhat exclusive, as in Study III, the aim was to identify those participants that were in excellent subjective and objective health, the “super healthy”, and compare their outcomes with other groups of different combinations of subjective and objective health.

6.2.7 Objective Health

Objective health in this thesis was defined as the absence of illnesses in Study III and as multimorbidity (disease count) in Study IV. The harsh definition of the

absence of all chosen illnesses in Study III was adopted because the aim was to identify those participants that were in excellent subjective and objective health, the "super healthy", and compare their outcomes with other groups of different combinations of subjective and objective health.

Earlies studies have compared mere SRH with disease count based PRH and found SRH a better predictor of institutionalization (Thygesen et al., 2009). Also, the combination of poor SRH and poor PRH has been found associated with a higher risk of death than the combinations of poor SRH but good PRH or good SRH but poor PRH (Giltay et al., 2012), indicating possible additive effect of the SRH on the PRH. We wanted to exclude the physician's clinical assessment from the equation and to compare the fully objective (absence of illnesses) and the subjective assessments of health and their combinations in predicting adverse effects.

However, for Study IV, the aim was not to factor in illnesses that were scarce in the population as it could have affected the prevalence of multimorbidity, which was desired to be based on common chronic conditions in the study population. For this reason, the conditions were somewhat different than those used in Study III.

Multimorbidity's association with institutionalization was assessed with different definitions as suggested in earlier research (Johnston et al., 2018). The choice of a disease count as the morbidity measure instead of comorbidity indices was justified as the aim was to assess the association of multiple chronic conditions (possibly not associated with each other) with institutionalization, instead of comorbidities (conditions that are associated with the index condition) (Valderas et al., 2009).

6.2.8 Institutionalization

The data on institutionalization were gathered from the electronic patient record system by individually investigating the participants' patient records, and coded by month and year of entry. This is a more precise method than used in earlier research where the data has been collected most often by interviews (Bravell et al., 2009; Hajek et al., 2015; Luppa et al., 2012; Luppa, Luck, Matschinger, et al., 2010).

For institutionalization analyses, the participants already living in an institution at baseline were naturally excluded, but we also excluded participants who had moved to another municipality as data on their institutionalization were not available. Also, when counting the prevalence of institutionalization in the study population, we only included participants who had deceased or been institutionalized during the follow-up period so that no participant still alive was categorized as not institutionalized when in fact they could have been institutionalized at a later date. The exact information on institutionalization (including all the possible options for

institutionalization: primary care long-term units, nursing homes and 24/7 assisted living units) is a strength of this thesis.

The follow-up period was long. In earlier research, often the follow-up period for institutionalization has been shorter ranging from four to nine years (Andel et al., 2007; Hajek et al., 2015; Luppa et al., 2012), but also longer follow-up periods of up to 30 years have been used (Bravell et al., 2009; Salminen et al., 2017).

6.2.9 Mortality

Mortality data were obtained from the official Finnish Cause of Death Registry using unique personal identification numbers up till the end of the follow-up period of 18 years. These data are robust as in Finland, all causes of deaths are recorded.

For Study V, which included a re-examination after the original follow-up period of 18 years, the data on mortality were gathered from the electronic patient record system in which the date of death is recorded even if it occurs in a different municipality. However, causes of death after the original follow-up period were not available for all participants if the death certificate was written in a different health care facility, or if there had been a forensic autopsy. The exact information on mortality is a strength of this thesis.

6.2.10 Re-examination

The re-examination took place circa 20 years after the baseline examination. The aim of the re-examination was to describe the participants still able to live at home at the high age of 84 years or older without daily formal or informal care and the possible factors leading to their SA. All participants still alive and living at home in June 2018 were invited. 62% of them participated in the re-examination. When excluding the participants with a need for daily formal or informal care, the 112 participants consisted 51% of the invited subjects. Of the non-participants, 83% responded by mail and we were able to do a non-response analysis, which is a strength to Study V (Hardy et al., 2009).

The re-examination mirrored the baseline examination but not all variables were re-examined, and also some were added according to the needs of future research. However, a multitude of variables were examined both at baseline and at re-examination providing robust follow-up data.

