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Malnutrition and obesity among older adults,

assessed by Mini Nutritional Assessment and the body mass index, respectively: prevalence and associations with mortality and urinary tract infection

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To my family,

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Abstract

Introduction: Malnutrition and obesity are health concerns among older (aged ≥ 65 years) adults, but the combination of them have not been studied thoroughly nor have they been thoroughly investigated in very old (aged ≥ 85 years) adults. The aims of this thesis were to investigate the prevalence, trends in prevalence and associations with mortality of malnutrition and obesity, assessed by Mini Nutritional Assessment (MNA) and the body mass index (BMI), respectively, and to examine the combined effects of these conditions on mortality. Malnutrition as a risk factor for urinary tract infection (UTI) was also investigated.

Material and Methods: The studies reported on in papers I and II were conducted with data from the Umeå85+/Gerontological Regional Database study, a population-based study of cohorts of very old adults. Data from all four Swedish cohorts (2000–2002, 2005–2007, 2010–2012 and 2015–2017), and from the 2000–2002 and 2005–2007 Swedish cohorts and a 2005–2006 Finnish cohort, respectively, were used. In the paper I study, trends in the prevalence of malnutrition (by MNA score) and obesity (by BMI) were investigated across cohorts. In the paper II study, the associations of MNA scores and BMI with 5-year mortality were investigated. The study reported on in paper III was conducted with data from the Senior Alert national quality registry; associations of Mini Nutritional Assessment–Short Form (MNA-SF) scores, BMI and 2-year mortality in older adults living in residential care facilities in Sweden were investigated. The study reported on in paper IV was conducted with data from the Frail Older People–Activity and Nutrition and Umeå Dementia and Exercise studies; risk factors for UTI among older adults in residential care facilities were investigated.

Results: In the paper I study, mean BMI increased between 2000–2002 and 2015–2017 and the prevalence of obesity were 13.4% and 18.3%, respectively; the prevalence of underweight were 7.6% and 3.0%, respectively. Mean MNA scores increased between 2000–2002 and 2010–2012 and were slightly lower in 2015–2017. The prevalence of malnutrition according to MNA scores in the four cohorts were 12.2%, 6.4%, 5.1% and 8.7%, respectively, and the prevalence of at risk thereof were 31.8%–37.2%. In the paper II study, 13.3% of participants were malnourished, and 40.3% were at risk thereof according to MNA scores, and malnutrition was more common among women than men. Twenty-

five percent of the population had BMIs ≥ 28.0 kg/m^2. Of those with malnutrition according to MNA scores, 17.4% had BMIs ≥ 24.7 kg/m^2; of those with good nutritional status according to MNA scores, 13.8% had BMIs < 22.2 kg/m^2. Compared to malnutrition according to MNA, lesser mortality was found in those with good nutritional status. Compared to individuals with BMI < 22.2 kg/m^2, lesser mortality was found in those with BMI ≥ 28.0 kg/m^2. In the paper III study, 14.6% of the population was malnourished, and 45.0% were at risk of malnutrition according to MNA-SF scores and 16.0% were obese. Compared to individuals with good nutritional status, greater mortality was found in those with malnutrition according to MNA-SF. Mortality was greater among underweight than among normal-weight participants and lesser among participants with obesity, including severe obesity. Higher BMIs were also associated with reduced mortality in subgroups defined by MNA-SF scores. In the paper IV study, malnutrition according to MNA scores was not a risk factor for UTI in the whole sample or in women. In men, the MNA score was associated with UTI in univariate analysis.

Conclusions: The results of this thesis highlight the importance of nutritional screening in older adults in residential care facilities and in very old adults, since malnutrition risk was common and associated with greater mortality among these populations. Malnutrition according to MNA was not a clear risk factor for UTI in older adults living in residential care facilities. Time trends indicated an increasing prevalence of obesity whereas no change in nutritional status according to MNA was observed among very old adults, although these trends need further investigation. The results also confirmed that higher BMIs were beneficial for survival in these populations, and in the residential care population this seems to apply also for BMIs reflecting severe obesity. Finally, in the residential care population, regardless of nutritional status according to MNA-SF, higher BMIs were associated with better survival.

Abbreviations

ADL	activities of daily living
ASA	acetyl-salicylic acid
BBS	Bergs Balance Scale
BIA	bioelectrical impedance analysis
BMI	body mass index
C	cohort
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CT	computed tomography
DFRI	Downton Fall Risk Index
DoMAP	Determinants of Malnutrition in Aged Persons
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, fourth edition
DXA	dual-energy X-ray absorptiometry
ESPEN	European Society for Clinical Nutrition and Metabolism
FOPANU	Frail Older People–Activity and Nutrition
GDS-15	15-item Geriatric Depression Scale
GERDA	Gerontological Regional Database
GLIM	Global Leadership Initiative on Malnutrition
HR	hazard ratio
I	instrumental
MMSE	Mini-Mental State Examination
MNA	Mini Nutritional Assessment
MNA-SF	Mini Nutritional Assessment–Short Form
MNS	Modified Norton Scale
MRI	magnetic resonance imaging
MST	Malnutrition Screening Tool
MUST	Malnutrition Universal Screening Tool
NPR	National Patient Register
NRS	Nutritional Risk Screening
P	personal
Q	quartile
RAPS	Risk Assessment Pressure Sore
ROAG	Revised Oral Assessment Guide
SA	Senior Alert
SD	standard deviation
SGA	Subjective Global Assessment
SNAQ	Simplified Nutritional Assessment Questionnaire

SSRI	selective serotonin reuptake inhibitor
UMDEX	Umeå Dementia and Exercise
UTI	urinary tract infection
WHO	World Health Organization

Original papers

The thesis is based on the following papers, which have been provided with permission from the publishers.

Paper I

Burman M, Hörnsten C, Öhlin J, Olofsson B, Nordström P, Gustafson Y. Prevalence of obesity and malnutrition in four cohorts of very old adults, 2000–2017. Manuscript.

Paper II

Burman M, Säätelä S, Carlsson M, Olofsson B, Gustafson Y, Hörnsten C. Body mass index, mini nutritional assessment, and their association with five-year mortality in very old people. J Nutr Health Aging. 2015 [1].

Paper III

Burman M, Hörnsten C, Gustafson Y, Olofsson B, Nordström P. Obesity may increase survival, regardless of nutritional status: A Swedish cohort study in nursing homes. Manuscript.

Paper IV

Burman M, Hörnsten C, Carlsson M, Rosendahl E, Nordström P, Olofsson B, Gustafson Y. Is malnutrition a risk factor for incident urinary tract infection among older people in residential care facilities. Jour Nursing Home Res. 2018 [2].

Sammanfattning på svenska

Introduktion

Undernäring är ett tillstånd där brist på näringsämnen har orsakat sjukdomar eller påverkat sjukdomsförlopp, kroppssammansättning eller funktionsförmåga. Åldrandet i sig, sjukdomar, läkemedel, munhälsa, fysisk och kognitiv funktion och sociala faktorer är kopplat till undernäring på olika sätt, speciellt hos äldre personer (≥ 65 år). Undernäring är därför vanligt bland äldre och är vanligare bland de som bor på särskilt boende. Däremot är förekomsten av undernäring mindre studerad bland de allra äldsta (≥ 85 år), och tidigare studier har visat hög men varierande förekomst. Dessutom är det få studier som har undersökt om förekomsten av undernäring har förändrats i den här åldersgruppen i Sverige. Undernäring har flera allvarliga konsekvenser, inklusive en ökad risk för död men även här behövs mer kunskap om hur kopplingen till död ser ut hos de allra äldsta. Undernäring är också associerat med en ökad risk för infektioner. I en tidigare studie från vår forskargrupp har man sett att det bland äldre personer på särskilt boende var vanligt att de med undernäring hade haft urinvägsinfektion föregående år. Huruvida undernäring är kopplat till en ökad risk för att drabbas av urinvägsinfektion är dock mindre studerat.

Förekomsten av fetma har ökat bland vuxna och äldre de senaste decennierna och i en svensk studie på personer som var 70 år under år 2000, så hade ungefär en femtedel av studiedeltagarna fetma. Om fetma ökar även bland de allra äldsta är dock mindre studerat. Fetma ökar risken för bl.a. hjärt-kärlsjukdom och typ 2 diabetes. Däremot tycks fetma vara kopplat till en bättre överlevnad hos de med etablerad hjärtsjukdom, t.ex. hjärtsvikt, vilket brukar kallas för the ”obesity paradox”. Det är dock inte klarlagt vad som orsakar att dessa samband ses i studier. Kopplingen mellan fetma och död är mindre studerad bland de allra äldsta, vilket även den kombinerade effekten av undernäring och fetma är, samt hur kopplingen mellan högre grad av fetma och död ser ut.

Livslängden ökar och de äldsta åldersgrupperna utgör en allt större del av befolkningen vilket gör att behovet av kunskap om undernäring och fetma i dessa åldersgrupper är stort. Syftet med den här avhandlingen var att undersöka förekomsten (samtliga delarbeten), inklusive tidstrender (delarbete I), av undernäring och fetma. Vidare var syftet att studera

kopplingen mellan undernäring, fetma och död bland de allra äldsta (delarbete II) och bland äldre på särskilt boende, inklusive högre grader av fetma (delarbete III), samt att undersöka om undernäring ökar risken för att få urinvägsinfektion bland äldre som bor på särskilt boende (delarbete IV).

Metod och resultat

I alla delarbeten har undernäring bedömts enligt screeninginstrumentet Mini Nutritional Assessment (MNA) eller dess kortare version MNA-SF och som identifierar en individ i risk för undernäring som bör utredas vidare för att utreda orsaker, planera åtgärder samt fastställa diagnos. MNA och MNA-SF delas in i tre kategorier utifrån fallande poängskala: normalt nutritionsstatus, risk för undernäring och undernäring.

Fetma har definierats med body mass index (BMI; kg/m^2) i samtliga delarbeten och i delarbete I och III delades BMI in i kategorier där undervikt definierades som BMI < 18.5 kg/m^2 och fetma som BMI ≥ 30 kg/m^2. I delarbete III delades fetma även upp i grad I, II och III. I delarbete II delades BMI in i kvartiler där lägsta kvartilen var BMI < 22.2 kg/m^2 och högsta var BMI ≥ 28.0 kg/m^2.

I delarbete I och II, inkluderades personer som var 85 år och äldre som undersöktes i sina hem. Undersökningarna har upprepats med fem års mellanrum mellan 2000–2002 och 2015–2017. I första delarbetet jämfördes förekomsten av undernäring och fetma mellan de fyra insamlingsomgångarna där totalt 1602 personer deltog. Undernäring enligt MNA förekom hos 5.1%–12.2% av deltagarna och en stor andel hade också risk för undernäring enligt MNA (31.8%–37.2%) vid de fyra insamlingsomgångarna. Medelvärdet av MNA ökade mellan första och tredje insamlingsomgången, men hade minskat igen till den sista insamlingsomgången. Samtidigt tycktes medelvärdet av BMI och förekomsten av fetma öka mellan första och fjärde datainsamlingen, där 13.4% av deltagarna hade fetma vid den första och 18.3% vid fjärde insamlingsomgången. I det andra delarbetet studerades kopplingen till fem-års mortalitet och av 832 inkluderade individer så var 13.3% undernärda och 40.3% i risk för undernäring enligt MNA. Undernäring var vanligare bland kvinnor än hos män. Jämfört med individer med undernäring enligt MNA sågs en lägre risk för död hos de med risk för undernäring och de med normalt nutritionsstatus. Individer med BMI

≥ 28.0 kg/m^2 hade en lägre risk för död jämfört med de med ett BMI < 22.2 kg/m^2.

Delarbete III baserades på information från det nationella kvalitetsregistret Senior Alert, vars syfte bland annat är att förebygga undernäring hos äldre. Studien inkluderade 47 686 äldre personer på särskilt boende i Sverige och 14.6% av deltagarna var undernärda, 45.0% var i risk för undernäring enligt MNA-SF och 16.0% hade fetma och de flesta hade fetma grad I (12.1%). Jämfört med individer med ett BMI ≥ 30 kg/m^2 så hade de med lägre BMI ökad risk för död. Jämfört med individer med normalvikt enligt BMI så hade de med undervikt en ökad risk för död och de med övervikt och fetma grad I, II och III en lägre risk för död. Undernäring och risk för undernäring var kopplat till en ökad risk för död, jämfört med normalt nutritionsstatus enligt MNA-SF. Vidare undersöktes hur olika BMI värden påverkade risken för död bland de som var undernärda eller i risk för undernäring enligt MNA-SF och ett högre BMI tycktes gynnsamt oavsett vilket nutritionsstatus som personen hade enligt MNA-SF.

I delarbete IV användes data från två studier där äldre personer på särskilda boenden i Västerbotten inkluderades, totalt 373 personer. Undernäring enligt MNA ökade inte risken för urinvägsinfektion. Dock kan det finnas en koppling mellan undernäring och risk för urinvägsinfektion hos män.

Diskussion

Risk för undernäring var vanligt bland äldre och de allra äldsta och dessa fynd stödjer tidigare studiers resultat, även om jämförelser med tidigare studier är svårt p.g.a. att deltagare i olika studier skiljer sig åt i t.ex. ålder, sjuklighet och hur stor andel som bor på särskilt boende. Orsakerna till de tidstrender som sågs i delarbete I är komplexa då flertalet faktorer kan kopplas till undernäring. Utifrån resultaten i delarbete I är det möjligt att spekulera kring bidragande faktorer. Det tycktes som om vissa sjukdomar ökade i delarbete I, vilket direkt eller indirekt kan leda till undernäring. Kvalitetsregistret Senior Alert spreds nationellt i Sverige mellan 2010 och 2014, genom statligt stöd och ekonomiska incitament. De flesta registreringarna i Senior Alert sker på särskilda boenden och det är möjligt att dessa insatser för att förebygga bland annat undernäring kan ha gett positiva effekter som motverkats av andra förändringar, t.ex. att en mindre andel av de äldre bor på särskilt boende, vilket innebär att de

individerna är sjukare, och att antalet vårdplatser på sjukhus minskat, vilket innebär att de äldre skrivs ut från sjukhus med ett större vårdbehov. Ett viktigt nästa steg är att undersöka vilka faktorer som är kopplade till undernäring bland de allra äldsta.

Undernäring var kopplat till en ökad risk för död bland de allra äldsta i delarbete II. Tidigare studier har visat att 1-års-mortalitet men inte 3- eller 5-års-mortalitet har varit kopplat till undernäring. Skillnaden mot resultaten i delarbete II kan bero på vilka som inkluderats i de olika studierna, samt vilka analyser som gjorts. Vidare ökade inte undernäring enligt MNA risken för urinvägsinfektion hos äldre som bor på särskilt boende i delarbete IV, såsom tidigare studier visat. Resultaten från delarbete IV behöver dock verifieras i fler studier.

Resultaten från delarbete II och III antyder att the obesity paradox kan vara gällande även för de allra äldsta och för äldre på särskilt boende och för dessa tycktes det gälla även högre grader av fetma. För äldre personer på särskilt boende tycktes även högre BMI gynnsamt för överlevnaden oavsett nutritionsstatus enligt MNA-SF. Det finns många tänkbara förklaringar till dessa fynd, t.ex. är de personer som lever till 85 års ålder är en selekterad grupp av individer. Ett högre BMI betyder även att personen har en energireserv att använda vid olika sjukdomstillstånd som kan ge upphov till ett lägre näringsintag eller en högre energiförbrukning. Det kan även finnas metodologiska aspekter som kan påverka de samband som observeras mellan BMI och risk för död. Att undersöka potentiella konsekvenser av fetma hos äldre är angeläget, särskilt om BMI ökar även bland de allra äldsta, vilket resultaten från delarbete I antyder.

Slutsats

I delarbetena i den här avhandlingen har undernäring och fetma studerats i olika datamaterial och populationer. Resultaten belyser vikten av att göra riskbedömningar av äldres näringstillstånd eftersom risk för undernäring enligt MNA och MNA-SF var vanligt förekommande bland äldre på särskilt boende och de allra äldsta, samt var kopplat till en ökad risk för död. Undernäring var däremot inte en riskfaktor för att äldre på särskilt boende skulle ådra sig urinvägsinfektion.

Tidstrenderna som observerades antyder att förekomsten av fetma ökade bland de allra äldsta. Däremot sågs det inte någon förändring av nutritionsstatus enligt MNA mellan 2000 och 2015.

Resultaten i den här avhandlingen bekräftar också att ett högre BMI är kopplat till en lägre risk för död bland äldre på särskilt boende och bland de allra äldsta, och för de äldre på särskilt boende tycktes det även gälla för högre grader av fetma. Dessutom, bland äldre på särskilt boende så tycktes ett högre BMI vara gynnsamt för överlevnaden oavsett nutritionsstatus enligt MNA-SF.

Resultaten från de ingående delarbetena tillför ny och uppdaterad kunskap om undernäring och fetma hos äldre på särskilt boende och personer 85 år och äldre. Resultaten belyser även behovet av studier som undersöker orsaker till både undernäring och fetma samt deras konsekvenser. Det gäller särskilt studier som inkluderar de allra äldsta eftersom de kommer utgöra en allt större grupp i samhället i framtiden, och där få studier finns.

Introduction

Malnutrition and underweight have historically been caused by hunger and starvation, but the panorama of malnutrition has changed with improvements in living conditions. Currently, malnutrition in developed countries is seen mostly among older adults and is a multifactorial process caused by ageing, medical conditions, medication use and psychological and social factors. Furthermore, dietary changes and more sedentary lifestyles have made overweight and obesity global concerns in all age groups, including older adults. This development has potential consequences and challenges for the health of older adults, especially since they comprise the fastest-growing age group in the world.

However, studies including older, and in particular very old adults are scarce. Subsequently, knowledge in areas such as the prevalence and trends of malnutrition and obesity, and their association with long-term mortality is lacking. This also apply for older adults in residential care facilities in Sweden, where information on how obesity, including more severe obesity, and malnutrition are associated with mortality, including the combination of them both. In previous research from the Department of Community Medicine and Rehabilitation, an association between malnutrition and having had a urinary tract infection (UTI) in the previous year has been reported. This raised the question if malnutrition could be a risk factor for this common infection, an area that has been scarcely investigated previously.

This thesis focused on the prevalence and trends of malnutrition and obesity, and their associations with mortality, in older and very old adults. Malnutrition was also examined as a risk factor for UTI.

Definitions of older and very old adults

According to the World Health Organization (WHO), older adults are aged ≥ 60 years and very old adults are aged ≥ 80 years [3]. In Sweden, the term ‘older adults’ usually refers to individuals aged ≥ 65 years; in this thesis, this definition of older adults is adopted and individuals aged ≥ 85 years are considered to be very old adults, unless indicated otherwise. To avoid ageism, the term ‘elderly’ is not used [4, 5].