The re-examination was performed as a collaboration of one study nurse and one study physician providing the best possible equivalent quality in interpretations. For example the “eyeball test” was assessed by the same person for each of the participants providing consistency. Also all measurements were done by the same study nurse.

Great time and effort was used to gather all the relevant information from the patient record system and chronic conditions were not dependent on self-report data, which could be unreliable. In the study of exceptional longevity in men (Yates et al., 2008), they followed the participants for 16 years but mostly by self-reported data. The advantage to that study was annual questionnaires, but only major illnesses were gathered from the patient records and the re-examination included only data on functional ability. Our re-examination included reviewing all the patient records and also the data on institutionalization and need of daily formal or informal care, an extensive interview and a clinical examination.

6.2.11 Statistical analyses

One of the strengths of this thesis is that the statistical analyses were performed in collaboration with a biostatistician and a data manager. In the analyses for institutionalization, death was used as a competing factor. The analyses were adjusted for necessary factors. Multivariable analyses were used when necessary.

For Study III, to count the RERI, AP and S_y, a previously described method was used (Andersson et al., 2005). For Study V, while examining the differences between the variables at baseline and re-examination among the same individuals, correlation between the repeated measurements was taken into account.

6.3 Results

6.3.1 Prevalence of Frailty (Study I)

The prevalence of frailty by FI (24%) was the same as the previously described global prevalence for community-dwelling adults aged 50 years or over using the accumulation of deficits frailty model (O'Caoimh et al., 2021), although the participants in our study were older. Prevalence of frailty by PRISMA-7 (17%), a phenotype based rather than accumulation of deficits based frailty tool, was higher than the described European prevalence for community-dwelling adults aged 45 years or over using phenotype based tools (12%) (O'Caoimh et al., 2018). This is probably explained by the difference in age. Both of these prevalence numbers were higher than the previously described global prevalence for community-dwelling older adults aged 65 years or over (10.7%) (Collard et al., 2012).

For the FS, the prevalence of frailty in our study was only 2%. Although the phenotype based tools have also previously been shown to yield a lower prevalence than other tools, this was even lower compared to those that range from circa 10% to 12% (Collard et al., 2012; O'Caoimh et al., 2018, 2021). This might have been the result of the modifications used for the FS in this thesis. A systematic review on

modifications of the phenotype criteria found that modifications affect the precision, especially the specificity, of the frailty tool (Theou et al., 2015), but it seems than in this study, the modifications also affected the sensitivity.

Only 20% (2% frail, 18% robust) of the participants were categorized identically with all three frailty tools. Also an earlier study comparing the concordance of the FI, a modified Fried phenotype-model, and a modified Tilburg Frailty Indicator (TFI) (Gobbens et al., 2010) found low concordance between the tools: 15.3% for frail and 83.9% for robust (Gonzalez-Colaço Harmand et al., 2017). This was, however, a much better result for concordance than in our study. The low concordance in our study could have been due to the modifications made in the FS and PRISMA-7, or to the fact that those phenotype-based tools often anyway yield a lower prevalence than the FI (O'Caoimh et al., 2021).

6.3.2 Prevalence of Institutionalization (Study II)

In this thesis, the prevalence of institutionalization was counted excluding the participants still alive at the end of the follow-up period of 18 years as they could still have been institutionalized during their lifetime. So only the participants institutionalized or deceased while living at home during the follow-up period were taken into account in the analyses on the prevalence of institutionalization.

In earlier research, the prevalence of institutionalization during the participants' lifetime has not often been reported as they have focused on the rate of institutionalization (Nihtilä et al., 2008; Salminen et al., 2017). However, also this approach of only including deceased or institutionalized participants has been used before in a study investigating trends in use and cost of LTC in Finland (Forma et al., 2017). The prevalence of institutionalization in their study among participants aged 70 years or over was a little over 40% from the year 2002 to 2011 (visualized in a figure only) (Forma et al., 2017). This is in line with our finding of the prevalence of institutionalization being 41%.

The mean age at time of institutionalization increased during the follow-up period, reflecting probably the increase in the LE and the improved care of chronic conditions. The mean time spent living in an institution decreased, reflecting probably the municipality's change in the policy of admitting older people into institutional care: people are nowadays admitted only after extensive formal home care has been utilized and found inadequate. This decrease in the mean time spent living in an institution is the opposite of what previous Finnish research reported: the time spent living in LTC increased during the follow-up period of 17 years (Aaltonen et al., 2019). Their study involved multiple municipalities and as the municipalities can each have their own procedures for admittance to LTC, the difference to our study could be explained by that.

6.3.3 Association of Frailty with Institutionalization (Study II)

Being frail or pre-frail according to the FI, pre-frail according to the FS and frail according to PRISMA-7 were all associated with a higher risk of institutionalization during the 10-year follow-up. Also being frail according to the FI and PRISMA-7 were associated with a higher risk of institutionalization during the 18-year follow-up.

Frailty by the FI has also previously been shown to predict institutionalization (Rockwood et al., 2006). Another study comparing the FI, TFI and a Fried phenotype based model, however, found no association of pre-frailty or frailty with institutionalization (Gonzalez-Colaço Harmand et al., 2017), but they categorized participants as robust or non-robust (including pre-frail and frail) and that might have weakened the results as they were close to statistical significance. A systematic review and meta-analysis on frailty as a predictor of institutionalization found frailty by phenotype-based tools, as well as by accumulation of deficits based tools, associated with an increased risk of institutionalization (Kojima, 2018a). Our findings are in line with earlier research.

To our knowledge, no other studies investigating the association of frailty by PRISMA-7 with institutionalization have been carried out.

6.3.4 Association of Self-Rated Health and Self-Reported Walking Ability with Institutionalization (Study II)

Both poor SRH and the inability to self-reportedly walk 400 meters were associated with a higher risk of institutionalization during the 10-year follow-up. However, the HRs for these were lower than for the frailty tools (FI and PRISMA-7). The number of participants in the frail categories according to FI and PRISMA-7 were higher than the number of participants in the poor SRH and the inability to walk –categories, and that could have diluted the effects.

For primary care purposes, the simple measures of SRH and self-reported walking ability would, however, be sufficient in identifying older people at higher risk of institutionalization. They could then be offered a CGA, and based on that, a plan for intervention.

6.3.5 Association of Frailty with Mortality (Study I)

Previously, FS and PRISMA-7 have been suggested for only screening of frailty (Dent et al., 2016), although others since have found FS a promising tool for mortality prediction (Kojima, 2018b). FI has been shown to have good specificity to frailty (Apóstolo et al., 2017), and to be good at predicting mortality (Song et al., 2010), but it is time-consuming which reduces its feasibility in the clinical setting

(Dent et al., 2016). In this thesis, pre-frailty and frailty by FS and FI, and also frailty by PRISMA-7 were associated with a higher risk of death during both follow-ups.

Even though FS categorized only 2% of the participants as frail, their HR for mortality was highest both in the unadjusted, and adjusted models during both follow-ups. FS is a simple and fast questionnaire based on self-report data and could be effectively used in the primary care setting for screening of frailty and an increased risk of death. Also pre-frailty by FS had similar HRs as pre-frailty by FI in the unadjusted and adjusted analyses during both follow-ups, suggesting that with feasibility in mind, the time-consuming FI could be replaced by the fast FS, especially if when screened positive for frailty, the individual would be referred to additional examinations. PRISMA-7 also performed well in the analyses predicting mortality, but with feasibility in mind, FS is faster to perform.

6.3.6 Subjective and Objective Health (Study III)

Altogether 420 participants were categorized as subjectively healthy, and 310 participants as objectively healthy, while 839 participants were categorized as subjectively unhealthy and 949 participants as objectively unhealthy. The participants in the "super healthy" (SO) group were expectedly younger, had more often higher than basic education, higher MMSE scores, and higher BMI scores than the participants in the "unhealthy" (UH) group.

Also, there was a difference between the BMI scores of the "super healthy" and the "worried but well" (O): the "worried but well" participants had higher BMI scores than the "super healthy". In addition to that, the "super healthy" had more often higher than basic education than the "worried but well". Perhaps the lower education and the higher BMI scores influenced their subjective health by lowering their SRH and/or satisfaction with life.