Demographic trends among older adults

The age group of older adults is growing rapidly worldwide [3] including in Sweden. In 2017, Sweden had a population of 10.1 million people, about 20% of whom were aged ≥ 65 years; this proportion is expected to increase to 25% by 2070 [6]. The number of people aged ≥ 80 years is expected to increase from 0.5 million in 2017 to 1.3 million in 2070 [6]. Life expectancy is also expected to increase, from 84 to 89 years in women and from 80 to 87 years in men, between 2017 and 2070 [6]. In Finland in 2000, the age group of old and very old constituted 15.0% and 1.5% of the population (total population of 5.2 million people), respectively, compared to 20.5% and 2.5% in 2015 (total population of 5.5 million people) [7]. Increased life expectancy historically has been driven by reduced mortality in younger age groups; currently, it is driven mainly by reduced mortality in older age groups, referred to as the epidemiological transition [6]. In adults aged ≥ 60 years, this reduction is attributable primarily to reduced mortality from cardiovascular diseases [6].

Health and social care of older adults in Sweden and Finland

This section describes the health and social care system of older adults in Sweden and Finland to give a context to the results of the studies in this thesis. In Sweden and internationally, 'ageing in place' policies are implemented with the aim of enabling older adults to live in their own homes as long as possible [3]. In Sweden, older adults can receive in-home help from home care and/or nursing services or live in residential care facilities. The terminology and conceptualisation of 'residential care' and 'nursing homes' vary among countries and have changed in recent decades; in this thesis, 'residential care facilities' is used to refer to facilities with nursing staff present at all times [8] and includes nursing homes, long-term care facilities, and group dwellings for people with dementia. When referring to previous research, the terminology used in these studies are primarily used. The number of people aged ≥ 80 years receiving public care for older adults increased greatly in Sweden in the 1960s and 1970s. Since the 1980s, this proportion has decreased, initially through the reduced use of home care services; in the last two decades, however, more older adults have been offered home care services than residential care [9]. Between 2001 and 2012, the percentage of people aged ≥ 80 years living in residential care facilities decreased from 21.7% to 15.6% [10]. In addition, changes in city council–run health care have

occurred; the decline in the number of hospital beds in past decades has resulted in the discharge of older adults with greater care needs than previously [11]. As a consequence of these changes, persons living in residential care facilities are expected to be older and frail [12]; indeed, lengths of stay in these units have decreased, with 10% of older adults who moved into them dying within an average of 85 days in 2006 and only 8 days in 2012 [13]. Also in Finland there has been a transformation in the care of older adults from the year of 2000, and in 2014, 8.7% of adults aged 75 years and older was living in residential care facilities [14].

Senior Alert

In the beginning of the 2000s the county council of Jönköping introduced a preventive care process locally. This work was the foundation of what later became a Swedish national quality register, Senior Alert (SA), in 2008 [15, 16]. The purpose of the preventive care process and register is to prevent older adults to develop malnutrition, pressure ulcer, falls, poor oral health (added 2011), and bladder dysfunction (added 2014), by performing risk assessments, initiating preventive actions and to evaluate the results [15, 16]. With a quality register, this work can be evaluated and compared locally as well as nationally and is a source for research and for developing the care of older adults [15, 16].

From 2010 to 2014, SA was spread nationally when the Ministry of health and social affairs decided to implement and fund the spread of the register in health care and social care in all of Sweden [15, 17], including economic incitements for performing risk assessments [17]. In the report from SA from 2019, it was estimated that around 70% of the individuals living in residential care facilities were registered in SA [18].

The ageing process

Ageing has biological, psychological and social components,
In short summary, the psychological ageing includes the individual's development in memory, learning ability, personality, and how the person perceives and adapts to the situation, while the social ageing includes the individual's social and economic situation etc, that is also affected by how the society is constructed [3, 19]. This section focuses on biological ageing, defined as a universal, intrinsic, progressive and irreversible process that reduces an individual's functional capacity [3,

19]. It causes reduced muscle mass and function (sarcopenia) [20], balance [21], bone mass [22], heart [23], lung [24] and renal function [25], and vision [21], as well as changes in the nervous system [26], and gastrointestinal tract [27]. Changes in hormonal systems that may impact nutrition also occur [28]. In addition, age-related changes in the urogenital tract that may influence urogenital conditions (e.g. urinary incontinence, pelvic organ prolapse, UTI) occur, although their distinction from other factors, such as comorbidity-associated changes, is difficult [29, 30]. Lack of oestrogen in women and prostate hyperplasia in men also affect the urinary tract [19]. Thus, age-related changes affect virtually all parts of the human body, although ageing is a diverse and individually variable process. The WHO define healthy ageing as older adults' ability to maintain and improve functional ability and generate well-being [3, 19]. The process of ageing is important, as it determines whether the years gained with increased life expectancy will be spent healthy.

Various diseases and multimorbidity (more than diagnosed conditions), and thus also polypharmacy, are more common in older than in younger adults [3, 31]. In a previous study, the most common diagnoses among older Swedish adults were hypertension, dementia and heart failure, and about half of the study population had multimorbidity [32]. Globally, chronic and non-communicable diseases, including cardiovascular diseases, cancer, chronic respiratory diseases, musculoskeletal diseases and mental and neurological disorders, contribute most to the burden of disease, measured by disability-adjusted life years (DALY), in individuals aged ≥ 60 years [33].

Ageing and immunology

There is an age-related decline in the immune system function, termed 'immunosenescence' [34]. Ageing is associated with a deteriorating defence against infections due to many factors as summarized by Yoshikawa et al [35] including thinner skin, weakened cough reflex, impaired capacity and emptying of the bladder. At a cellular level both the innate and the adaptive immune system may be involved in the increased susceptibility to infection in older adults [34]. Also, it has been suggested that a dysregulation and constant stimulation of the immune system is involved in the low-grade and chronic inflammation, referred to as inflammaging [34]. Comorbidities (e.g., diabetes mellitus and stroke) and use of medications has also been associated with increased risk of

infections [35]. Infections may present with atypical symptoms disproportional to their severity, and fever may be absent, in older adults, making diagnosis more challenging, especially in individuals with cognitive decline [35]. The most common infections occurring in community-dwelling older adults are respiratory infections (i.e., bronchitis and pneumonia), UTI, and gastrointestinal infections; those that are most common in residential care facilities are pneumonia, UTI, and skin and soft-tissue infections [35].

Ageing and nutrition

Age-related changes may affect older adults' nutritional status. Furthermore, energy expenditure and physical activity, and thus energy requirements, decrease with age; energy requirements are 20%–30% lower among 80-year-olds than among 30-year-olds [19]. Despite this reduction, the need for nutrients does not change; thus, older adults require high-quality, nutrient-rich diets [36]. The European Society for Clinical Nutrition and Metabolism (ESPEN) and the National Board of Health and Welfare in Sweden recommend a protein intake of ≥ 1.0 g protein/kilogram body weight/day in healthy older adults [36, 37]. The protein requirement is even higher with disease, medical treatment or surgery or malnutrition risk [36, 37].

Ageing and body composition

The body composition (proportions of bone, muscle and fat mass) changes with age [19]. Height is reduced and between the ages of 30 and 80 years, women and men can lose up to 6 and 5 cm height, respectively [38]. Body weight decreases from the age of 60–70 years [39-41], and there is a loss of muscle mass and muscle function (sarcopenia) [40, 42], which results in an increased proportion of body fat and intraabdominal and intramuscular redistribution of fat mass [40]. The co-existence of sarcopenia and obesity is termed 'sarcopenic obesity' [43]. In addition, the percentage of body water decreases due to decreased muscle mass and proportionally increased fat mass [19].

Body composition measurement

Body composition is assessed by anthropometric measurements, including the waist circumference, waist-to-hip ratio and body mass index (BMI). Whereas the BMI is an indirect measure of total body fat, the waist circumference and waist-to-hip ratio provide more information

on fat mass distribution. Underwater weighing and bioelectrical impedance also can be used to assess body composition and fat mass. Furthermore, several imaging techniques [e.g. dual-energy X-ray absorptiometry (DXA), ultrasound, magnetic resonance imaging (MRI), computed tomography (CT)] can be used to measure body composition; they provide precise information, but are less available than anthropometric techniques in clinical settings [44].

The BMI

The BMI, an indirect measure of body fat, is a well-established, easy and cost-effective metric. It is a measure of a person's weight in relation to their height, calculated as weight (in kilograms) divided by height (in metres) squared [45]. The BMI is used to categorise persons as underweight, normal-weight, overweight and obese. The WHO's cut-offs for these categories, based on the negative consequences of overweight and obesity on morbidity and mortality in adults, are often used (Table 1) [45].

Table 1 The WHO's BMI-based classification [45]

BMI categories	**BMI (kg/m^2)**
Underweight	< 18.5
Normal-weight	18.5 – 24.9
Overweight	25.0 – 29.9
Obesity	≥ 30.0
Obesity class I	30.0 – 34.9
Obesity class II	35.0 – 39.9
Obesity class III	≥ 40.0

BMI, body mass index; WHO, World Health Organization

Although widespread and easy to use, the BMI as a measure of adiposity has some limitations. It does not enable distinction between fat and lean mass; for example, individuals with more muscle or bone mass have higher BMIs [46]. It also does not enable the consideration of fat mass distribution, although visceral obesity is more dangerous than lower-body obesity [46]. Nor does it enable consideration of the larger percentage of body fat in women than in men [47]. Finally, self-measured weight and height may be under- or overestimated [48].

BMI in older adults

The use of the BMI for older adults has been questioned; several limitations must be considered, as the BMI does not enable consideration of sex, age or body composition [49]. Individuals, and especially women, lose height with age, resulting in false increases in the BMI of 1.6 units in women and 1.2 units in men between the ages of 30 and 80 years [38]. Furthermore, due to the age-related loss of lean mass, the body composition of older adults differs from that of their younger counterparts. The argument has been made that different BMI cut-offs should be used for older adults because of altered associations with mortality, but no consensus on age-related thresholds has been reached. The WHO cut-offs are used in many studies of older adults, enabling comparison.

Overweight and obesity according to the BMI

Definitions

The term 'overnutrition' encompasses overweight and obesity and refers to excessive fat mass due to a positive energy balance [45, 50]. Obesity can be accompanied by malnutrition when the food consumed is of poor quality or an acute or chronic condition is contributing to poor nutritional status [50]. Furthermore, excess body weight has been suggested to contribute to malnutrition by increasing inflammatory processes [50].

Aetiology

In general, overweight and obesity are caused by excess energy intake in relation to expenditure. In older adults, however, obesity is a more complex process due to age-related changes, including sarcopenia and the redistribution of and increase in fat mass [40, 42]. Obesity, and especially sarcopenic obesity, is associated with self-reported limitations in physical function [51], which may create a vicious cycle of further weight gain, functional limitations and inactivity in these individuals.

Prevalence

Overweight and obesity are common among adults in Europe, and their prevalence has increased in the last four decades [52]. In European adults aged 60–69 years, the prevalence of overweight (BMI $\geq$ 25 kg/m^2) decreased from 64.0% in 2005 to 62.7% in 2013, while obesity (BMI $\geq$ 30 kg/m^2) increased from 18.8% to 20.5% [53]. For individuals aged

≥ 80 years, the prevalences of overweight and obesity ranged from 51.3% to 56.2% and from 13.7% to 15.3%, respectively. In this age group, overweight, but not obesity, increased between 2005 and 2013 [53]. The prevalence of overweight and obesity among Finnish 90-year-olds were 31.9% and 6.6%, respectively in 2000 [54] and those among older nursing home inhabitants in Europe were 27% and 14%, respectively (year not specified) [55]. In Swedish populations, increasing prevalence of overweight, obesity, and obesity class II-III have been observed in adults (aged 18–74 years) between 1995 and 2017 [56]. In 2017, overweight, obesity, and obesity class II-III were seen in 55.1%, 16.6%, and 4.2% of the study population, respectively [56]. Also in Swedish 70-year olds, overweight and obesity have increased between 1971 and 2000 [57]. In 2000, 23.8% of women and 20.0% of men had obesity [57].

Consequences

Obesity, and abdominal fat in particular, is a risk factor for diabetes mellitus, insulin resistance, dyslipidaemia, hypertension, coronary heart disease, stroke, sleep apnoea, gall bladder disease, osteoarthritis, gout, reproductive system abnormalities, low back pain, some cancers, premature death and dementia [45, 58]. In obese individuals, higher BMIs have been associated with a decrease in income, and increase in social transfer payments, and in health care costs [59], and greater estimated health care usage, despite reduced life expectancy has been reported in obese individuals, compared to those with normal-weight [60].

Mortality

The association of overweight and obesity with mortality among older adults has been investigated. In general, many studies have shown that overweight is not associated with greater mortality [61-63], and that BMIs in the overweight range are preferable for older adults.

Although obesity is associated with several chronic diseases such as cardiovascular disease [64], type 2 diabetes mellitus [65], some cancer forms [66], and with mortality [67]. In those with established disease such as malignancy [68], chronic obstructive pulmonary disease [69] and cardiovascular disease [70], obesity has been associated with increased survival, in the so called obesity paradox. Indeed, the association between obesity and mortality in older adults is more complex. Obesity, defined as BMI ≥ 30.0 kg/m^2 [61, 71], or obesity class I [62, 63, 71], has

not been associated with mortality in some studies, but was associated with greater mortality in a meta-analysis [72]. More heterogeneous results have been obtained for severe (classes II and III) obesity, ranging from an association with a greater mortality risk to no significant association with mortality [62, 63, 71]. However, comparison of study findings is somewhat problematic due to the use of different inclusion criteria, methods, follow-up durations and definitions of obesity.

Among older adults in nursing homes, overweight and obesity have been associated with reduced mortality in the short (6 months) and long (up to 9 years) terms [55, 73, 74]. However, Grabowski et al. [75] reported that the association between high BMIs and mortality differed between individuals already residing in these facilities in 1996 and those newly admitted during that year. Among those newly admitted, but not among existing residents, greater mortality was associated with BMIs > 35 kg/m^2 and > 40 kg/m^2; BMIs > 28 kg/m^2 were not associated with greater mortality in either group [75]. Few studies have investigated the associations of obesity classes with mortality among older adults in residential care facilities [75].

Janssen and Mark [72] found that 5 of 32 studies in which high BMIs were not associated clearly with mortality included individuals aged ≥ 75 years. Studies of this association in very old individuals are scarce relative to those conducted with other age groups [54, 61, 76-80]. Comparison of existing findings is difficult because of the use of different methods, follow-up durations and BMI thresholds. Lisko et al. [54] found no association between BMI and 4-year mortality in 90-year-old women, whereas overweight 90-year-old men had a lower risk of mortality than did those who were normal-weight [54]. In a larger Danish study of 93-year-olds, the least mortality was found among individuals with BMIs ≥ 28 kg/m^2 [78]. In an even larger study of very old Chinese adults, in which BMIs were categorised according to Chinese guidelines, mortality rates were lower among normal-weight, overweight and obese women and men than among underweight individuals [79]. In contrast, Stessman et al. [76] reported less mortality among overweight and obese women than among normal-weight women, and no association between BMI and 3-year mortality in men, in an Israeli population of 85-year-olds [76]. Thinggaard et al. [77] found greater mortality in overweight individuals, except among men aged 90–94 years, and reported that the association between BMI and mortality might become less U-shaped

with increasing age in individuals aged 70–95 years [77]. Thus, higher BMIs appear to be associated with greater survival of older individuals, but this association needs to be confirmed in diverse populations and settings.

Underweight according to the BMI

Definitions

According to the WHO's cut-offs, underweight is defined as a BMI < 18.5 kg/m^2 [45]. Low BMIs (BMI < 20 kg/m^2 for those aged < 70 years and < 22 kg/m^2 for those aged > 70 years) indicate poor nutritional status and is a criterion for the diagnosis of malnutrition [81]. In addition, low BMI and weight loss are proposed to grade the severity of malnutrition according to the Global Leadership Initiative on Malnutrition (GLIM) criteria for malnutrition diagnosis [81]

Aetiology

In general, body weight increases during adulthood, peaking at about 60–70 years of age and declining thereafter [19, 39, 40]. Malnutrition can lead to underweight, consequently, factors associated with malnutrition might also be associated with underweight.

Prevalence

The prevalence of underweight has decreased since the 1960s, and is 0.8% among older adults in the United States [82]. The prevalence among very old adults has been reported at 1.2–3.0%, and has been greater among inhabitants of residential care facilities (11.0%) [54, 55, 83].

Consequences

The association of lower BMIs with increased mortality is acknowledged widely [62, 63], including among older adults residing in care facilities [73, 84] and in study populations including very old individuals [77-80].

Malnutrition

Definitions

In 2017, ESPEN published a consensus of definitions and terminology for nutritional disorders [50]. Malnutrition was defined as a state of

nutrient deficiency (lack of intake or uptake) that adversely affects body composition, leading to reduced physical and mental function and impaired clinical outcome [50]; this definition is also used in the Swedish guidelines for the prevention and treatment of malnutrition [36]. Malnutrition and undernutrition are often used synonymously [50]; in this thesis, the term 'malnutrition' is used.

Deficiencies in micronutrients is also a nutritional disorder [50] with reported deficiencies and negative health effects in older adults in e.g., vitamin B_1, vitamin B_6, vitamin B_{12}, vitamin C, vitamin D, folate, calcium, zink, iron, and magnesium [85]. These micronutrient deficiencies may require food records and/or blood tests for there recognition.

Aetiology

Malnutrition is a multifactorial process, with age-related changes, including anorexia of ageing (i.e. age-related reduction of appetite and energy intake), contributing [86, 87]. The nutritional status is also affected by chronic and acute diseases [88], which can entail cachexia (muscle mass loss associated with diseases and inflammatory activity) [89]. Malnutrition also can be caused by psychological or socio-economic factors [86, 90]. The 2019 Determinants of Malnutrition in Aged Persons (DoMAP) model lays out potential causes of malnutrition and their modes of action (Figure 1) [90]. According to this model, key factors in the development of malnutrition are reduced food intake, reduced bioavailability of nutrients and greater nutrient demand [90]. These factors can be affected directly and indirectly via various pathways. An infection may negatively affect nutritional status via for example an increased metabolic demand, an inflammatory process, potential side effects of medications, anorexia and may lead to hospitalisation, physical inactivity and eating difficulty. In addition, associations are bidirectional, as malnutrition negatively affects the immune system function [91].