6.3.7 Association of Subjective and Objective Health with Institutionalization (Study III)

Being "unhealthy" did not increase the risk of institutionalization when compared to the "super healthy" in the adjusted analyses during both follow-ups. The rates of institutionalization per 1000 person-years were, however, different: 7.7 and 14.2 for the "super healthy", and 26.2 and 33.2 for the "unhealthy" during the 10- and 18-year follow-ups, respectively.

For the "unworried but ill" (S) and the "worried but well", the rates of institutionalization per 1000 person-years were again similar to each other for the both follow-ups, but for institutionalization, the rates were a little higher for the "unworried but ill" than the "worried but well", in contrast to the rates for mortality,

but not statistically significant. There was a trend but the statistical power was too low. Being "worried but well" has earlier been associated with a higher risk of institutionalization (Giltay et al., 2012).

All in all, the categorization of participants into four groups of combined health information was not good at predicting institutionalization in our study.

6.3.8 Association of Subjective and Objective Health with Mortality (Study III)

After adjusting for age, BMI, MMSE scores, and education, the "unhealthy" had a significantly higher mortality risk when compared to the "super healthy" during both follow-ups. The mortality rates per 1000 person-years for the "super healthy" and "unhealthy" were very different during the both follow-ups (16.0 and 37.7 for the "super healthy", and 69.1 and 79.9 for the "unhealthy", respectively). From the survival curves it can be seen, that the difference in mortality rates for the "unhealthy" and "super healthy" starts early and continues throughout the follow-up period.

Poor subjective health had an additive effect on poor objective health in predicting mortality. This effect has also been shown earlier (Giltay et al., 2012). The combination of poor subjective and objective health was still notable for mortality after 18 years, as suggested by the AP that was still significant after 18 years. This is a similar result to previous studies with follow-up periods of 18 (Desalvo & Muntner, 2011) and 27 (Wuorela et al., 2020) years. The individual's subjective health can be thought to include also the experienced disability linked to their chronic conditions as the mere existence of a chronic condition does not take into account its induced disability. By including the experienced disabilities, the subjective health measure can include more factors than objective health measures (Jylhä, 2009). A recent study suggested incorporating the SRH as a measure of subjective health into the assessment of an older person's health as it was almost as good at predicting mortality as objective health measured by frailty, at least during a shorter, less than 10 years, of follow-up (Wuorela et al., 2020).

The mortality rates per 1000 person-years during the 10-year follow-up were quite similar for the "unworried but ill", and the "worried but well", but differed somewhat during the 18-year follow-up (44.0 and 38.6 for the S and the O, respectively). This might be due to the longer follow-up during which new chronic conditions affecting mortality could be acquired, or that subjective health is able to encompass something that objective health is not when it comes to predicting survival during longer follow-ups. The simple SRH has indeed been shown to predict mortality during longer, up to 21-year follow-up periods (Idler et al., 2000), although

it has been shown to predict short-term mortality better than long-term (Benyamini et al., 2003; Wuorela et al., 2020).

6.3.9 Chronic Conditions and Multimorbidity (Study IV)

Multimorbidity was common in the study population. If the traditional definition of multimorbidity (at least two chronic conditions) had been used, multimorbidity prevalence would have been 96%. In this study population, the definition of multimorbidity was considered more applicable when defined as having four or more, or five or more chronic conditions with prevalences of 70% and 46%, respectively.

The prevalence of multimorbidity has been shown to increase over the last decades (Uijen & van de Lisdonk, 2009). They found that in the year 2005, the prevalence of multimorbidity defined by four or more chronic conditions was approximately 55% in participants aged 75 years or over. When considering the whole population, the prevalence of four or more chronic conditions was 2.6% in the year 1985, and 7.5% in the year 2005. Uijen and van de Lisdonk (2009) found that while having four or more chronic conditions in the year 1985 was an exception, in the year 2005 it was as common as having two or three chronic conditions. These participants were patients of the Dutch General Practitioners' and the researchers report that the increase is not likely due to the effects of starting registration, or a change in classification, or coding rules, as these factors had remained unchanged during the years (Uijen & van de Lisdonk, 2009). Also, they standardized their data to the year 2000 to take into account the ageing population (Uijen & van de Lisdonk, 2009).