General and age-related factors	Older age	Anorexia of ageing	Functional decline	Multi-morbidity
	Poly-pharmacy	Frailty	Hospitalisation	Low education
Indirect effects	Stroke	Parkinson's disease	Cancer	Gastrointestinal disease
	Depression	Dementia	Cognitive impairment	COPD
	Infection	Inflammatory disease	Surgery	Psychological distress
	Pain	Medication	Dry mouth	Poor dental health
	Oral pain	Physical inactivity	Mobility limitations	Sensory impairment
	Loss of interest in life	Poor quality of meals	Poor quality of care	Poverty
	Loneliness			
Direct effects	Poor appetite	Diarrhoea	Nausea	Dysphagia
	Mal-absorption	Chewing problems	Vomiting Tremor	Unwilling to eat
	Forgetting to eat	Difficulties to shop, prepare and eating food	Increased metabolic rate	Hyper-activity
	Inflammation		Lack of food	Restrictive diet

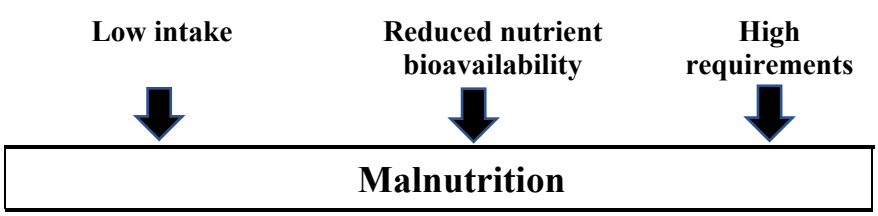


Figure 1 Factors associated with the development of malnutrition, according to the Determinants of Malnutrition in Aged Persons model. Adapted from Figure 2 in Volkert et al. [90]. COPD, Chronic obstructive pulmonary disease.

Many studies of factors associated with malnutrition among older adults have been cross-sectional; few have been prospective. A systematic review of prospective studies revealed low- to moderate-quality evidence for the associations of some risk factors with malnutrition, and conflicting results for other potential risk factors [92]. They reported moderate-quality evidence for hospitalisation, eating dependence, poor appetite and poor self-perceived health and physical function as risk factors for malnutrition [92]. However, the authors stated that these results should be interpreted with caution because of several limitations of the included studies, and indicated that additional studies are needed [92].

Nutritional screening and assessment

Screening for the risk of malnutrition is the first step in nutrition-based care provision. It may be followed by the assessment of nutritional status for diagnosis and the identification of possible causes and potential interventions [36, 93]. Tools used for screening older adults include the Mini Nutritional Assessment–Short Form (MNA-SF), Malnutrition Screening Tool (MST), Malnutrition Universal Screening Tool (MUST), Nutritional Risk Screening 2002 (NRS 2002) and Simplified Nutritional Assessment Questionnaire (SNAQ) [93]. Those used for assessment include the Mini Nutritional Assessment (MNA) and Subjective Global Assessment (SGA) [93]. The MUST was developed to use in different settings [94] and the SGA has been validated for use with older adults. In addition, the MST has been validated for use with older adults receiving hospital and ambulatory care, but not long-term care [95]; the NRS 2002 was developed to identify hospitalised patients who would benefit from nutritional treatment [96]; and the SNAQ can be used to identify individuals at risk of weight loss over 6 months in community and long-term care settings [97]. The MNA is a validated and widely used tool developed in the mid-1990s for the identification of malnutrition risk in older adults [98], including in very old adults and older persons living in residential care [99]. It was developed for nutritional screening in older adults [98, 100, 101] and composes 18 questions with information in four areas: anthropometric measurements (BMI, weight loss, mid arm and calf circumference), basic dietary questions, general assessment, and a subjective assessment, with a maximum score of 30 [98]. The MNA-SF was developed to enable screening in two steps. It constitutes 6 questions from the full MNA regarding anthropometric measurements (BMI and weight loss), general assessment and a dietary question. If this screening

identifies a nutritional risk, the full MNA provides an assessment [98, 102, 103]. Its maximum score is 14 and the MNA-SF performs well in predicting low MNA scores [98]. Table 2 presents the thresholds for the MNA and MNA-SF. Notably, none of these tools provides information on nutritional intake or energy expenditure, which are important factors in the assessment of nutritional status. Information on dietary intake can be gathered using food records (preferably over 7 days), 24-hour recall, food frequency questionnaires or complete dietary histories; food records seem to be the best option for older adults [104].

Table 2 MNA and MNA-SF thresholds

MNA categories	**MNA (0–30)**	**MNA-SF (0–14)**
Good nutritional status	24–30	12–14
Risk of malnutrition	17–23.5	8–11
Malnutrition	< 17	< 8

MNA, Mini Nutritional Assessment; MNA-SF, Mini Nutritional Assessment–Short Form

Diagnosis

When malnutrition is suspected, due to clinical signs or in situations where it is common or a major risk, screening to detect this risk should be performed. Individuals experiencing unintentional weight loss, eating difficulties or underweight (BMI < 20 kg/m^2 for those aged < 70 years and < 22 kg/m^2 for those aged > 70 years) are deemed to be at risk of malnutrition [36]. Risk screening can also be performed using instruments such as the MNA [36]. When the risk of malnutrition is identified, a comprehensive assessment should be performed, covering dietary intake, energy and nutrient requirements, anthropometrics, socioeconomic and psychosocial factors that may affect nutritional status, along with a thorough examination of the individual's medical conditions and medications [36], and areas that should be included in this examination are illustrated in Figure 1. It is also important to evaluate if micronutrient deficiencies may be present [85].

Various definitions of malnutrition have been proposed; recently, the GLIM provided criteria for the diagnosis of this condition and grading of its severity [81]. The GLIM criteria are used to define malnutrition on the

basis of phenotype and aetiology (the presence of at least one criterion of each type is required; Table 3). When the risk of malnutrition is identified, the assessment of nutritional status for diagnosis is recommended [81]. These diagnostic criteria are used in the Swedish guidelines for the prevention and treatment of malnutrition [36].

In the papers included in this thesis, when referring to malnutrition or the risk thereof, this is according to the screening tools MNA or MNA-SF. Thus, identifying individuals with a malnutrition risk that would need an assessment to make the diagnosis.

Table 3 GLIM criteria for the diagnosis of malnutrition [81]

Phenotype	
Weight loss	> 5% the last 6 months or > 10% beyond 6 months
Low BMI	< 70 years: < 20 kg/m^2 or > 70 years: < 22 kg/m^2
Reduced muscle mass	DXA, BIA, CT, or MRI to measure body composition or Physical examination, anthropometric and functional measure (mid-arm, calf circumference, hand-grip strength)
Aetiology	
Reduced food intake or assimilation	≤ 50% of energy requirement > 1 week or a reduction > 2 weeks or chronic gastrointestinal conditions
Inflammation	Due to chronic, or acute disease or injury

BIA, bioelectrical impedance analysis; BMI, body mass index; CT, computed tomography; DXA, dual-energy X-ray absorptiometry; GLIM, Global Leadership Initiative on Malnutrition; MRI, magnetic resonance imaging.

Nutritional care in older adults

Following the nutritional assessment an individualised nutritional care plan should be made with goals regarding dietary intake and BMI/body weight [37]. Because of the complex nature of malnutrition, the care should be individualised, comprehensive and part of a multidisciplinary team intervention, and include efforts to increase dietary intake and targeting potential causes [36, 37]. Protein and energy supplementation has been associated with weight gain older adults [105]. However, multifactorial and multidisciplinary interventions in very old community-dwelling might need further investigation [106].

Prevalence of malnutrition according to MNA and MNA-SF scores

The prevalence of malnutrition is associated with the level of dependence and varies among settings; it is lower in communities than in residential care facilities (Table 4) [98, 107].

Table 4 Prevalence of malnutrition, according to MNA scores, from a systematic review and meta-analysis [107]

Setting	**Malnutrition**	**Risk of malnutrition**
Community	3.1% (2.3–3.8)	26.5% (22.4–32.7)
Home care service	8.7% (5.8–11.7)	47.5% (40.9–54.2)
Nursing homes	17.5% (14.3–20.6)	48.0% (44.2–51.8)
Long-term care	28.7% (21.4–36.0)	49.0% (43.6–54.4)
Hospital	22.0% (18.9–25.2)	45.6% (42.7–48.6)

Information from 240 studies conducted in Europe, Asia, America, Australia, and Africa were analysed and data are presented with 95% confidence intervals. MNA, Mini Nutritional Assessment.

In Swedish populations, the reported prevalence of malnutrition and the risk thereof, defined by MNA scores, are 8% and 41%, respectively, among individuals receiving home care [108] and 15.0%–17.7% and 40.3%–66.0%, respectively, among older adults living in residential care facilities [109, 110].

Among very old individuals the prevalence of malnutrition risk has been reported variously as 34.5% among community-dwelling 85-year-olds in Spain (MNA score ≤ 23.5) [111], 76.1% of community-dwelling adults aged ≥ 90 years in China (MNA-SF ≤ 11) [112], 28.4% among Spanish adults aged ≥ 90 years of which one fourth of the population were living in institutions (MNA-SF < 11) [113], and as 66% among adults aged ≥ 90 years in Belgium where the majority was residing in nursing homes (MNA-SF ≤ 11 [114]. Furthermore, 53.1% and 42.5% of very old Japanese nursing home inhabitants were categorised as malnourished and at risk, respectively, according to MNA-SF scores [115].

Few studies have involved investigation of whether the prevalence of malnutrition among very old adults is changing. A study of older Swedish nursing home residents suggested that this prevalence decreased between 1996 and 2010, when malnutrition was assessed using the MNA and MNA-SF, respectively [116]. In contrast, this prevalence, according to MNA-SF assessment, was similar in 2008 and 2013 in a population of older adults receiving home care or living in nursing homes in Belgium [117]. While Saarela et al. [118] reported that this prevalence, according to the MNA score, increased among older adults in nursing homes and assisted living facilities in Finland between 2003, 2007 and 2011 [118].

Consequences of malnutrition

Whereas good nutritional status has been associated with successful ageing, as defined by physical and cognitive function [119], malnutrition has several potential serious consequences in older adults, including negative effects on the musculoskeletal system that lead to functional decline and disability, an increased incidence of falls and increased risk of fracture, poor wound healing and an increased risk of pressure ulcers [120]. Malnutrition has also been associated with delayed postoperative recovery, with admission to hospital and length of stay [120], and postoperative delirium in older adults with hip fracture [121]. Malnutrition has also been associated with greater hospital costs [122].

Infections including UTI

Malnutrition is associated with dysfunction of the immune system [123] and increased risk of infection [120]. Furthermore, with reduced immune function, infections are prolonged and reduce the nutritional reserve [124]. UTIs are very common among older adults in community and residential care settings [125]. They are not associated with increased

mortality in healthy older adults. With increasing age, however, the rate of hospitalisation for pyelonephritis increases [125], and the risk of developing uroseptic shock is greater for hospitalised patients with UTIs aged ≥ 80 years [126]. Among older adults in nursing homes, UTI in the previous 2 years was associated with increased mortality during a 1-year follow-up period [127]. The increasing incidence of UTI with age is explained partly by the increase in bacterial colonisation (bacteriuria) due to age-related changes, including mechanical and urothelial changes, the lack of oestrogen in women and prostatic hypertrophy in men [91]. Risk factors for UTI in very old adults include previous UTI, cognitive impairment, disability in activities of daily living (ADL) and urinary incontinence [128]. In a large study conducted in nursing homes in the United States, Castle et al. [129] identified indwelling urinary catheter use as the strongest risk factor for UTI; other factors were white ethnicity, disabilities in ADL, depression and the use of antidepressants and hypnotic medications, whereas cognitive impairment was protective. Malnutrition was not included as a potential risk factor in that study [129]. Poorer nutritional status was associated with UTI diagnosis in the previous year among older Swedish adults in residential care facilities [110]. However, the BMI and malnutrition defined by the MNA score were not associated with UTIs in older adults receiving home care in Taiwan (0.8% was categorized as having a good nutritional status) [130]. Similar results regarding the association of malnutrition with UTI risk were obtained in a study from the United States published in 1988 [131].

Mortality

Increased short- and long-term mortality have been observed among malnourished older adults in Swedish and other European studies [108, 132-134]. Similar associations have been found for older adults living in nursing homes [109, 116, 135], although conflicting results have been reported [127]. Studies of very old populations are scarce, although existing findings suggest that short-term, but not long-term, mortality is predicted by nutritional status. Specifically, poorer nutritional status was associated with increased 1-year mortality [136], but not 3-year [137, 138], or 5-year [113, 139] mortality, in very old adults. Malnutrition was, however, an independent risk factor for 3-year mortality in hospitalised adults aged ≥ 90 years [140].

Rationale

The age group of older and very old adults is growing rapidly, globally and in Sweden, leading to changes in care provision. As a larger proportion of this population receives help at home, individuals in residential care facilities are older and frailer. Furthermore, health care systems have changed in past decades, with reduced numbers of hospital beds. Hence, studies providing new and updated information are essential.

Malnutrition is seen mainly in older adults, and the prevalence of obesity is increasing in this age group. Whether the prevalence of malnutrition and/or obesity is increasing among very old adults have shown heterogenous results.

Malnutrition is associated with increased mortality, but this association and that between obesity and mortality need to be confirmed in very old adults, for whom studies are scarce. Also, the association between severe obesity and mortality in older adults living in residential care facilities has not been studied thoroughly. Furthermore, the BMI and nutritional status are related, and obesity and malnutrition can co-exist, but we have little knowledge about the association of the combination of BMI and nutritional status with mortality in the residential care population.

UTIs are common among older adults living in residential care facilities. Although the nutritional status is associated with infection, and previous UTI has been associated with malnutrition, malnutrition has not been examined thoroughly as a risk factor for UTI. The identification of potentially preventable risk factors for UTI is important.

Aims

The overall aim of this thesis was to determine the prevalence of and temporal trends in malnutrition and obesity, defined by the MNA score and the BMI, respectively, among older adults. In addition, the associations of malnutrition and (severe) obesity, alone and combined, with mortality were examined. Finally, whether malnutrition is a risk factor for UTI was investigated.

Specific aims of the studies reported on in the papers included in this thesis

In the paper I study, the aim was to investigate whether the prevalence of obesity, underweight, and malnutrition in four cohorts of very old adults in northern Sweden changed between 2000−2002 and 2015−2017.

The aim of the paper II study was to investigate the prevalence of malnutrition, assessed by the BMI and MNA, and the associations of the BMI and MNA score with 5-year mortality, in very old adults in northern Sweden and western Finland.

The aim of the study reported on in paper III was to investigate the association between obesity and mortality, including the examination of potential heterogeneity in this association among obesity classes I–III. Furthermore, the combined effect of the BMI and nutritional status, according to MNA-SF scores, among older nursing home residents in Sweden was investigated.

Finally, the aim of the paper IV study was to investigate whether malnutrition is a risk factor for incident UTI in a population of older adults living in residential care facilities in northern Sweden.

Materials and Methods

This thesis is based on data from three studies: the Umeå85+/Gerontological Regional Database (GERDA) study, the Frail Older People–Activity and Nutrition (FOPANU) study, and the Umeå Dementia and Exercise (UMDEX) study. It also incorporates data from the Swedish Senior Alert (SA) national quality registry. An overview of the studies included in this thesis is provided in Table 5.

Table 5 Summary of studies included in the thesis

	Paper I	Paper II	Paper III	Paper IV
Data	Umeå85+/ GERDA	Umeå85+/ GERDA	Quality register SA	FOPANU, UMDEX
Assessment years	2000–2002 (Swe), 2005–2007 (Swe), 2010–2012 (Swe), 2015–2017 (Swe)	2000–2002 (Swe), 2005–2007 (Swe), 2005–2006 (Fin)	2012–2013	2002 (FOPANU), 2011–2012 (UMDEX)
Populations	≥ 85 years, living in the community or residential care in northern Sweden	≥ 85 years, living in the community or residential care in northern Sweden and western Finland	≥ 65 years, living in residential care in Sweden	≥ 65 years, living in residential care in northern Sweden
Sample size	1602	832	47,686	373
Living in residential care facility n (%)	C1: 136/343 (39.7), C2: 116/342 (33.9), C3: 132/409 (32.3), C4: 135/508 (26.6)	359/832 (43.1)	47,686 (100)	373 (100)

Table 5 continued. Summary of studies included in the thesis

	Paper I	Paper II	Paper III	Paper IV
Nutritional assessment	MNA < 17, 17–23.5, 24–30	MNA < 17, 17–23.5, 24–30	MNA-SF 0–7, 8–11, 12–14	MNA < 17, 17–23.5, 24–30
BMI (kg/m^2)	< 18.5, 18.5–24.9, 25.0–29.9, ≥ 30.0	< 22.2, 22.2–24.6, 24.7–27.9, ≥ 28.0	< 18.5, 18.5–24.9, 25.0–29.9, ≥ 30.0, 30.0–34.9, 35.0–39.9, ≥ 40.0	Mean ± SD
Outcomes	Time trends in prevalence of MNA score and the BMI	5-year mortality	2-year mortality	Incidence of UTI
Analyses	Chi-squared test and analysis of variance	Chi-squared test, independent samples *t* test, analysis of variance, Cox regression models	Chi-squared test, analysis of variance, Cox regression models	Chi-squared test, independent samples *t* test, Cox regression models

BMI, body mass index; C1, cohort in 2000–2002; C2, cohort in 2005–2007; C3, cohort in 2010–2012; C4, cohort in 2015–2017; Fin, Finland; FOPANU, Frail Older People–Activity and Nutrition study; GERDA, Gerontological Regional Database; MNA, Mini Nutritional Assessment; MNA-SF, Mini Nutritional Assessment–Short Form; SA, Senior Alert; SD, standard deviation; Swe, Sweden; UMDEX, Umeå Dementia and Exercise study; UTI, urinary tract infection

Data collection

Papers I and II

Umeå85+/GERDA study
The GERDA study, a continuation of the Umeå85+ study, was initiated in 2000. Its aim was to gather broad information on general health and socio-economic factors associated with healthy ageing among very old adults in northern Sweden. The study had a cross-sectional and a longitudinal design. Data were collected in the urban municipality of Umeå and in five rural municipalities (Dorotea, Malå, Sorsele, Storuman and Vilhelmina) every 5 years (2000–2002, 2005–2007, 2010–2012 and 2015–2017), with new and previous participants invited to participate at each timepoint. The study was expanded to include two municipalities in Finland (Korsholm and Vaasa) in the second round of data collection (included in paper II) and two additional municipalities in Finland (Korsnäs and Malax) in the third round of data collection (not included in this thesis). It was a collaboration among the Department of Community Medicine and Rehabilitation, Division of Geriatric Medicine, and the Department of Nursing and Social Science at Umeå University in Sweden and the Novia University of Applied Sciences, University of Vaasa and Åbo Akademi University in Finland.

Eligible participants were identified from the population registers of the Swedish National Tax Board and Finnish Population Register Centre. Persons living in the selected municipalities on 1 January in the year of data collection and aged 85, 90 and ≥ 95 years were selected. As the 85-year-olds formed a relatively large group, every other individual of this age was selected by randomly choosing if persons with even or odd numbers in the population register should be included. Survivors and non-responders from previous data collection rounds were invited to participate in each of the second through fourth rounds. Potential participants were sent a letter with information about the study and contacted by telephone 2 weeks later to provide additional information and obtain informed consent; the oldest participants were contacted first. When cognitive impairment was suspected, a close relative was contacted to discuss participation. Participants were only included if they gave their consent and when applicable if their close relative did not have any objections.

One or several home visits were scheduled; data were collected via a standardised structured interview that included measurements and the administration of several questionnaires, as well as enquiry about sociodemographic, medical histories and medication use. Home visitation took approximately 2 hours and was performed by trained assessors (physiotherapists, registered nurses, medical students and physicians). Assessors were trained by first being informed about the content and how to perform the structured interview. Then they accompanied a colleague during interviews and then performed a supervised interview. During the home visits, participants were also asked to grant permission for the researchers to access their medical records and/or, when applicable, to provide contact information for a close relative or caregiver for the acquisition of additional information. Participants could decline any portion of study participation.

Paper III

Senior Alert

The paper III study used data from the national quality registry Senior Alert that has been described in detail in the introduction [15, 16]. Risk assessments performed in the care preventive process include the administration of the MNA-SF [102] or three screening questions (to determine the presence of involuntary weight loss, eating difficulty and/or BMI < 20 kg/m^2 for those aged < 70 years and < 22 kg/m^2 for those aged > 70 years) to identify individuals at risk of malnutrition. For pressure ulcers the Modified Norton Scale (MNS) [141, 142] or Risk Assessment Pressure Sore (RAPS) scale [143] is used. For falls, the Downton Fall Risk Index (DFRI) [144] or two screening questions ('Has the person fallen in the last year?' and 'Do you think the person will fall without preventive action?') are used. For oral health, the Revised Oral Assessment Guide (ROAG) [145] is used. Bladder dysfunction is assessed. When a risk is registered, a team-based risk analysis is performed, preventive actions are planned and executed, and their effects are evaluated [15, 16]. Older adults can be assessed and registry entries for them created at any point of contact with the health care system; for example in hospitals, in residential care facilities and by home care services [18]. Caregivers are obliged to inform individuals about SA registration before performing it, and individuals can withdraw their information from the registry at any time, so called opt-out [16].

Paper IV

The study reported on in paper IV was based on data from the FOPANU and UMDEX studies.

FOPANU

The FOPANU study was a cluster-randomised controlled trial with an exercise intervention (consisting of 45 minutes of exercise, five times every two weeks vs. a control activity while sitting down, e.g., singing, reading) and a nutrition intervention (consisting of a protein-enriched energy supplement vs a placebo, both were milk-based drinks with 408 kilo Joule per 100 g vs 191 kilo Joule per 100 g) performed with older adults in residential care facilities in Umeå, northern Sweden, in 2002 [146]. The inclusion criteria were age ≥ 65 years, Mini-Mental State Examination (MMSE) [147] score ≥ 10, dependence in personal (P)-ADL according to the Katz index [148], ability to stand up from a chair with armrests with help from no more than one person, and physician's approval to participate. Participants provided oral informed consent, and this was confirmed by close relatives when cognitive impairment was confirmed or suspected. The intervention period was 3 months, and participants were reassessed at 3 and 6 months.

UMDEX

The UMDEX study was a cluster-randomised controlled trial conducted in 2011–2012 to investigate the effect of an exercise intervention in older people with dementia living in residential care facilities in Umeå, northern Sweden [149]. The inclusion criteria were the same as in the FOPANU study, with the addition of dementia diagnosis, ability to hear speech produced at usual volume from a distance of 1 meter and ability to understand instructions in Swedish. Informed oral consent was provided by the participants and was confirmed by a close relative. The intervention period was 4 months, and participants were reassessed at 4 and 7 months. The intervention was similar to the exercise intervention in the FOPANU study, i.e., 45 minutes of exercise, five times every two weeks vs. a control activity while sitting down, e.g., singing and reading.

Participants

Paper I

This study was conducted with data from all four Swedish cohorts of the Umeå85+/GERDA study. Individuals who participated with home visitation and medical records review for whom BMIs and MNA scores were available were included. Participants in the four cohorts were considered as separate cohorts, thus survivors from previous cohorts were assigned to their new age group if they fulfilled inclusion criteria. Figure 2 illustrates the flow of this study.

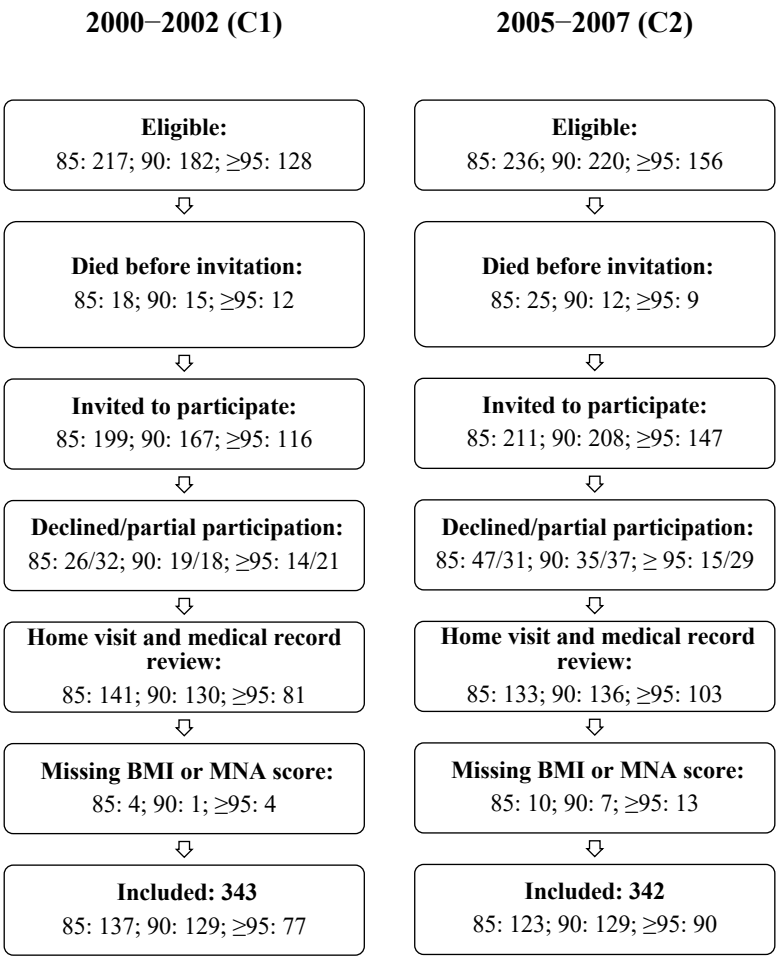
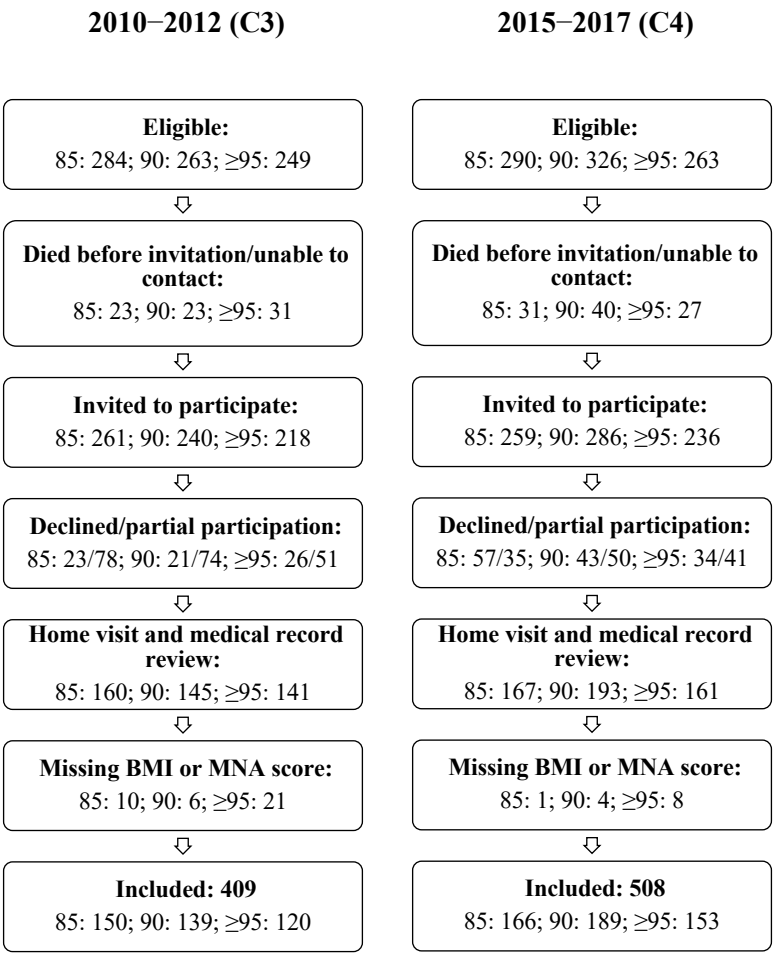


Figure 2 Flow of participant selection for the paper I study with data collection in the years 2000–2002, 2005–2007, 2010–2012, and 2015–2017, according to age groups (85 years, 90 years, ≥ 95 years). BMI, body mass index; C, cohort; MNA, Mini Nutritional Assessment.


2010–2012 (C3)
2015–2017 (C4)
Eligible:
85: 284; 90: 263; ≥95: 249
Eligible:
85: 290; 90: 326; ≥95: 263
Died before invitation/unable to contact:
85: 23; 90: 23; ≥95: 31
Died before invitation/unable to contact:
85: 31; 90: 40; ≥95: 27
Invited to participate:
85: 261; 90: 240; ≥95: 218
Invited to participate:
85: 259; 90: 286; ≥95: 236
Declined/partial participation:
85: 23/78; 90: 21/74; ≥95: 26/51
Declined/partial participation:
85: 57/35; 90: 43/50; ≥95: 34/41
Home visit and medical record review:
85: 160; 90: 145; ≥95: 141
Home visit and medical record review:
85: 167; 90: 193; ≥95: 161
Missing BMI or MNA score:
85: 10; 90: 6; ≥95: 21
Missing BMI or MNA score:
85: 1; 90: 4; ≥95: 8
Included: 409
85: 150; 90: 139; ≥95: 120
Included: 508
85: 166; 90: 189; ≥95: 153

Paper II

The study reported on in paper II was conducted with data from members of the first (2000–2002) and second (2005–2007) Swedish cohorts, and the 2005–2006 Finish cohort, of the Umeå85+/GERDA study. Participants who underwent home visitation and for whom MNA scores or BMIs were available were included. Each participant was included once; survivors from the first cohort were included in the second cohort. Figure 3 illustrates the flow of this study.

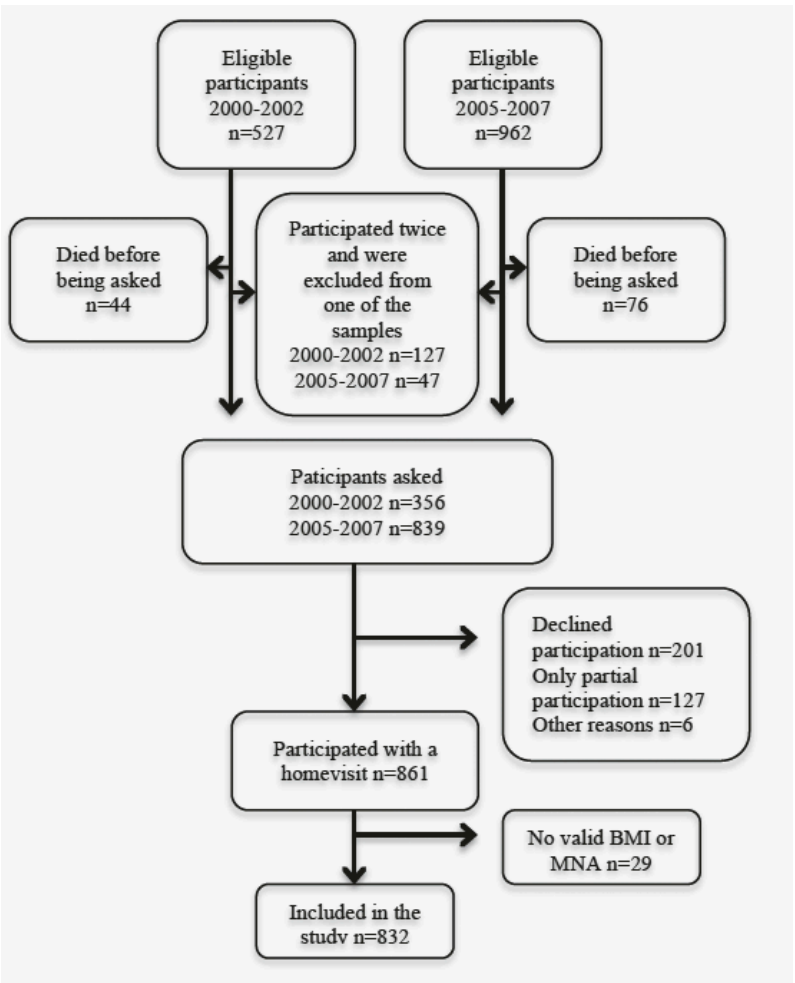


Figure 3 Flow of participant selection for the paper II study. BMI, body mass index; MNA, Mini Nutritional Assessment.

Paper III

For the study reported on in paper III, eligible individuals were older adults living in residential care facilities in Sweden with SA registration between 1 January 2012 and 31 December 2013. Exclusion criteria were documented death before SA registration, missing MNA-SF score or BMI, body weight < 20 kg or > 210 kg, height < 100 cm or > 210 cm and BMI < 10 kg/m^2 or > 70 kg/m^2.

Paper IV

This study included participants in the FOPANU and UMDEX studies (n = 191 and 186, respectively) with documented MNA scores. No individual participated in both studies. Figure 4 illustrates the flow of this study.

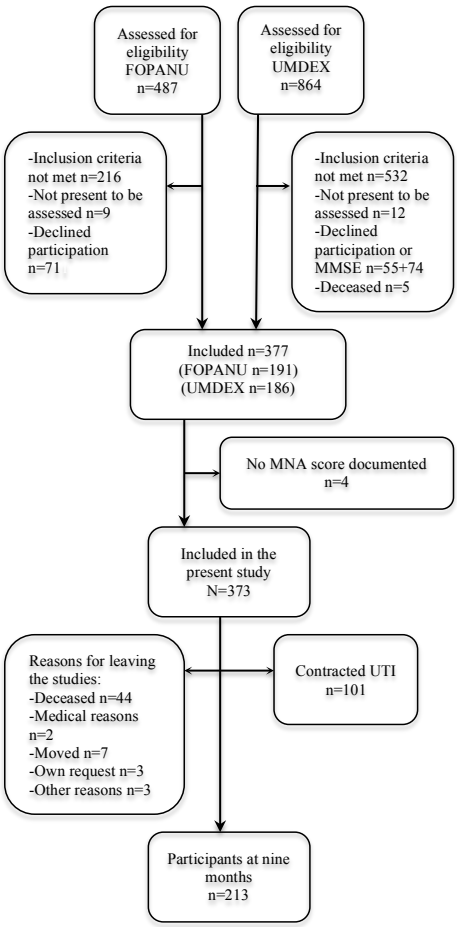


Figure 4 Flow of participant selection from the FOPANU and UMDEX studies (paper IV). FOPANU, Frail Older People–Activity and Nutrition; MMSE, Mini-Mental State Examination; MNA, Mini Nutritional Assessment; UMDEX, Umeå Dementia and Exercise; UTI, urinary tract infection.

Measurements and outcomes

Papers I and II

In the Umeå85+/GERDA study, a wide range of measurements was taken and information collected. Those relevant to the studies reported on in papers I and II are described here.

The MNA was used to assess the risk of malnutrition [98] and divided according to applied thresholds shown in Table 2. Height was measured with a folding ruler and weight was measured with an ordinary calibrated bathroom scale and BMI was calculated. The WHO's BMI-based categories are shown in Table 1 [45]. These categories were used in the study reported on in paper I, with obesity defined as BMI ≥ 30.0 kg/m^2. For the study reported on in paper II, BMIs were divided into quartiles (Q1, < 22.2 kg/m^2; Q2, 22.2–24.6 kg/m^2; Q3, 24.7–27.9 kg/m^2; Q4, ≥ 28.0 kg/m^2).

The MMSE was used to assess cognitive function. This instrument is composed of six types of items: orientation, registration, attention and calculation, recall, language and copying. Scores range from 0 to 30, with lower scores indicating cognitive impairment [147].

The 15-item Geriatric Depression Scale (GDS-15) [150] was used to screen for depressive symptoms. Its items are yes/no questions about symptoms of depression relevant to older adults. Scores range from 0 to 15; scores of 5–10 indicate mild depression and those of 10–15 indicate moderate to severe depression [150, 151]. In the study reported on in paper I, the scores of participants who answered ≥ 10 questions were imputed (total score / total number of questions answered × 15) to avoid missing values. The scores of individuals who answered < 10 questions were recorded as missing [152].

The Barthel ADL Index [153, 154] was used to assess personal activities of daily living (P-ADL) in 10 items including feeding, bowel control, bladder control, grooming, toileting, bathing, dressing, transfer, walking, and climbing stairs. Scores range from 0 to 20, with higher scores indicating greater independence in P-ADL [153, 154].

In the study reported on in paper I, the Katz ADL index [148] was used for the construction of ADL staircases and assessment of independence

in P-ADL (including bathing, dressing, toileting, transfer, bowel and bladder control, and feeding) and instrumental ADL (including shopping groceries, cooking, cleaning, and transportation; I-ADL) [155]. The results were dichotomised as independence in all 10 activities assessed or dependence in one or more activities.

Participants, close relatives and/or caregivers provided information about the participants' current and previous medical diagnoses and medication use. Such data were also collected from medical records and/or based on a combination of assessment, medical record review and interviews. Diagnoses of depression and dementia disorders were based on the Swedish version of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV) [156]. The same geriatrician evaluated and made final diagnoses for all participants in all cohorts. Most diagnoses were recorded as present when participants had the conditions at the time of data collection or in their histories. Exceptions were myocardial infarction (occurring in the previous year), UTI (present at the time of data collection or in the previous year) and malignancy (present in the previous 5 years). Medications were classified according to the Anatomical Therapeutic Chemical Classification system and reported as used regularly or *pro re nata* (in paper I) or only regularly (paper II). Dates of death were gathered from medical records, death certificates and the National Tax Agency's records in Sweden, and from medical records and the Finnish Population Register Centre's database in Finland. Maximum follow-up durations in the paper I and paper II studies were 2 and 5 years, respectively.