The prevalence of multimorbidity in our study was higher than found in the Dutch population (Uijen & van de Lisdonk, 2009). Our study population was older (aged 84 years or over at the end of the follow-up), and also, the follow-up in our study ended at the end of 2016, while theirs ended in 2005. The increase in prevalence of multimorbidity they found from 1985 till 2005 could have of course continued from 2005 till 2016 also in Finland.

Also, a systematic review found that there is great heterogeneity in the prevalence of multimorbidity, and the heterogeneity is highest in persons aged 75 years or over (Fortin et al., 2012). When defining multimorbidity as having two or more chronic conditions and using the general population as the study population instead of a primary care population used by Uijen and van de Lisdonk (2009), Fortin et al. (2012) found that the prevalence of multimorbidity at the age of 85 years or over was approximately 45–65%. Using the primary care setting, the prevalence of multimorbidity defined as having three or more chronic conditions in participants

aged 85 years or over, was approximately 60% (Fortin et al., 2012). The prevalence increased with age in most of the studies reviewed (Fortin et al., 2012).

The increase in multimorbidity is probably due to multiple factors. Many diseases increase in prevalence with age and the population is ageing. Improved diagnostics and new treatment options especially in primary care increase the need for early diagnostics.

All in all, our study population was very multimorbid and the use of multimorbidity definitions greater than the often used two or more chronic conditions was warranted.

6.3.10 Association of Chronic Conditions and Multimorbidity with Institutionalization (Study IV)

Dementia, mood disorders and neurological disorders were associated with a higher risk of institutionalization in our study. This is in line with earlier research (Aaltonen et al., 2019; Hajek et al., 2015; Halonen et al., 2019; Luppa, Luck, Weyerer, et al., 2010; Nihtilä et al., 2008; Salminen et al., 2017, 2020). For participants without dementia, having mood disorders or neurological disorders were associated with an increased risk of institutionalization. This too is in line with earlier research (Luppa, Luck, Matschinger, et al., 2010), were they found that depression and functional impairment, that neurological disorders often lead to, were associated with an increased risk of institutionalization.

In our study, malignant neoplasms, ischaemic heart disease, atrial fibrillation and renal failure were associated with a lower risk of institutionalization. For malignant neoplasms, this is most likely due to the mortality associated with them: people die earlier in life and don't end up needing institutional care before death. In an earlier study, however, malignant neoplasms were associated with an increased risk of institutional care (Gaugler et al., 2007; Koller et al., 2014). The difference might be due to the differences in health care systems. In Finland, palliative care is often provided at the persons own home with the aid of the municipality's at-home hospital and formal home care.

For ischeamic heart disease, earlier research has shown an association of increased risk of institutionalization in participants without a dementia diagnosis (Luppa, Luck, Matschinger, et al., 2010). In our study, ischeamic heart disease was, however, associated with a decreased risk of institutionalization in participants without dementia and in all participants. The proportions of participants with ischaemic heart disease were high in both the community-dwelling and institutionalized participants, but higher in the community-dwelling participants. Perhaps the new cardiological treatments have enabled the people with chronic heart disease to live with less disability, and at home longer than before, or they perish due

to heart related disease before the onset of disability leading to the need of institutional care.

For renal failure, an earlier Finnish study showed an increase in the risk of institutionalization related to renal disease (Salminen et al., 2020). In our study, however, it was associated with a decreased risk of institutionalization. Atrial fibrillation was associated with a decreased risk of institutionalization in our study, but stroke was not. Stroke has been identified as a factor leading to increased risk of institutionalization in earlier research (Aaltonen et al., 2019; Andel et al., 2007; Banaszak-Holl et al., 2004; Gaugler et al., 2007; Koller et al., 2014; Nihtilä et al., 2008; Nuutinen et al., 2017). Perhaps the number of participants with stroke was too low to make any conclusions, or the rehabilitation of stroke has improved leading to less disability than before.