Smoking habits were reported as current, history and never, and these data were dichotomised as current and previous or never smokers in both studies. Participants' housing situations were categorised as living in the community (in paper I referred to as 'free-living') (living in an apartment or house, regardless of receipt of home care), residential care (living in a facility with private apartments or rooms and staff available day and night) and living alone (regardless of type housing). Education levels were reported as number of years in school (paper II) and classified accordingly: 0 to 5 years; 6 to 7 years; 8 to 9 years; and 10 years or more (paper I).

Paper III
Nutritional Status was assessed using the MNA-SF with thresholds according to Table 2 [102]. Participants were assigned to the WHO's BMI-based categories, with obesity subdivided into classes I–III (Table 1) [45].

Diagnoses were collected from the National Patient Register (NPR), which fully covers diagnoses made in hospitals since 1987 and outpatient specialised care provided since 2001 [157, 158]. The register does not, however, include diagnoses from primary care. The diagnoses are coded according to the Swedish version of the International Classification of Diseases and Related Health Problems, Tenth Revision [159, 160]. Those for which data were extracted were chronic obstructive pulmonary disease (COPD), dementia, diabetes, hip fracture, myocardial infarction, rheumatoid arthritis, renal failure, stroke and the diagnose was considered prevalent if it was registered in the National Patient Register up to the date of study inclusion. Information on participants' disposable income and education levels was collected from Statistics Sweden, a government agency that generates official statistics. Mortality information was obtained from the National Board of Health and Welfare's Cause of Death Register [161]. Individuals were followed for a maximum of 2 years from the date of SA registration.

Paper IV
Measurements and assessments were performed, and information on medical diagnoses and medication use was collected, at baseline. The MNA was used to assess nutritional status and divided accordingly (Table 2). Participants' BMIs were calculated.

The MMSE [147], GDS-15 [150, 151] and Barthel ADL Index [153] were used to assess cognitive function, depressive symptoms, and level of dependence in P-ADL, respectively. Participants' balance was assessed using the Bergs Balance Scale (BBS), with possible scores ranging from 0 to 56 and higher scores indicating a better balance [162].

Information on all diagnoses, including the incidence of UTI, was gathered systematically. In the FOPANU study, the registered nurse at the facility collected data on diagnoses, drug prescriptions and clinical characteristics from participants' medical records. In the UMDEX study, physicians involved in the study performed this data collection. In both

studies, a geriatrician reviewed the available information to make final diagnoses; depression and dementia disorders were diagnosed using the DSM-IV criteria [156]. Data from participants with UTIs at baseline were included in the 'UTI in the previous year' variable, as the majority (26/33) of these participants had also had UTIs in the previous year. The incidence of UTI was determined based on clinical diagnoses made by the participants' treating physicians, which in turn were based on clinical symptoms and the results of urinary dipstick tests, bacterial culture and/or laboratory tests. The maximum follow-up duration was 9 months.

Ethical considerations

The Umeå85+/GERDA study was approved by the Regional Ethical Review Board in Umeå, the Swedish Ethical Review Authority (nos. §99-326, §05-063M, §09-178M, 2020-01428) and the Ethics Committee of Vaasa Central Hospital (no. §05-07). The study in which SA data were used was approved by the Regional Ethical Review Board in Umeå (nos. 2013-86-31M, 2013-456-32M). The FOPANU and UMDEX studies were approved by the Ethics Committee of the Medical Faculty of Umeå University (no. §391/01) and the Regional Ethical Review Board in Umeå (no. 2011–205–31M), respectively.

Statistical analyses

Paper I

Differences in sex and age between participants and non-participants were examined using the chi-squared test and the independent-samples *t* test, respectively. Differences over time were examined by cohort and age group, and in the subgroup of individuals living in residential care facilities, using analysis of variance for continuous variables and the chi-squared test for categorical variables. Sensitivity analyses were performed with the exclusion of individuals who participated in the study more than once. Cox regression models were constructed with and without the interaction terms (BMI(continuous) × cohort; BMI (categorized) × cohort; MNA(continuous) × cohort; MNA (categorized) × cohort), adjusted for sex and age, and likelihood ratio tests were performed to explore differences between cohorts in the associations of the BMI and MNA score with 2-year mortality. $P < 0.05$ was taken to indicate significance. Most analyses were performed using SPSS (version 25; IBM Corporation, Armonk, NY, USA); mortality analyses were

performed using R (version 4.0.3; The R Foundation for Statistical Computing, Vienna, Austria).

Paper II

Potential differences in sex and age between participants and non-participants were analysed using the chi-squared test and the independent-samples *t* test, respectively. Differences between women and men and among age groups were explored using the chi-squared test for categorical variables and the independent-samples *t* test or analysis of variance for continuous variables. For comparisons among age groups in which BMIs and MNA scores were included as categorical variables, these values were dichotomised (< 22.2 and ≥ 22.2 kg/m^2 and < 17 and ≥ 17, respectively).

Associations of the BMI and MNA score with 5-year mortality in the whole sample (adjusted for sex and age) and by sex and age group were examined using Cox regression models, with BMIs and MNA scores included as categorical variables. Reference groups were BMI < 22.2 kg/m^2 and MNA score < 17. Additional analyses were performed with other reference groups. Correlations between the BMI and MNA score were examined using Pearson's correlation coefficient. The association between BMI/MNA and survival times was (also) plotted using a scatter plot with a smooth curve drawn using local polynomial regression fitting. $P < 0.05$ was taken to indicate significance. Analyses were performed using SPSS (version 20; SPSS Inc., Chicago, IL, USA).

Paper III

Potential differences in sex and age between participants and non-participants were analysed using the chi-squared test and the independent-samples *t* test, respectively. Participants were divided into groups according to MNA-SF categories, and differences among groups were examined using the chi-squared test for categorical variables and the Welch one-way analysis of variance for continuous variables. Cox regression models were used to analyse the associations of the BMI and MNA-SF score with 2-year mortality. Proportional-hazard assumptions for the included variables against time were tested using tests of Schoenfeld residuals. As this analysis revealed that the BMI and MNA-SF score violated the assumption that mortality occurred proportionally during follow-up, analyses were performed for every 6 months of follow-up. The analyses were adjusted (for age, level of education, disposable

income, dementia, hip fracture, COPD, renal failure, rheumatoid arthritis, myocardial infarction, stroke, and diabetes), and variables other than the BMI and MNA-SF score that violated the proportional-hazard assumption were stratified. Analyses were performed for obesity classified as BMI ≥ 30.0 kg/m^2 and as classes I–III. Differences between women and men were explored using likelihood ratio tests of models with the interaction term (BMI(continuous) × sex; BMI(categorized) × sex; MNA(continuous) × sex; MNA(categorized) × sex) and models without interaction terms. $P < 0.05$ was considered to indicate significance. The analyses were performed in R (version 3.5.0; The R Foundation for Statistical Computing).

Paper IV

Comparison between groups, based on incident UTI, was performed using the chi-squared test and independent-samples *t* test for categorical and continuous variables, respectively. Variables associated with incident UTI in bivariate analyses with $P < 0.15$ were included in univariate Cox regression models. Variables associated significantly with UTI in these analyses were included in multivariable Cox regression models. The incontinence variable from the Barthel ADL Index was excluded from multivariable analyses due to correlation with the total score of the Barthel ADL Index. The analyses were adjusted for intervention type (physical and nutritional). Sensitivity analyses were performed with the exclusion of data from participants with UTIs at baseline and for women and men separately. The diagnosis of gynaecological disease and prostate disease were included in analyses of data from women and men, respectively. $P < 0.05$ was considered to indicate significance. The analyses were performed with the SPSS software (version 22.0; IBM Corporation).

Results

Results from the four papers are presented according to topic (participants characteristics, prevalence and trends over time in MNA and BMI, the combination of them both, and their associations with mortality and UTI). To clarify the results presented from paper II, results for the associations of MNA score and the BMI with 5-year mortality, obtained using different reference categories, are presented in Tables 19 and 22, respectively. Results are presented according to participants' age as adults aged 85 years and older (paper I and II) and adults aged 65 years and older (paper III and IV) and according to living arrangements, i.e., living in the community and living in residential care facilities.

Participants

Adults aged ≥ 85 years (Paper I and II)

In the study reported in paper I, 1602 out of 2814 (56.9%) eligible individuals participated (C1, 65.1%; C2, 55.9%; C3, 51.4%; C4, 57.8%). Mean age did not differ between participants and non-participants in analyses of the individuals in all the cohorts (89.9 ± 4.6 and 90.0 ± 4.7 years, respectively) or in analyses of the four cohorts separately, while a larger proportion of eligible men participated compared to eligible women in analysis of the individuals in all the cohorts (60.5% vs 55.3%, $p = 0.009$) and in the third cohort (60.2% vs 47.1%, $p < 0.001$). The characteristics of the paper I study participants are presented by cohort in Table 6 (characteristics of the participants according to age groups are presented in Tables 7–9). Women were in majority in all four cohorts, and mean age in the fourth cohort was 90.2 ± 4.6 years and did not differ among cohorts. The proportion of individuals living in residential care facilities decreased between the first and fourth cohorts (overall $p < 0.001$). Mean MMSE and Barthel ADL Index scores did not differ among cohorts, but the mean GDS-15 score and independence according to the ADL staircase did. In addition, the prevalence of several diagnoses and medications used differed among cohorts; for example, dementia disorders were present in 26.8%, 33.3%, 36.7% and 40.0% of the participants in the first through fourth cohorts, respectively (overall $p = 0.001$).

Table 6 Baseline characteristics of paper I study participants, according to cohorts

Characteristic	2000–2002 (C1) (*n* = 343)	2005–2007 (C2) (*n* = 342)	2010–2012 (C3) (*n* = 409)	2015–2017 (C4) (*n* = 508)	*p*
Women	243 (70.8)	231 (67.5)	253 (61.9)	334 (65.7)	0.069
Age mean (years)	89.5 ± 4.5	90.1 ± 4.4	89.8 ± 4.7	90.2 ± 4.6	0.182
Age range (years)	85–103	84–104	84–105	84–102	
Age group (years)					0.160
85	137 (39.9)	123 (36.0)	150 (36.7)	166 (32.7)	
90	129 (37.6)	129 (37.7)	139 (34.0)	189 (37.2)	
≥95	77 (22.4)	90 (26.3)	120 (29.3)	153 (30.1)	
Living in residential care facilities	136 (39.7)	116 (33.9)	132 (32.3)	135 (26.6)	0.001
<8 years education (*n* = 1524)	255 (75.2)	237 (78.0)	289 (73.7)	310 (63.4)	<0.001
Current smoker (*n* = 1595)	14 (4.1)	11 (3.2)	9 (2.2)	9 (1.8)	0.204
Barthel ADL Index (0–20; *n* = 1599)	16.2 ± 5.9	16.7 ± 5.0	16.9 ± 4.8	16.5 ± 5.5	0.338
Independence in P-ADL & I-ADL[a] (*n*=1599)	79 (23.1)	96 (28.1)	72 (17.6)	100 (19.8)	0.003
GDS-15 score (*n* = 1486)	3.8 ± 2.7	3.7 ± 2.7	3.5 ± 2.5	3.3 ± 2.5	0.014
MMSE score (*n* = 1567)	21.8 ± 7.8	21.0 ± 6.8	21.7 ± 6.5	21.8 ± 6.8	0.299
Diagnoses					
Constipation	139 (40.5)	168 (49.1)	200 (48.9)	273 (53.7)	0.002
COPD	48 (14.0)	56 (16.4)	84 (20.5)	89 (17.5)	0.120
Dementia disorder	92 (26.8)	114 (33.3)	150 (36.7)	203 (40.0)	0.001
Depressive disorder	93 (27.1)	141 (41.2)	181 (44.3)	208 (40.9)	<0.001
Diabetes mellitus	45 (13.1)	46 (13.5)	80 (19.6)	85 (16.7)	0.049
Diarrhoea	34 (9.9)	45 (13.2)	53 (13.0)	115 (22.6)	<0.001
Heart failure	85 (24.8)	96 (28.1)	154 (37.7)	146 (28.7)	0.001
Hip fracture	70 (20.4)	54 (15.8)	78 (19.1)	92 (18.1)	0.453
Hypertension	189 (55.1)	235 (68.7)	328 (80.2)	404 (79.5)	<0.001
Malignancy[b]	36 (10.5)	31 (9.1)	60 (14.7)	92 (18.1)	<0.001
Myocardial infarction[c]	12 (3.5)	11 (3.2)	10 (2.4)	2 (0.4)	
Parkinson's disease	9 (2.6)	5 (1.5)	2 (0.5)	5 (1.0)	
Stroke	68 (19.8)	75 (21.9)	103 (25.2)	105 (20.7)	0.274
Thyroid disease	40 (11.7)	47 (13.7)	89 (21.8)	108 (21.3)	<0.001
Urinary tract infection[d]	99 (28.9)	92 (26.9)	83 (20.3)	75 (14.8)	<0.001

Table 6 continued. Baseline characteristics of paper I study participants, according to cohorts

	2000–2002 (C1)	2005–2007 (C2)	2010–2012 (C3)	2015–2017 (C4)	
Drug prescriptions					
Number of drugs[e]	6.4 ± 4.4	8.2 ± 5.1	8.6 ± 4.4	8.3 ± 4.6	<0.001
Analgesics	253 (73.8)	264 (77.2)	326 (79.7)	368 (72.4)	0.055
Antidepressants	56 (16.3)	56 (16.4)	82 (20.0)	100 (19.7)	0.359
Cholinesterase inhibitors	7 (2.0)	14 (4.1)	7 (1.7)	14 (2.8)	0.194
Corticosteroids, oral	18 (5.2)	25 (7.3)	16 (3.9)	25 (4.9)	0.212
Diuretics	167 (48.7)	170 (49.7)	230 (56.2)	221 (43.5)	0.002
Drugs for acid-related symptoms	42 (12.2)	77 (22.5)	110 (26.9)	124 (24.4)	<0.001
Insulin	11 (3.2)	8 (2.3)	35 (8.6)	37 (7.3)	<0.001
Laxatives	122 (35.6)	135 (39.5)	155 (37.9)	184 (36.2)	0.696
Mirtazapine	2 (0.6)	11 (3.2)	13 (3.2)	24 (4.7)	
Neuroleptics	28 (8.2)	23 (6.7)	13 (3.2)	18 (3.5)	0.003
Opioids	70 (20.4)	72 (21.1)	64 (15.6)	71 (14.0)	0.016
Oral antihyperglycemics	19 (5.5)	33 (9.6)	36 (8.8)	23 (4.5)	0.008
Paracetamol	144 (42.0)	183 (53.5)	234 (57.2)	299 (58.9)	<0.001
SSRIs	47 (13.7)	47 (13.7)	60 (14.7)	73 (14.4)	0.975
Vitamin B_{12}	87 (25.4)	146 (42.7)	133 (32.5)	154 (30.3)	<0.001

Data are presented as mean ± standard deviation or *n* (%), unless otherwise indicated. Differences in mean values were examined using one-way analysis of variance. Differences in proportions were analysed using the chi-squared test. [a]According to the ADL staircase. [b]In the previous 5 years. [c]In the previous year. [d]At present or in the previous year. [e]Regular use and *pro re nata.* ADL, activities of daily living; C, cohort; COPD, chronic obstructive pulmonary disease; GDS-15, 15-item Geriatric Depression Scale; I, instrumental; MMSE, Mini-Mental State Examination; P, personal; SSRI, selective serotonin reuptake inhibitor.

Table 7 Baseline characteristics of paper I study participants aged 85 years, according to cohorts

Characteristic	2000–2002 (C1) (*n* = 137)	2005–2007 (C2) (*n* = 123)	2010–2012 (C3) (*n* = 150)	2015–2017 (C4) (*n* =166)	*p*
Women	91 (66.4)	78 (63.4)	82 (54.7)	101 (60.8)	0.210
Age mean (years)	85.0 ± 0.0	85.7 ± 0.5	84.8 ± 0.4	85.0 ± 0.3	<0.001
Living in residential care facilities	24 (17.5)	25 (20.3)	23 (15.3)	16 (9.6)	0.071
<8 years education (*n* = 566)	98 (71.5)	97 (82.2)	101 (68.7)	87 (53.0)	<0.001
Current smoker (*n* = 574)	8 (5.9)	5 (4.1)	5 (3.3)	4 (2.4)	
Barthel ADL Index (0−20; *n* = 575)	18.5 ± 3.8	18.0 ± 4.3	18.3 ± 3.8	18.3 ± 4.2	0.723
Independence in P-ADL & I-ADL[a] (*n*=573)	50 (36.8)	58 (47.2)	48 (32.0)	66 (40.2)	0.074
GDS-15 score (*n* = 554)	3.5 ± 2.4	3.3 ± 2.6	3.3 ± 2.4	2.6 ± 2.2	0.014
MMSE score (*n* = 570)	24.5 ± 5.4	23.4 ± 5.6	23.7 ± 5.1	24.6 ± 5.7	0.172
Diagnoses					
Constipation	37 (27.0)	51 (41.5)	57 (38.0)	66 (39.8)	0.057
COPD	17 (12.4)	23 (18.7)	41 (27.3)	27 (16.3)	0.009
Dementia disorder	27 (19.7)	28 (22.8)	34 (22.7)	40 (24.1)	0.835
Depressive disorder	32 (23.4)	46 (37.4)	57 (38.0)	56 (33.7)	0.036
Diabetes mellitus	18 (13.1)	19 (15.4)	29 (19.3)	32 (19.3)	0.416
Diarrhoea	8 (5.8)	12 (9.8)	15 (10.0)	29 (17.5)	0.011
Heart failure	25 (18.2)	23 (18.7)	43 (28.7)	36 (21.7)	0.122
Hip fracture	18 (13.1)	13 (10.6)	16 (10.7)	19 (11.4)	0.903
Hypertension	99 (72.3)	86 (69.9)	124 (82.7)	136 (81.9)	0.016
Malignancy[b]	16 (11.7)	13 (10.6)	34 (22.7)	33 (19.9)	0.012
Myocardial infarction[c]	3 (2.2)	4 (3.3)	1 (0.7)	2 (1.2)	
Parkinson's disease	4 (2.9)	3 (2.4)	0 (0.0)	3 (1.8)	
Stroke	27 (19.7)	27 (22.0)	33 (22.0)	27 (16.3)	0.547
Thyroid disease	20 (14.6)	14 (11.4)	35 (23.3)	31 (18.7)	0.052
Urinary tract infection[d]	33 (24.1)	30 (24.4)	20 (13.3)	24 (14.5)	0.018

Table 7 continued. Baseline characteristics of paper I study participants aged 85 years, according to cohorts

	2000−2002 (C1)	2005−2007 (C2)	2010−2012 (C3)	2015−2017 (C4)	
Drug prescriptions					
Number of drugs[e]	5.5 ± 3.8	7.7 ± 5.0	8.0 ± 4.3	7.4 ± 4.1	<0.001
Analgesics	95 (69.3)	88 (71.5)	107 (71.3)	111 (66.9)	0.796
Antidepressants	22 (16.1)	16 (13.0)	26 (17.3)	28 (16.9)	0.774
Cholinesterase inhibitors	4 (2.9)	3 (2.4)	3 (2.0)	8 (4.8)	
Corticosteroids, oral	5 (3.6)	11 (8.9)	3 (2.0)	6 (3.6)	
Diuretics	57 (41.6)	56 (45.5)	75 (50.0)	65 (39.2)	0.240
Drugs for acid-related symptoms	15 (10.9)	28 (22.8)	40 (26.7)	41 (24.7)	0.006
Insulin	6 (4.4)	5 (4.1)	15 (10.0)	12 (7.2)	0.151
Laxatives	27 (19.7)	38 (30.9)	35 (23.3)	35 (21.1)	0.146
Mirtazapin	1 (0.7)	6 (4.9)	5 (3.3)	3 (1.8)	
Neuroleptics	7 (5.1)	11 (8.9)	4 (2.7)	4 (2.4)	0.035
Opioids	16 (11.7)	27 (22.0)	16 (10.7)	14 (8.4)	0.005
Oral antihyperglycaemics	8 (5.8)	15 (12.2)	17 (11.3)	5 (3.0)	0.008
Paracetamol	48 (35.0)	57 (46.2)	71 (47.3)	81 (48.8)	0.077
SSRIs	19 (13.9)	10 (8.1)	16 (10.7)	24 (14.5)	0.333
Vitamin B_{12}	31 (22.6)	48 (39.0)	33 (22.0)	47 (28.3)	0.007

Data are presented as mean ± standard deviation or *n* (%), unless otherwise indicated. Differences in mean values were examined using one-way analysis of variance. Differences in proportions were analysed using the chi-squared test.