For multimorbidity, having five of more chronic conditions was associated with an increased risk of institutionalization also in the adjusted analyses. Multimorbidity by different definitions has been shown to increase the risk of institutionalization in older adults (Koller et al., 2014; Salminen et al., 2020). Salminen et al. (2020) found multimorbidity defined as having two or more chronic conditions, and Koller et al. (2014) multimorbidity defined as having three or more chronic conditions to be associated with an increased risk of institutionalization in older adults aged 65 years or over (Koller et al., 2014; Salminen et al., 2020). In the very old population, Halonen et al. (2019) found that multimorbidity defined as three or more, or as four or more chronic conditions was associated with an increased risk of institutionalization in the very old, aged 90 years or over, population (Halonen et al., 2019).

In light of the high prevalence of having multiple chronic conditions found in this Finnish study population, we suggest using five or more chronic conditions as the cut-off for multimorbidity when assessing older adults' risk of institutionalization associated with multimorbidity.

6.3.11 Describing the Successful Agers (Study V)

The functional and cognitive ability of the successful agers, the ones still able to live at home without daily informal or formal care at the age of 84 years or older, had naturally worsened during the follow-up period of 20 years, but most of them were still satisfied with their lives.

Frailty by all three tools used had increased during the follow-up. This was expected, as frailty increases with age (O'Caoimh et al., 2021). The FS still identified only 21% as frail, when PRISMA-7 categorized 75%, and the FI 46% as frail. The modifications used for FS could have affected its ability to identify frailty. For PRISMA-7, as it gives one point for all who are 85 years or older and it requires

three points to categorize an individual as frail, it is not surprising that three out of four successful agers were categorized as frail by PRISMA-7. PRISMA-7 is not therefore the best choice in identifying frailty in people over 85 years of age as it tends to over screen (Clegg et al., 2015). Also, the modifications used for PRISMA-7 could have impacted the results in this study.

Objective health measured by the number of chronic conditions had worsened during the 20 years. However, only 21% of these successful agers had five or more chronic conditions which in Study IV was found to be associated with a higher risk of institutionalization. This finding in Study V strengthens our findings in Study IV.

Results for gait speed and grip strength were in line with previous research of older adults aged 84 years or over (Finnish Institute for Health and Welfare, 2018; Hollman et al., 2011; Lusardi et al., 2003; Werle et al., 2009). This depicts probably the fact that the participants in studies determining reference values have often better functional ability than those who choose not to participate, the non-response bias, which seemed to be present also in our study (Banack et al., 2019; Kelfve et al., 2013) . Also, the mean gait speed for both women and men in our study was over 0.8 m/s. This has previously been shown to be a cut off for survival: predicted life expectancy at the median for age and gender occurs at about 0.8 m/s and faster gait speeds predict survival beoynd the median (Studenski et al., 2011). Perhaps these successful agers will continue to age successfully.

Subjective health was defined the same as in Study III and the definition was quite strict. Still, one in four met all these three criteria (good SRH, self-reported ability to walk 400 meters and good satisfaction with life) at the chronological age of 84 years or older.

More of the successful agers rated their SRH now as poor than at baseline, but still over three fourths assessed their SRH as at least moderate despite having more chronic conditions. For satisfaction with life, only three participants (3%) reported poor satisfaction with life at baseline and only one participant (1%) at re-examination. Almost all of the successful agers regarded their satisfaction with life as at least moderate despite that they had more illnesses, their functional and cognitive ability had worsened and they were more often frail than at baseline. This could suggest that ageing successfully does not necessarily mean the absence of illness, disability or frailty, but could be possible for also ill, disabled and frail persons if they were given the necessary social and environmental support, and thus felt satisfied with their lives.

Successful agers having such good satisfaction with life despite hardships could suggest them having high resilience (MacLeod et al., 2016). They had the sensation of ageing successfully and were quite satisfied with their lives even though their health and functional ability was worse both objectively and subjectively. This

finding is similar to earlier research investigating centenarians and near-centenarians (Jopp et al., 2016).

6.3.12 Personal Biological Age and "Eyeball Test" (Study V)

The mean PBA of the successful agers was lower than their CA at baseline and at re-examination. In fact, the difference was greater at re-examination. Despite the fact that most of the participants were categorized as pre-frail by the FI at baseline and re-examination, their PBA was still lower than their CA depicting that while they were pre-frail, they were not as pre-frail as their CA would suggest. They were indeed successful agers and more so at re-examination than at baseline.