[a]According to the ADL staircase. [b]In the previous 5 years. [c]In the previous year. [d]At present or in the previous year. [e]Regular use and *pro re nata*.

ADL, activities of daily living; C, cohort; COPD, chronic obstructive pulmonary disease; GDS-15, 15-item Geriatric Depression Scale; I, instrumental; MMSE, Mini-Mental State Examination; P, personal; SSRI, selective serotonin reuptake inhibitor.

Table 8 Baseline characteristics of paper I study participants aged 90 years, according to cohorts

Characteristic	2000−2002 (C1) (n = 129)	2005−2007 (C2) (n = 129)	2010−2012 (C3) (n = 139)	2015−2017 (C4) (n = 189)	*p*
Women	90 (69.8)	85 (65.9)	90 (64.7)	116 (61.4)	0.488
Age mean (years)	90.0 ± 0.0	89.8 ± 0.4	89.9 ± 0.4	89.8 ± 0.7	0.010
Living in residential care facilities	58 (45.0)	40 (31.0)	46 (33.1)	41 (21.7)	<0.001
<8 years education (n = 557)	96 (75.0)	81 (73.0)	95 (70.9)	121 (65.8)	0.311
Current smoker (n = 584)	4 (3.1)	5 (3.9)	3 (2.2)	3 (1.6)	
Barthel ADL Index (0−20)	16.3 ± 5.3	17.2 ± 4.5	16.9 ± 4.9	17.2 ± 4.7	0.364
Independence in P-ADL & I-ADL[a]	24 (18.6)	34 (26.4)	20 (14.4)	29 (15.3)	0.043
GDS-15 score (n = 549)	4.0 ± 2.8	3.8 ± 2.9	3.6 ± 2.6	3.1 ± 2.2	0.021
MMSE score (n = 579)	21.6 ± 7.6	20.6 ± 6.8	21.4 ± 6.8	21.8 ± 6.2	0.488
Diagnoses					
Constipation	57 (44.2)	64 (49.6)	66 (47.5)	97 (51.3)	0.640
COPD	21 (16.3)	18 (14.0)	28 (20.1)	37 (19.6)	0.486
Dementia disorder	31 (24.0)	45 (34.9)	53 (38.1)	74 (39.2)	0.031
Depressive disorder	41 (31.8)	57 (44.2)	66 (47.5)	75 (39.7)	0.054
Diabetes mellitus	19 (14.7)	17 (13.2)	31 (22.3)	32 (16.9)	0.204
Diarrhoea	15 (11.6)	14 (10.9)	12 (8.6)	44 (23.3)	<0.001
Heart failure	37 (28.7)	39 (30.2)	52 (37.4)	56 (29.6)	0.372
Hip fracture	26 (20.2)	19 (14.7)	28 (20.1)	29 (15.3)	0.457
Hypertension	67 (51.9)	97 (75.2)	109 (78.4)	154 (81.5)	<0.001
Malignancy[b]	15 (11.6)	13 (10.1)	14 (10.1)	37 (19.6)	0.028
Myocardial infarction[c]	7 (5.4)	4 (3.1)	3 (2.2)	0 (0.0)	
Parkinson's disease	2 (1.6)	2 (1.6)	1 (0.7)	1 (0.5)	
Stroke	28 (21.7)	25 (19.4)	45 (32.4)	36 (19.0)	0.022
Thyroid disease	17 (13.2)	21 (16.3)	28 (20.1)	39 (20.6)	0.305
Urinary tract infection[d]	39 (30.2)	28 (21.7)	27 (19.4)	25 (13.2)	0.003

Table 8 continued. Baseline characteristics of paper I study participants aged 90 years, according to cohorts

	2000–2002 (C1)	2005–2007 (C2)	2010–2012 (C3)	2015–2017 (C4)	
Drug prescriptions					
Number of drugs[e]	7.0 ± 4.8	7.9 ± 4.7	8.7 ± 4.6	8.2 ± 4.2	0.022
Analgesics	100 (77.5)	103 (79.8)	111 (79.9)	130 (68.8)	0.053
Antidepressants	26 (20.2)	24 (18.6)	34 (24.5)	38 (20.1)	0.661
Cholinesterase inhibitors	2 (1.6)	9 (7.0)	2 (1.4)	4 (2.1)	
Corticosteroids, oral	12 (9.3)	10 (7.8)	8 (5.8)	15 (7.9)	0.747
Diuretics	74 (57.4)	57 (44.2)	76 (54.7)	89 (47.1)	0.096
Drugs for acid-related symptoms	20 (15.5)	25 (19.4)	30 (21.6)	47 (24.9)	0.231
Insulin	4 (3.1)	3 (2.3)	13 (9.4)	15 (7.9)	
Laxatives	49 (38.0)	49 (38.0)	58 (41.7)	65 (34.4)	0.604
Mirtazapin	1 (0.8)	0 (0.0)	5 (3.6)	12 (6.3)	
Neuroleptics	10 (7.8)	7 (5.4)	6 (4.3)	2 (1.1)	
Opioids	36 (27.9)	24 (18.6)	19 (13.7)	23 (12.2)	0.002
Oral antihyperglycaemics	6 (4.7)	11 (8.5)	16 (11.5)	16 (8.5)	0.248
Paracetamol	57 (44.2)	71 (55.0)	78 (56.1)	105 (55.6)	0.153
SSRIs	23 (17.8)	23 (17.8)	26 (18.7)	24 (12.7)	0.421
Vitamin B_{12}	38 (29.5)	60 (46.5)	49 (35.3)	56 (29.6)	0.009

Data are presented as mean ± standard deviation or *n* (%), unless otherwise indicated. Differences in mean values were examined using one-way analysis of variance. Differences in proportions were analysed using the chi-squared test.

[a]According to the ADL staircase. [b]In the previous 5 years. [c]In the previous year. [d]At present or in the previous year. [e]Regular use and *pro re nata*.

ADL, activities of daily living; C, cohort; COPD, chronic obstructive pulmonary disease; GDS-15, 15-item Geriatric Depression Scale; I, instrumental; MMSE, Mini-Mental State Examination; P, personal; SSRI, selective serotonin reuptake inhibitor.

Table 9 Baseline characteristics of paper I study participants aged ≥ 95 years, according to cohorts

Characteristic	2000–2002 (C1) (n = 77)	2005–2007 (C2) (n = 90)	2010–2012 (C3) (n = 120)	2015–2017 (C4) (n = 153)	*p*
Women	62 (80.5)	68 (75.6)	81 (67.5)	117 (76.5)	0.177
Age mean (years)	96.6 ± 1.8	96.4 ± 2.1	96.0 ± 2.2	96.2 ± 2.0	0.156
Living in residential care facilities	54 (70.1)	51 (56.7)	63 (52.5)	78 (51.0)	0.038
<8 years education (n = 401)	61 (82.4)	59 (78.7)	93 (83.8)	102 (72.3)	0.127
Current smoker (n = 437)	2 (2.6)	1 (1.1)	1 (0.8)	2 (1.3)	
Barthel ADL Index (0–20; n = 438)	12.0 ± 7.5	14.4 ± 5.9	15.2 ± 5.3	13.5 ± 6.4	0.004
Independence in P-ADL & I-ADL[a]	5 (6.5)	4 (4.4)	4 (3.3)	5 (3.3)	
GDS-15 score (n = 383)	4.3 ± 3.0	4.1 ± 2.3	3.8 ± 2.4	4.2 ± 2.9	0.558
MMSE score (n = 418)	17.3 ± 9.7	18.2 ± 7.0	19.6 ± 7.0	18.7 ± 7.4	0.240
Diagnoses					
Constipation	45 (58.4)	53 (58.9)	77 (64.2)	110 (71.9)	0.105
COPD	10 (13.0)	15 (16.7)	15 (12.5)	25 (16.3)	0.743
Dementia disorder	34 (44.2)	41 (45.6)	63 (52.5)	89 (58.2)	0.127
Depressive disorder	20 (26.0)	38 (42.2)	58 (48.3)	77 (50.3)	0.003
Diabetes mellitus	8 (10.4)	10 (11.1)	20 (16.7)	21 (13.7)	0.547
Diarrhoea	11 (14.3)	19 (21.1)	26 (21.7)	42 (27.5)	0.151
Heart failure	23 (29.9)	34 (37.8)	59 (49.2)	54 (35.3)	0.031
Hip fracture	26 (33.8)	22 (24.4)	34 (28.3)	44 (28.8)	0.621
Hypertension	23 (29.9)	52 (57.8)	95 (79.2)	114 (74.5)	<0.001
Malignancy[b]	5 (6.5)	5 (6.5)	12 (10.0)	22 (14.4)	0.098
Myocardial infarction[c]	2 (2.6)	3 (3.3)	6 (5.0)	0 (0.0)	
Parkinson's disease	3 (3.9)	0 (0.0)	1 (0.8)	1 (0.7)	
Stroke	13 (16.9)	23 (25.6)	25 (20.8)	42 (27.5)	0.273
Thyroid disease	3 (3.9)	12 (13.3)	26 (21.7)	38 (24.8)	
Urinary tract infection[d]	27 (35.1)	34 (37.8)	36 (30.0)	26 (17.0)	0.001

Table 9 continued. Baseline characteristics of paper I study participants aged ≥ 95 years, according to cohorts

	2000–2002 (C1)	2005–2007 (C2)	2010–2012 (C3)	2015–2017 (C4)	
Drug prescription					
Number of drugs[e]	6.7 ± 4.4	9.3 ± 5.7	9.1 ± 4.3	9.2 ± 5.3	0.002
Analgetics	58 (75.3)	73 (81.1)	108 (90.0)	127 (83.0)	0.053
Antidepressants	8 (10.4)	16 (17.8)	22 (18.3)	34 (22.2)	0.184
Cholinetserase inhibitors	1 (1.3)	2 (2.2)	2 (1.7)	2 (1.3)	
Corticosteroids, oral	1 (1.3)	4 (4.4)	5 (4.2)	4 (2.6)	
Diuretics	36 (46.8)	57 (63.3)	79 (65.8)	67 (43.8)	<0.001
Drugs for acid-related symptoms	7 (9.1)	24 (26.7)	40 (33.3)	36 (23.5)	0.002
Insulin	1 (1.3)	0 (0.0)	7 (5.8)	10 (6.5)	
laxatives	46 (59.7)	48 (53.3)	62 (51.7)	84 (54.9)	0.729
Mirtazapin	0 (0.0)	5 (5.6)	3 (2.5)	9 (5.9)	
Neuroleptics	11 (14.3)	5 (5.6)	3 (2.5)	12 (7.8)	
Opioids	18 (23.4)	21 (23.3)	29 (24.2)	34 (22.2)	0.986
Oral antihyperglycaemics	5 (6.5)	7 (7.8)	3 (2.5)	2 (1.3)	
Paracetamol	39 (50.6)	55 (61.1)	85 (70.8)	113 (73.9)	0.002
SSRI	5 (6.5)	14 (15.6)	18 (15.0)	25 (16.3)	0.208
Vitamine B_{12}	18 (23.4)	38 (42.2)	51 (42.5)	51 (33.3)	0.023

Data are presented as mean ± standard deviation or *n* (%), unless otherwise indicated. Differences in mean values were examined using one-way analysis of variance. Differences in proportions were analysed using the chi-squared test.

[a]According to the ADL staircase. [b]In the previous 5 years. [c]In the previous year. [d]At present or in the previous year. [e]Regular use and *pro re nata*.

ADL, activities of daily living; C, cohort; COPD, chronic obstructive pulmonary disease; GDS-15, 15-item Geriatric Depression Scale; I, instrumental; MMSE, Mini-Mental State Examination; P, personal; SSRI, selective serotonin reuptake inhibitor.

The paper II study had a participation rate at 69.6% (832 out of 1195 persons being asked) and there were no differences in the proportion of women and men ($p = 0.378$), while participants were older than those who did not participate (90.2 ± 4.6 vs. 89.6 ± 4.6 years, $p = 0.022$). The characteristics of paper II study participants are presented in Table 10 according to sex and age groups. Women comprised 70.0% of the sample and were older on average than men. About half (56.9%) of the participants were community-dwelling. Several diagnoses were more common in women than in men; women also took more drugs regularly and had lower MMSE and Barthel ADL Index scores than did men.

Adults aged ≥ 65 years living in residential care facilities (Paper III and IV)

Out of 49,604 potential participants in the study reported on in paper III, the final sample consisted of 47,686 individuals. In total, 1918 people were excluded due to death before SA registration ($n = 273$), missing MNA-SF score ($n = 1612$), weight < 20 kg ($n = 1$), missing weight ($n = 17$), height < 100 cm ($n = 11$), height > 210 cm ($n = 1$), BMI < 10 kg/m^2 ($n = 2$) and BMI > 70 kg/m^2 ($n = 1$). The characteristics of paper III study participants are presented according to MNA-SF categories in Table 11. The mean age of the 47,686 participants (70.0% women) was 86.3 ± 7.4 years and there were no differences in the proportion of women (69.6%) and men between participants and non-participants, while those excluded were older (86.8 ± 7.3 years, $p = 0.006$). A majority of the diagnoses were more prevalent among malnourished participants, except for myocardial infarction and diabetes mellitus that were more common among those with good nutritional status.

After the exclusion of four individuals due to missing MNA scores, the final sample in the paper IV study comprised 373 participants. The baseline characteristics of these individuals are presented in Table 12. The mean age of the paper IV study sample (74.0% women) was 84.9 ± 6.8 years. Dementia was present in 76.4% of participants, and the mean MMSE score was 16.3 ± 4.6. The mean Barthel ADL Index was 12.0 ± 4.4.

Table 10. Baseline characteristics of paper II study participants

Characteristics	**Women (n=582)**	**Men (n=250)**	***p***	**85 years (n=290)**	**90 years (n=306)**	**≥ 95 years (n=236)**
Women				188(64.8)	209(68.3)	185(78.4)
Age mean	90.6±4.7	89.3±4.0	<0.001			
Living in Sweden	420(72.2)	189(75.6)	0.305	204(70.3)	234(76.5)	171(72.5)
Community-dwelling	299(51.4)	174(69.6)	<0.001	213(73.4)	184(60.1)	76(32.2)
Living alone	540(93.1)	153(61.4)	<0.001	206(71.0)	264(86.8)	223(94.9)
Education years	6.7±2.2	6.9±2.4	0.290	6.8±1.9	6.9±2.4	6.4±2.5
Current smoker	18(3.1)	12(4.8)	0.239	12(4.2)	12(3.9)	6(2.6)
Depressive disorders	224(39.0)	74(29.6)	0.010	95(32.8)	121(39.8)	82(35.5)
Dementia disorder	257(44.2)	74(29.6)	<0.001	85(29.3)	117(38.2)	129(54.7)
Hypertension	377(64.8)	140(56.0)	0.017	206(71.0)	204(66.7)	107(45.3)
Myocardial infarction*	20(3.4)	7(2.8)	0.635	8(2.8)	13(4.2)	6(2.5)
Heart failure	206(35.5)	68(27.2)	0.020	75(25.9)	105(34.3)	94(40.0)
Stroke	123(21.1)	55(22.0)	0.780	70(24.1)	61(19.9)	47(19.9)
Diabetes mellitus	88(15.1)	36(14.4)	0.789	52(17.9)	49(16.0)	23(9.7)
Malignancy**	51(20.5)	41(7.0)	<0.001	36(12.5)	38(12.4)	18(7.6)
COPD	82(14.1)	56(22.4)	0.003	46(15.9)	51(16.7)	41(17.4)
Numbers of drugs taken regularly	7.3±4.2	5.6±3.9	<0.001	6.3±4.0	7.0±4.3	7.0±4.1
MMSE score	19.0±8.5	21.9±6.3	<0.001	22.6±6.7	20.0±7.6	16.4±8.8
Barthel ADL Index (0−20)	14.6±6.5	17.3±4.7	<0.001	17.4±4.9	15.9±5.6	12.4±7.0

Values are presented as *n* (%) or mean ± standard deviation. * In the previous year. ** In the previous 5 years. ADL, activities of daily living; COPD, chronic obstructive pulmonary disease; MMSE, Mini-Mental State Examination.

Table 11 Baseline characteristics of paper III study participants

	Whole sample	**MNA-SF 0–7**	**MNA-SF 8–11**	**MNA-SF 12–14**	***p***
Number	47,686	6970	21,459	19,257	<0.001
Age, mean (SD)	86.3 (7.4)	86.7 (7.2)	86.3 (7.4)	86.3 (7.4)	<0.001
Women, n (%)	33,374 (70.0)	5121 (73.5)	15,231 (71.0)	13,022 (67.6)	<0.001
Level of education, n (%)					<0.001
<9 years	26,534 (57.1)	3666 (54.2)	11,811 (56.5)	11,057 (58.9)	
9–12 years	15,744 (33.9)	2435 (36.0)	7104 (34.0)	6205 (33.0)	
>12 years	4159 (9.0)	669 (9.9)	1975 (9.5)	1515 (8.1)	
Income*, mean (SD)	167 (202)	164 (188)	165 (193)	170 (217)	0.013
Diagnoses, n (%)					
Dementia	15,193 (31.9)	2948 (42.3)	7628 (35.5)	4617 (24.0)	<0.001
Hip fracture	10,399 (21.8)	2066 (29.6)	4992 (23.3)	3341 (17.3)	<0.001
COPD	2567 (5.4)	438 (6.3)	1142 (5.3)	987 (5.1)	0.001
Renal failure	1227 (2.6)	180 (2.6)	532 (2.5)	515 (2.7)	0.46
Rheumatoid arthritis	1059 (2.2)	161 (2.3)	509 (2.4)	389 (2.0)	0.048
Myocardial infarction	6460 (13.5)	874 (12.5)	2799 (13.0)	2787 (14.5)	<0.001
Stroke	10,764 (22.6)	1604 (23.0)	5016 (23.4)	4144 (21.5)	<0.001
Diabetes mellitus	7765 (16.3)	989 (14.2)	3336 (15.5)	3440 (17.9)	<0.001

Differences between groups (defined by MNA-SF categories) were analysed using chi-squared test for categorical variables and using Welch one-way analysis of variance tests for continuous variables. COPD, chronic obstructive pulmonary disease; MNA-SF, Mini Nutritional Assessment-Short Form; SD, standard deviation. *Disposable income, in 1000 SEK per year.

Table 12 Baseline characteristics of paper IV study participants

Characteristic	Total (N=373)	UTI (n=101)	No UTI (n=272)	*p*
Women	276 (74.0)	85 (84.2)	191 (70.2)	0.006
Age, mean	84.9±6.8	85.6±6.7	84.6±6.8	0.203
BMI	26.2±5.1	26.4±4.9	26.1±5.2	0.598
GDS-15 score	4.1±3.2	4.0±3.1	4.1±3.2	0.672
MMSE score	16.3±4.6	15.2±4.0	16.7±4.8	0.005
BBS score	27.9±14.7	28.4±14.8	26.3±14.3	0.224
Barthel ADL Index (0−20)	12.0±4.4	11.2±4.1	12.3±4.5	0.028
MNA, mean	20.8±3.2	20.4±3.4	20.9±3.2	0.208
MNA score categ.				
<17	41 (11.0)	13 (12.9)	28 (10.3)	
17–23.5	270 (72.4)	77 (76.2)	193 (71.0)	
24–30	62 (16.6)	11 (10.9)	51 (18.8)	
Diagnoses				
Angina	100 (26.8)	28 (27.7)	72 (26.5)	0.808
Arthritis	105 (28.2)	36 (35.6)	69 (25.4)	0.050
Atrial fibrillation	68 (18.2)	17 (16.8)	51 (18.8)	0.670
Constipation, prev. month	223 (59.8)	65 (64.4)	158 (58.1)	0.273
Chronic lung disease	67 (18.0)	17 (16.8)	50 (18.4)	0.729
Dementia disorder	285 (76.4)	82 (81.2)	203 (74.6)	0.185
Depressive disorder	220 (59.0)	60 (59.4)	160 (58.8)	0.919
Diabetes mellitus	65 (17.4)	15 (14.9)	50 (18.4)	0.424
Diarrhoea, prev. month	31 (8.3)	6 (5.9)	25 (9.2)	0.312
Gastric ulcer	50 (13.4)	16 (15.8)	34 (12.5)	0.400
Gynaecologic dis.[a] (n=276)	24 (8.7))	11 (12.9)	13 (6.8)	0.095
Myocardial infarction, prev. year	8 (2.1)	3 (3.0)	5 (1.8)	0.502
Heart failure	107 (28.7)	41 (40.6)	66 (24.3)	0.002
Hypertension	180 (48.3)	61 (60.4)	119 (43.8)	0.004
Malignancy, prev. 5 years	42 (11.3)	12 (11.9)	30 (11.0)	0.817
Osteoporosis	114 (30.6)	34 (33.7)	80 (29.4)	0.428
Other infection, prev. year	85 (22.8)	24 (23.8)	61 (22.4)	0.785
Pace maker	25 (6.7)	7 (6.9)	18 (6.6)	0.914
Pneumonia, prev. year	35 (9.4)	17 (16.8)	18 (6.6)	0.003
Prostate disease[b] (n=97)	40 (41.2)	10 (62.5)	30 (37.0)	0.059
Sleeping disorder	145 (38.9)	35 (34.7)	110 (40.4)	0.308
Stroke	109 (29.2)	31 (30.7)	78 (28.7)	0.704
Urinary catheter	24 (6.4)	10 (9.9)	14 (5.1)	0.096
Urinary incontinence[c]	127 (34.0)	45 (44.6)	82 (30.1)	0.009
Urinary retention	13 (3.5)	4 (4.0)	9 (3.3)	0.760
UTI, prev. year	151 (40.5)	66 (65.3)	85 (31.3)	<0.001

Table 12 continued. Baseline characteristics of paper IV study participants

	Total (N=373)	UTI (n=101)	No UTI (n=272)	
Drug prescriptions				
Number of drugs	8.7±4.2	9.4±4.5	8.5±4.0	0.053
Analgesics, excl. ASA	220 (59.0)	59 (58.4)	161 (59.2)	0.892
SSRI	150 (40.2)	45 (44.6)	105 (38.6)	0.298
Benzodiazepines	114 (30.6)	25 (24.8)	89 (32.7)	0.138
Diuretics	181 (48.5)	53 (52.5)	128 (47.1)	0.352
Laxatives	202 (54.2)	57 (56.4)	145 (53.3)	0.590

Values are presented as *n* (%) or mean ± standard deviation. ADL, activities of daily living; ASA, acetyl-salicylic acid; BBS, berg balance scale; BMI, body mass index; GDS, geriatric depression scale; MMSE, Mini-Mental State Examination; MNA, Mini Nutritional Assessment; SSRI, selective serotonin reuptake inhibitor; UTI, urinary tract infection. [a]based on number of UTI (n=85) in women (n=276); [b]based on number of UTI (n=16) in men (n=97); [c]According to item in the Barthel ADL Index.

MNA and MNA-SF score

In adults aged ≥ 85 years (Paper I and II)

Differences in MNA scores among paper I study cohorts are presented in Table 13. The mean MNA score increased between the first and third cohorts (from 23.2 ± 4.7 to 24.2 ± 3.6), and decreased to 23.3 ± 4.2 in the fourth cohort (overall $p = 0.002$). This score did not differ between the first and fourth cohorts. Similar results were obtained for 90-year-olds and ≥ 95-year-olds. In the whole sample, malnutrition according to MNA was present in 12.2%, 6.4%, 5.1% and 8.7% of the first through fourth cohorts, respectively; 31.8%, 36.8%, 32.0% and 37.2% of participants in these cohorts, respectively, were at risk thereof (overall $p = 0.004$). In the four cohorts, 2.0–4.2% of 85-year-olds, 3.6–12.4% of 90-year-olds and 10.8–27.3% of ≥ 95-year-olds were malnourished according to MNA. These proportions differed significantly among cohorts for the oldest age group, following the same trend as the results for the whole sample (overall $p = 0.002$; Table 13).

For paper II study participants, 13.3% of participants were malnourished (17.0% of women and 4.4% of men) and 40.3% were at risk of malnutrition according to MNA scores. Malnutrition was present in 5.3%, 11.3% and 25.2% of 85-year-olds, 90-year-olds and ≥ 95-year-

olds, respectively. The distributions of MNA scores according to sex and age group are presented in Table 14.

Table 13 Differences in MNA score among paper I study cohorts

	2000–2002 (C1) (*n* = 343)	**2005–2007 (C2) (*n* = 342)**	**2010–2012 (C3) (*n* = 409)**	**2015–2017 (C4) (*n* = 508)**	***p***
Whole sample					
Mean MNA score	23.2 ± 4.7	23.7 ± 3.9	24.2 ± 3.6[a]	23.3 ± 4.2[b]	0.002
MNA score categ.					0.004
<17	42 (12.2)	22 (6.4)	21 (5.1)	44 (8.7)	
17.0–23.5	109 (31.8)	126 (36.8)	131 (32.0)	189 (37.2)	
24–30	192 (56.0)	194 (56.7)	257 (62.8)	275 (54.1)	
85 years					
Mean MNA score	24.9 ± 3.2	24.8 ± 3.5	25.0 ± 3.2	24.9 ± 3.5	0.991[c]
MNA score categ.					0.792
<17	5 (3.6)	3 (2.4)	3 (2.0)	7 (4.2)	
17.0–23.5	35 (25.5)	34 (27.6)	44 (29.3)	38 (22.9)	
24–30	97 (70.8)	86 (69.9)	103 (68.7)	121 (72.9)	
90 years					
Mean MNA score	22.8 ± 4.6	23.6 ± 3.8	24.2 ± 3.4[a]	23.3 ± 4.1	0.039
MNA score categ.					0.074
<17	16 (12.4)	8 (6.2)	5 (3.6)	12 (6.3)	
17.0–23.5	46 (35.7)	53 (41.1)	46 (33.1)	75 (39.7)	
24–30	67 (51.9)	68 (52.7)	88 (63.3)	102 (54.0)	
≥ 95 years					
Mean MNA score	20.6 ± 5.7	22.3 ± 4.3	23.1 ± 3.9[a]	21.4 ± 4.2[b]	0.001
MNA score categ.					0.002
<17	21 (27.3)	11 (12.2)	13 (10.8)	25 (16.3)	
17.0–23.5	28 (36.4)	39 (43.3)	41 (34.2)	76 (49.7)	
24–30	28 (36.4)	40 (44.4)	66 (55.0)	52 (34.0)	

Data are presented as mean ± standard deviation or *n* (%). Differences in mean values were examined using one-way analysis of variance with Bonferroni correction. Differences in proportions were analysed using chi–squared test. Post-hoc tests: [a]significant difference vs. C1; [b]significant difference vs. C3; [c]no significant difference. MNA, Mini Nutritional Assessment.

Table 14 Differences in MNA score among paper II study participants, according to sex and age groups

	Whole sample (n=782)	**Women (n=553)**	**Men (n=229)**	***p***	**85 years (n=265)**	**90 years (n=291)**	**≥ 95 years (n=226)**	***p***
Mean MNA score	22.5±4.6	22.0±4.8	23.8±3.7	<0.001	23.9±3.8	22.6±4.4	20.7±5.1	<0.001
MNA score categ.								
< 17	104(13.3)	94(17.0)	10(4.4)		14(5.3)	33(11.3)	57(25.2)	<0.001
17–23.5	315(40.3)	228(41.2)	87(38.0)		93(35.1)	129(44.3)	93(41.2)	
24–30	363(46.4)	231(41.8)	132(57.6)		158(59.6)	129(44.3)	76(33.6)	

Values are presented as n (%) or mean ± standard deviation. Differences in proportions were analysed using the chi-squared test, and in analyses of age groups, MNA (< 17 and ≥ 17) was dichotomized. Differences in mean values were examined using the independent-samples *t* test or one-way analysis of variance. MNA, Mini Nutritional Assessment

In adults aged ≥ 85 years living in residential care facilities (Paper I and II)

In the paper I study, subgroup analyses using one-way analysis of variance with Bonferroni correction, showed that the mean MNA score was higher in the third cohort (21.7 ± 3.8) than in the first cohort (20.1 ± 5.0), and lower in the fourth cohort (19.5 ± 4.3) than in the second (21.1 ± 3.8) and third cohorts, among very old individuals living in residential care facilities (overall $p < 0.001$). In the paper II study, subgroup analysis revealed that 25.9% of very old adults living in residential care facilities and 3.4% of those residing in the community were malnourished, according to MNA scores ($p < 0.001$). The risk of malnutrition was present in 54.9% and 28.8% of these groups, respectively ($p < 0.001$).

In adults aged ≥ 65 years living in residential care facilities (Paper III and IV)

Of paper III study participants, 14.6% were malnourished and 45.0% were at risk thereof, according to MNA-SF scores. Results of this study are presented in Table 15. One-third of participants, including 42.3% of those categorised as malnourished and 24.0% of those with good nutritional status according to MNA-SF scores, had dementia diagnoses (overall $p < 0.001$; Table 11). Of the paper IV study participants, 11.0% were malnourished and 72.4% were at risk of malnutrition, according to MNA scores (Table 12).

Table 15 BMIs and MNA-SF scores in the paper III study population

	Whole sample	**MNA-SF 0–7**	**MNA-SF 8–11**	**MNA-SF 12–14**	***P***
Number	47,686	6970 (14.6)	21,459 (45.0)	19,257 (40.4)	<0.001
BMI, mean (SD)	25.1 (5.2)	20.8 (4.5)	24.4 (4.9)	27.4 (4.5)	<0.001
BMI categories, n (%)					<0.001
<18.5	3959 (8.3)	2288 (32.8)	1671 (7.8)	0 (0.0)	
18.5–24.9	21,445 (45.0)	3641 (52.2)	11,385 (53.1)	6419 (33.3)	
25.0–29.9	14,655 (30.7)	750 (10.8)	5728 (26.7)	8177 (42.5)	
≥30.0	7627 (16.0)	291 (4.2)	2675 (12.5)	4661 (24.2)	
BMI obesity class I-III, n (%)					<0.001†
30.0–34.9	5774 (12.1)	225 (3.2)	2034 (9.5)	3515 (18.3)	
35.0–39.9	1419 (3.0)	46 (0.7)	493 (2.3)	880 (4.6)	
≥40.0	434 (0.9)	20 (0.3)	148 (0.7)	266 (1.4)	
Mean MNA-SF, score (SD)	10.4 (2.6)	5.6 (1.5)	9.8 (1.1)	12.8 (0.8)	<0.001

Differences between groups (defined by MNA-SF categories) were examined using the chi-squared test for categorical variables and the Welch one-way analysis of variance test for continuous variables. Data are presented as mean ± standard deviation or *n* (%), unless otherwise indicated. †Analyses of all BMI categories with obesity divided in class I, II, and III. BMI, body mass index (kg/m^2); MNA-SF, Mini Nutritional Assessment-Short Form; SD, standard deviation.

The BMI

In adults aged ≥ 85 years (Paper I and II)

BMI results from paper I are presented in Table 16. In the whole sample, the mean BMI increased between the first and fourth cohorts (overall $p < 0.001$); Bonferroni-corrected analyses revealed differences between the fourth cohort and the first and second cohorts. Increases in the mean BMI from the first to the fourth cohort were also seen in 85-year-olds (overall $p = 0.001$) and ≥ 95-year-olds (overall $p = 0.008$; Table 16).

The proportions of BMI categories differed significantly among the four cohorts in the chi-squared analysis of the whole sample (overall $p = 0.006$; Table 16). Thirteen point four per cent, 12.0%, 13.7% and 18.3% of the first through fourth cohorts, respectively, were obese, 28.6%, 35.4%, 36.2% and 35.8% of these cohorts, respectively, were overweight, and 7.6%, 5.3%, 4.4% and 3.0% of participants, respectively, were underweight.

Obesity was present in 12.4%–24.1% of 85-year-olds, 10.1%–17.8% of 90-year-olds and 5.8%–13.1% of ≥ 95-year-olds. In the first through fourth cohorts, the prevalence of underweight ranged from 1.2% to 2.9% among 85-year-olds, from 3.2% to 8.5% among 90-year-olds, and from 4.6% to 14.3% among ≥ 95-year-olds (Table 16).

In the paper II study population, the mean BMI did not differ between women and men, and the mean BMI appeared to be lower in ≥ 95-year-olds compared to 85-year-olds (overall $p < 0.001$). One-fourth of the whole sample had BMIs in the highest quartile (≥ 28.0 kg/m^2). Half of the whole sample, 59.4% of 85-year-olds, 48.7% of 90-year-olds and 42.8% of ≥ 95-year-olds had BMIs ≥ 24.7 kg/m^2. Furthermore, one-fourth of the whole sample, 17.4% of 85-year-olds, 26.2% of 90-year-olds and 32.3% of ≥ 95-year-olds had BMIs in the lowest quartile (< 22.2 kg/m^2). BMI distributions by sex and age group are presented in Table 17.

Table 16 Differences in BMI among paper I study cohorts

	2000–2002 (C1) (n = 343)	**2005–2007 (C2)** (n = 342)	**2010–2012 (C3)** (n = 409)	**2015–2017 (C4)** (n = 508)	***p***
Whole sample					
BMI, mean	24.8 ± 4.7	24.9 ± 4.1	25.4 ± 4.2	26.0 ± 4.7[a,b]	<0.001
BMI categories					0.006
<18.5	26 (7.6)	18 (5.3)	18 (4.4)	15 (3.0)	
18.5–24.9	173 (50.4)	162 (47.4)	187 (45.7)	218 (42.9)	
25.0–29.9	98 (28.6)	121 (35.4)	148 (36.2)	182 (35.8)	
≥30.0	46 (13.4)	41 (12.0)	56 (13.7)	93 (18.3)	
85 years					
BMI, mean	25.6 ± 4.2	25.7 ± 4.0	26.2 ± 4.4	27.4 ± 4.7[a,b]	0.001
BMI categories					0.112
<18.5	4 (2.9)	3 (2.4)	4 (2.7)	2 (1.2)	
18.5–24.9	72 (52.6)	55 (44.7)	63 (42.0)	57 (34.3)	
25.0–29.9	44 (32.1)	44 (35.8)	54 (36.0)	67 (40.4)	
≥30.0	17 (12.4)	21 (17.1)	29 (19.3)	40 (24.1)	
90 years					
BMI, mean	25.0 ± 4.9	24.7 ± 4.0	25.3 ± 4.1	25.7 ± 4.5	0.191[c]
BMI categories					0.227
<18.5	11 (8.5)	5 (3.9)	6 (4.3)	6 (3.2)	
18.5–24.9	53 (41.1)	70 (54.3)	65 (46.8)	83 (43.9)	
25.0–29.9	42 (32.6)	41 (31.8)	48 (34.5)	67 (35.4)	
≥30.0	23 (17.8)	13 (10.1)	20 (14.4)	33 (17.5)	
≥ 95 years					
BMI, mean	23.0 ± 4.5	24.3 ± 4.2	24.5 ± 3.7	25.0 ± 4.6[a]	0.008
BMI categories					0.003
<18.5	11 (14.3)	10 (11.1)	8 (6.7)	7 (4.6)	
18.5–24.9	48 (62.3)	37 (41.1)	59 (49.2)	78 (51.0)	
25.0–29.9	12 (15.6)	36 (40.0)	46 (38.3)	48 (31.4)	
≥30.0	6 (7.8)	7 (7.8)	7 (5.8)	20 (13.1)	

Data are presented as mean ± standard deviation or n (%). Differences in mean values were examined using one-way analysis of variance with Bonferroni correction. Differences in proportions were examined using the chi–squared test. Post hoc tests: [a]significant difference vs. C1; [b]significant difference vs. C2; [c]no significant difference. BMI, body mass index (kg/m^2); C, cohort.