PBA has earlier been found a better predictor of mortality than CA although in a shorter follow-up of originally older participants (Mitnitski et al., 2002). Our findings support that as these survivors were mostly biologically younger than their years.

The concordance with the "eyeball test" and the difference between the CA and PBA was poor in regarding the frail participants, the ones with a PBA higher than their CA. The "eyeball test" has also earlier been found to be poor at identifying the frail individuals (Jain et al., 2014). However, the "eyeball test" was better at identifying the participants with a PBA lower than their CA, the successful agers.

6.4 Strengths and Limitations

The strength of this thesis is a large sample size of unselected participants aged 64 years or older at baseline, with a high participation rate enabling broad generalizability to the community-dwelling older population. The municipality of Lieto was a semi-industrialized mid-size municipality with 12 % of the population aged 65 or older, in comparison with the whole country at 15 %, at baseline (Official Statistics of Finland, 2018). This enables generalizability to most of the municipalites in Finland.

Also, the use of multiple data sources to gather the data on chronic conditions, institutionalization and mortality makes the data robust. The dates of institutionalization were gathered from the electronic patient record system and are therefore more exact compared to earlier studies in which the information was gathered by interview (Bravell et al., 2009; Hajek et al., 2015; Luppa et al., 2012).

A long follow-up time makes the analyses on predicting outcomes clinically relevant. Also, the use of 10- and 18-year follow-up periods enabled identifying some predicting factors that would have been overlooked if only the 18-year follow-up was used.

All our analyses were designed together with a statistician and a data manager enabling high quality statistical analyses and a comprehensive consideration of adjustable variables.

Frailty tools used in this thesis (Studies I, II and V) were validated and commonly used (Apóstolo et al., 2017; Clegg et al., 2015; Lopez et al., 2012), although our modifications to the FS and PRISMA-7 could have impacted the results. For institutionalization analyses, we used death as a competing factor, which strengthens the statistical base of our results.

The definition of subjective health for Studies III and V was comprehensive and in line with the WHO definition of health (World Health Organization, 1948), and the definition of objective health was intentionally quite strict to enable the analyses on subjectively and objectively healthy, the "super healthy" participants. For Study III we used a previously described method of assessing biological interaction (Andersson et al., 2005) to describe the interaction between subjective and objective health.

The data on acquired chronic conditions and multimorbidity were also gathered from multiple data sources and it included all the conditions acquired during the follow-up period (Studies IV and V). This same approach has been used also earlier (Bravell et al., 2009; Hajek et al., 2015; Luppa et al., 2012). Also, for these studies, the chronic conditions assessed were intentionally selected as conditions that could impact the individual's health and/or wellbeing instead of including all, or a broader selection of conditions (as in Study III). Dementia was not surprisingly the highest risk factor for institutionalization and therefore we also analyzed other chronic conditions in participants without dementia to find the conditions predicting higher risk of institutionalization among this population.

For Study V the strengths are an extensive re-examination of the original participants after a 20-year follow-up period including most of the variables studied at baseline and also some additional variables, the use of multiple data sources to gather the information needed, the non-response analysis and consistency in the examination brought by the fact that the same study physician and study nurse performed all the re-examinations together.

The limitations to this thesis are the only baseline data used to predict adverse effects in Studies I, II and III. Especially the institutionalization analyses can suffer from this as institutionalization is multifactorial. Also, at baseline, we did not have the data on formal or informal care available for analyses and the use of and the possibility of the use of formal or informal care of course affects the risk of institutionalization (Gaugler et al., 2007; Nuutinen et al., 2017; Salminen et al., 2020). The modifications used in the frailty indices could have impacted the results. Despite these limitations, we did investigate the medical records of all participants

in order to find the exact date of institutionalization and for Study IV, all the relevant diagnoses of chronic conditions acquired during the follow-up period.

For Study V, the low number of re-examined participants included in the analyses is a limitation. However, we managed to get a mail response from a substantial number of non-participants and were able to conduct a non-response analysis which can be considered a strength to this study (Hardy et al., 2009). The analysis showed little difference between the successful agers and the non-participants, but there was a difference in functional ability so non-response bias, a common challenge in ageing research (Banack et al., 2019; Kelfve et al., 2013), at least on that account, seems to be present.

6.5 Implications for Clinics and Future Research

6.5.1 Implications for Clinics

Frailty should be screened for among community-dwelling older adults in primary care to better target interventions to prevent, delay or reverse the cascade of frailty. FS could be used as a screening tool to find persons in need of a more elaborate evaluation. With our modifications it might, however, under-screen and thus also pre-frailty, in addition to frailty, should lead to additional evaluations. The possibility of generating the FI straight from the electronic patient record system should be explored and utilized as a more sensitive way to identify pre-frail and frail older adults. Without the possibility of electronic retrieval, it is too time-consuming for the clinical setting.

Combining easy-to-use self-reported tools of SRH and walking-ability to the evaluation of an older person's health could be useful in identifying those at higher risk of institutionalization. A CGA should then be performed and targeted interventions based on that should ensue.

Dementia, neurological disorders and mood disorders should be identified and treated (when possible) early on. Identifying these chronic conditions and multimorbidity as the risk factors of institutionalization among the older people visiting primary care professionals should lead to a broader evaluation of functional abilities and needs of care.

The combination of subjective and objective health was associated with mortality but not institutionalization. Subjective health had an additive effect on objective health in predicting mortality. The subjective evaluation of an older person's health should be taken into account more often in primary care as it seems to add to the objective evaluation. Poor subjective health should lead to additional evaluations.

Satisfaction with life should be identified as a possible factor leading to ageing successfully and the factors leading to not being satisfied with life should be addressed if possible.

6.5.2 Implications for Future Research

We aim to investigate these successful agers further by analyzing their modifiable risk factors (blood pressure, heart rate, smoking, alcohol use, BMI, life long habit of exercice, blood cholesterol and glucose) and health behavior influenced chronic conditions (hypertension, coronary heart disease, peripheral artery disease, chronic heart failure, chronic obstructive pulmonary disease and diabetes), and to compare these results to a reference population of the same age at baseline, but who were institutionalized or had deceased during the follow-up period of 20 years. The aim is to investigate the possible difference in these traditional risk factors among the successful agers and the unsuccessful agers.

Also, we are constructing SA models similarly to earlier studies on Finnish nonagenarians (Nosraty et al., 2015, 2019). We aim to compare our successful agers to a reference population of the same age at baseline, but who were institutionalized or had deceased during the follow-up period of 20 years to investigate whether these models also work in predicting institutionalization or mortality in a younger population and during a longer follow-up period.

To strengthen the results presented in this thesis, the same variables would be of interest to study in another population.

These same variables could also be studied in a later birth cohort to see if the predictors for institutionalization and mortality change over time. The policy is in favour of home care instead of institutional care and substantial care needs that earlier would have been met only in institutional care, are now considered manageable in home care. With the population ageing, however, a need for a different policy might arise as an answer to the increasing number of older people in need of both home care and institutional care. Technological advancements might on the other hand enable living at home for a larger number of older people than nowadays. The policy changes and possible technological advancements might change the predictors for institutionalization and advancements in health care might change the predictors for mortality in the future.

7 Conclusions

Frailty according to several definitions is prevalent among community-dwelling older adults and predicts institutionalization and mortality. SRH and self-reported walking ability are feasible measurements in clinical practice to predict institutionalization among community-dwelling older adults. Subjective health combined with objective health predict mortality, and poor subjective health has an additive effect on poor objective health in predicting mortality. Having dementia, a mood or a neurological disorder, and/or having five or more chronic conditions is associated with a higher risk of institutionalization. Successful agers had few of these risk factors, were satisfied with their lives and were biologically younger than their chronological age both at baseline and after a 20-year follow-up period.

In regard to these findings, the following conclusions can be drawn:

- Frailty was associated with institutionalization and mortality, and SRH and self-reported walking ability with institutionalization in this community-dwelling population of older people.
- The combination of subjective and objective health was associated with mortality but not with institutionalization among this study population. Dementia, mood or neurological disorders were associated with a higher risk of institutionalization. Multimorbidity, defined as having five or more chronic conditions instead of the commonly used definition of two conditions, was associated with a higher risk of institutionalization.
- Successful agers had a biological age younger than their chronological age, and were satisfied with their lives both at baseline and after a 20-year follow-up period.

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