Table 17 Differences in BMI among paper II study participants, according to sex and age groups

	Whole sample (n=803)	**Women (n=558)**	**Men (n=245)**	***p***	**85 years (n=281)**	**90 years (n=302)**	**≥ 95 years (n=220)**	***p***
BMI, mean	25.1±4.5	25.1±4.7	25.1±3.8	0.938	26.1±4.3	24.9±4.4	24.1±4.4	<0.001
BMI categories								
< 22.2	199(24.8)	144(25.8)	55(22.4)		49(17.4)	79(26.2)	71(32.3)	0.001
22.2–24.6	196(24.4)	135(24.2)	61(24.9)		65(23.1)	76(25.2)	55(25.0)	
24.7–27.9	207(25.8)	134(24.0)	73(29.8)		81(28.8)	77(25.5)	49(22.3)	
≥ 28.0	201(25.0)	145(26.0)	56(22.9)		86(30.6)	70(23.2)	45(20.5)	

Values are presented as n (%) or mean ± standard deviation. Differences in proportions were analysed using the chi-squared test, with BMI (< 22.2 and ≥ 22.2) dichotomized. Differences in mean values were examined using the independent-samples *t* test or one-way analysis of variance. BMI, body mass index (kg/m^2).

In adults aged ≥ 85 years living in residential care facilities (Paper I)

In the paper I study, subgroup analyses revealed that the mean BMIs of participants living in residential care facilities in the first through fourth cohorts were 24.1 ± 5.3, 24.9 ± 4.3, 25.4 ± 4.3 and 25.8 ± 5.2 kg/m^2, respectively. Thus, the mean BMI increased between the first and fourth cohorts in this subgroup (overall $p = 0.024$).

In adults aged ≥ 65 years living in residential care facilities (Paper III and IV)

In the paper III study population, 30.7% of participants were overweight, 16.0% were obese (class I, 12.1%; class II, 3.0%; class III, 0.9%) and 8.3% were underweight (Table 15). In the paper IV study population, the mean BMI was 26.2 ± 5.1 kg/m^2 (Table 12).

The MNA and MNA-SF score and mortality

In adults aged ≥ 85 years (Paper II)

In the study reported on in paper II, 5-year mortality rates were lower among participants with good nutritional status than among malnourished individuals (according to MNA scores) in the whole sample and in all subgroups defined according to sex and age (Table 18). Mortality rates also were lower among individuals at risk of malnutrition than among those categorised as malnourished, except among men and 90-year-olds. Results obtained in analyses using other reference groups are presented in Table 19 The association between MNA scores and 5-year mortality appeared to be linear; survival increased with the MNA score. In the study reported on in paper I, likelihood ratio tests revealed that the association between the MNA score and 2-year mortality did not differ among the four cohorts (continuous MNA $p = 0.126$; categorical MNA, $p = 0.451$).

Table 18 Adjusted and unadjusted associations between MNA scores and 5-year mortality among paper II study participants

		Hazard Ratio (95 % Confidence Interval)			
	MNA < 17	**MNA 17–23.5**	***p***	**MNA 24–30**	***p***
Whole sample	1	0.538 (0.425–0.680)	<0.001	0.257 (0.201–0.329)	<0.001
Whole sample, adjusted	1	0.608 (0.478–0.774)	<0.001	0.298 (0.229–0.386)	<0.001
Women	1	0.497 (0.385–0.644)	<0.001	0.229 (0.173–0.303)	<0.001
Men	1	0.584 (0.301–1.135)	0.113	0.272 (0.140–0.527)	<0.001
85 years	1	0.512 (0.274–0.958)	0.036	0.311 (0.168–0.575)	<0.001
90 years	1	0.696 (0.464–1.043)	0.079	0.260 (0.168–0.402)	<0.001
≥ 95 years	1	0.599 (0.426–0.844)	0.003	0.381 (0.263–0.552)	<0.001

Data are derived from Cox regression analyses. Analysis of the whole sample was adjusted for sex and age. MNA, Mini Nutritional Assessment.

Table 19 Associations of MNA scores with 5-year mortality in the paper II study population (alternate reference groups)

	Hazard Ratio (95 % Confidence Interval)					
	MNA < 17	***p***	**MNA 17–23.5**	***p***	**MNA 24–-30**	***p***
Whole sample	1.859 (1.470-2.350)	< 0.001	1		0.478 (0.397-0.575)	< 0.001
Whole sample	3.889 (3.044-4.969)	< 0.001	2.092 (1.739-2.517)	< 0.001	1	
Women	2.010 (1.554-2.601)	< 0.001	1		0.460 (0.364-0.580)	< 0.001
Women	4.373 (3.299-5.796)	< 0.001	2.175 (1.723-2.747)	< 0.001	1	
Men	1.711 (0.881-3.323)	0.113	1		0.465 (0.341-0.635)	< 0.001
Men	3.679 (1.897-7.134)	< 0.001	2.150 (1.575-2.934)	< 0.001	1	
85 years	1.952 (1.044-3.648)	0.036	1		0.607 (0.429-0.859)	0.005
85 years	3.214 (1.738-5.943)	< 0.001	1.647 (1.164-2.329)	0.005	1	
90 years	1.437 (0.959-2.154)	0.079	1		0.374 (0.275-0.507)	< 0.001
90 years	3.845 (2.489-5.939)	< 0.001	2.675 (1.971-3.631)	< 0.001	1	
≥ 95 years	1.668 (1.185-2.348)	0.003	1		0.636 (0.460-0.880)	0.006
≥ 95 years	2.622 (1.811-3.796)	< 0.001	1.572 (1.136-2.173)	0.006	1	

Data were obtained by unadjusted Cox regression analysis. MNA, Mini Nutritional Assessment.

In adults aged ≥ 65 years living in residential care facilities (Paper III)

In the study reported on in paper III, adjusted Cox regression analyses revealed greater 2-year mortality among individuals with malnutrition and at risk thereof than among those with good nutritional status according to MNA-SF scores during all follow-up timeframes (Table 20).

Table 20 Adjusted Cox proportional hazards for associations of BMI and MNA-SF scores with 2-year all-cause mortality during follow-up intervals

		Hazard Ratio (95 % Confidence Interval)				
	Deaths n(%)	0–24 months (n = 47,686)	0–6 months (n = 47,686)	6–12 months (n = 40,283)	12–18 months (n = 33,704)	18–24 months (n = 27,190)
Deaths n(%)	*p* <0.001*	23,335 (48.9)	7403 (15.5)	6579 (16.3)	5209 (15.5)	4144 (15.2)
BMI categ.	*p* <0.001**					
≥30.0	2757 (36.1)	1	1	1	1	1
25.0–29.9	6354 (43.4)	1.17 (1.12–1.22)	1.24 (1.13–1.36)	1.12 (1.03–1.22)	1.19 (1.09–1.31)	1.13 (1.02–1.25)
18.5–24.9	11,519(53.7)	1.58 (1.51–1.65)	1.84 (1.70–2.01)	1.48 (1.37–1.61)	1.52 (1.39–1.67)	1.44 (1.31–1.59)
<18.5	2705 (68.3)	2.56 (2.42–2.71)	3.45 (3.13–3.80)	2.26 (2.03–2.51)	2.31 (2.04–2.60)	1.92 (1.67–2.21)
BMI categ.	*p* <0.001**					
18.5–24.9	11,519(53.7)	1	1	1	1	1
<18.5	2705 (68.3)	1.62 (1.55–1.69)	1.87 (1.75–2.00)	1.52 (1.40–1.66)	1.51 (1.37–1.67)	1.33 (1.18–1.50)
25.0–29.9	6354 (43.4)	0.74 (0.72–0.76)	0.67 (0.63–0.71)	0.75 (0.71–0.80)	0.78 (0.73–0.84)	0.79 (0.73–0.84)
30.0–34.9	2106 (36.5)	0.63 (0.60–0.66)	0.55 (0.50–0.60)	0.66 (0.60–0.72)	0.65 (0.59–0.72)	0.69 (0.62–0.77)
35.0–39.9	482 (34.0)	0.62 (0.56–0.68)	0.48 (0.39–0.58)	0.70 (0.59–0.83)	0.64 (0.53–0.77)	0.69 (0.56–0.84)
≥40.0	169 (38.9)	0.80 (0.69–0.94)	0.71 (0.53–0.96)	0.87 (0.65–1.15)	0.83 (0.60–1.15)	0.82 (0.57–1.17)
MNA-SF categ.	*p* <0.001**					
12–14	7023 (36.5)	1	1	1	1	1
8–11	11,444(53.3)	1.74 (1.69–1.79)	2.10 (1.97–2.23)	1.68 (1.59–1.78)	1.72 (1.62–1.83)	1.48 (1.38–1.58)
0–7	4868 (69.8)	2.98 (2.87–3.10)	4.78 (4.48–5.11)	2.50 (2.32–2.69)	2.33 (2.14–2.54)	2.01 (1.82–2.22)

Analyses were of MNA-SF scores (ref. 12–14), BMIs with obesity defined as BMI ≥ 30.0 kg/m^2 (ref.) and BMIs with obesity divided into class I, II, III (ref. 18.5–24.9 kg/m^2). They were adjusted for age, sex, education level, disposable income, dementia, hip fracture, chronic obstructive pulmonary disease, renal failure, rheumatoid arthritis, myocardial infarction, stroke and diabetes. BMI, body mass index (kg/m^2); MNA-SF, Mini Nutritional Assessment–Short Form. * *P* value for number of deaths in follow-up intervals. ***P* values for numbers of deaths in BMI categories and MNA-SF categories.

The BMI and mortality

In adults aged ≥ 85 years (Paper II)

In the study reported on in paper II, compared to BMIs < 22.2 kg/m^2, unadjusted and adjusted analyses showed less mortality among individuals with BMIs ≥ 28.0 kg/m^2, in the whole sample and separately among women and men. BMIs of 24.7–27.9 kg/m^2 were associated with less mortality than were BMIs < 22.2 kg/m^2 in analyses of the whole sample, women and 90-year-olds. (Table 21). Results obtained in analyses using other reference groups are presented in Table 22. The association between BMI and mortality was plotted, and it seemed as if survival was increasing until a BMI of approximately 25 kg/m^2 and plateauing thereafter. In the study reported on in paper I, likelihood ratio tests revealed that the association between BMI and 2-year mortality did not differ among the four cohorts (continuous BMI, $p = 0.932$; categorical BMI, $p = 0.401$).

In adults aged ≥ 65 years living in residential care facilities (Paper III)

In the study reported on in paper III, less 2-year mortality was observed among obese individuals (those with BMIs ≥ 30.0 kg/m^2) than among overweight, normal-weight and underweight individuals during all follow-up periods. In the analysis performed with obesity classes, less mortality was found for overweight and obesity classes I–II than for normal-weight, whereas greater mortality was found for underweight, in all follow-up periods. Less mortality was also found for obesity class III in the follow-up period of 24 months and in analysis of the first 6 months (Table 20).

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Table 21 Unadjusted and adjusted associations of BMI quartiles with 5-year mortality in the paper II study

		Hazard Ratio (95 % Confidence Interval)					
	BMI < 22.2	**BMI 22.2–24.6**	***p***	**BMI 24.7–27.9**	***p***	**BMI ≥ 28.0**	***p***
Whole sample	1	0.765 (0.609–0.961)	0.022	0.563 (0.445–0.710)	<0.001	0.623 (0.494–0.786)	<0.001
Whole sample, adjusted	1	0.808 (0.642–1.016)	0.068	0.630 (0.498–0.797)	<0.001	0.739 (0.584–0.936)	0.012
Women	1	0.840 (0.640–1.101)	0.207	0.479 (0.357–0.644)	<0.001	0.644 (0.490–0.848)	0.002
Men	1	0.618 (0.405–0.945)	0.026	0.726 (0.491–1.075)	0.110	0.572 (0.369–0.885)	0.012
85 years	1	0.928 (0.571–1.506)	0.761	0.695 (0.430–1.121)	0.136	0.654 (0.407–1.050)	0.079
90 years	1	0.641 (0.443–0.926)	0.018	0.474 (0.324–0.693)	<0.001	0.703 (0.485–1.018)	0.062
≥ 95 years	1	0.975 (0.674–1.411)	0.895	0.752 (0.513–1.103)	0.145	0.825 (0.555–1.225)	0.340

Data were obtained by Cox regression analysis. Analysis of the whole sample was adjusted for sex and age. BMI, body mass index (kg/m^2). Analyses adjusted for sex and age.

Table 22 Associations of BMI with 5-year mortality in the paper II study population (alternate reference groups)

	Hazard Ratio (95 % Confidence Interval)							
	BMI < 22.2	***p***	**BMI 22.2–24.6**	***p***	**BMI 24.7–27.9**	***p***	**BMI ≥ 28.0**	***p***
Whole sample								
	1.307 (1.040-1.643)	0.022	1		0.735 (0.578-0.936)	0.012	0.814 (0.641-1.035)	0.094
	1.778 (1.408-2.245)	< 0.001	1.360 (1.069-1.731)	0.012	1		1.108 (0.868-1.414)	0.412
	1.605 (1.273-2.025)	<0.001	1.228 (0.966-1.561)	0.094	0.903 (0.707-1.152)	0.412	1	
Women								
	1.191 (0.908-1.562)	0.207	1		0.572 (0.421-0.774)	< 0.001	0.767 (0.578-1.019)	0.068
	2.086 (1.553-2.803)	< 0.001	1.752 (1.292-2.374)	< 0.001	1		1.344 (0.990-1.825)	0.058
	1.552 (1.180-2.042)	0.002	1.303 (0.981-1.731)	0.068	0.744 (0.548-1.010)	0.058	1	
Men								
	1.617 (1.058-2.472)	0.026	1		1.175 (0.782-1.766)	0.439	0.925 (0.589-1.450)	0.733
	1.377 (0.930-2.037)	0.110	0.851 (0.566-1.280)	0.439	1		0.787 (0.517-1.198)	0.264
	1.749 (1.130-2.707)	0.012	1.082 (0.689-1.697)	0.733	1.271 (0.834-1.935)	0.264	1	
85 years								
	1.078 (0.664-1.750)	0.761	1		0.749 (0.475-1.182)	0.214	0.705 (0.450-1.107)	0.129
	1.440 (0.892-2.324)	0.136	1.335 (0.846-2.107)	0.214	1		0.942 (0.604-1.468)	0.791
	1.529 (0.952-2.454)	0.079	1.418 (0.904-2.225)	0.129	1.062 (0.681-1.655)	0.791	1	
90 years								
	1.561 (1.079-2.257)	0.018	1		0.739 (0.496-1.101)	0.137	1.097 (0.742-1.620)	0.643
	2.112 (1.443-3.090)	< 0.001	1.353 (0.908-2.016)	0.137	1		1.484 (0.994-2.216)	0.054
	1.423 (0.983-2.061)	0.062	0.912 (0.617-1.347)	0.643	0.674 (0.451-1.006)	0.054	1	
≥ 95 years								
	1.025 (0.709-1.483)	0.895	1		0.771 (0.514-1.157)	0.209	0.845 (0.557-1.284	0.431
	1.330 (0.906-1.950)	0.145	1.297 (0.864-1.946)	0.209	1		1.097 (0.714-1.684)	0.673
	1.213 (0.816-1.801)	0.340	1.183 (0.779-1.796)	0.431	0.912 (0.594-1.400)	0.673	1	

Data were obtained by unadjusted Cox regression analysis. BMI, body mass index (kg/m^2)

The MNA and MNA-SF score and BMI (Paper II and III)

Of paper II study participants classified as malnourished according to MNA scores, 17.4% had BMIs ≥ 24.7 kg/m^2; 13.8% of participants in this study with good nutritional status according to MNA scores had BMIs < 22.2 kg/m^2. Of those at risk of malnutrition according to MNA scores, 28.1% and 27.8% had BMIs < 22.2 kg/m^2 and ≥ 28.0 kg/m^2, respectively (Table 23). The Pearson coefficient of correlation between the BMI and MNA score was 0.351 ($p < 0.001$).

Of paper III study participants, 15.0% classified as overweight or obese and 52.2% classified as of normal-weight according to BMIs were malnourished according to MNA-SF scores. Overweight or obesity was seen in 39.2% of those at risk of malnutrition according to MNA-SF scores. In addition, 57.8% of underweight individuals were classified as malnourished according to MNA and 42.2% of these individuals were categorised as being at risk of malnutrition according to MNA-SF scores. Good nutritional status according to MNA-SF scores were seen in 55.8% and 61.1% of those classified as overweight and obese according to the BMI, respectively (Table 15).

The MNA-SF score, BMI and mortality (Paper III)

In the study reported on in paper III, adjusted analyses revealed greater mortality among individuals with good nutritional status according to MNA-SF scores who were overweight or of normal-weight than among those with BMIs ≥ 30.0 kg/m^2 and MNA-SF scores of 12–14 (Table 24). The mortality rate was higher than the latter group among individuals at risk of malnutrition (MNA-SF scores of 8–11), regardless of BMI, with an increasing trend observed for lower BMIs. Compared with that among individuals with BMIs ≥ 30.0 kg/m^2 and MNA-SF scores of 12–14, the mortality rate was greater among malnourished individuals (those with MNA-SF scores of 0–7) in all BMI categories and was particularly high among underweight individuals; confidence intervals overlapped for the other BMI categories. Similar associations were found in all follow-up periods, except among individuals with MNA-SF scores of 12–14 and BMIs of 25.0–29.9 kg/m^2 for the first 18 months of follow-up.

Table 23 BMIs and MNA scores in the paper II study population

	MNA < 17 (n=92)			MNA 17–23.5 (n=299)			MNA 24–30 (n=362)		
	Whole sample	**Women**	**Men**	**Whole sample**	**Women**	**Men**	**Whole sample**	**Women**	**Men**
BMI categ.									
< 22.2	60 (65.2)	53 (64.6)	7 (70.0)	84 (28.1)	55 (25.3)	29 (35.4)	50 (13.8)	33 (14.3)	17 (12.9)
22.2–24.6	16 (17.4)	16 (19.5)	0 (0.0)	64 (21.4)	47 (21.7)	17 (20.7)	106 (29.3)	66 (28.7)	40 (30.3)
24.7–27.9	7 (7.6)	5 (6.1)	2 (20.0)	68 (22.7)	46 (21.2)	22 (26.8)	118 (32.6)	73 (31.7)	45 (34.1)
≥ 28.0	9 (9.8)	8 (9.8)	1 (10.0)	83 (27.8)	69 (31.8)	14 (17.1)	88 (24.3)	58 (25.2)	30 (22.7)
BMI Mean	21.4 ± 4.6	21.2 ± 4.6	22.3 ± 4.9	25.2 ± 4.8	25.5 ± 5.0	24.2 ± 4.1	25.8 ± 3.6	25.9 ± 3.8	25.6 ± 3.3

Values are presented as n (%) or mean ± standard deviation. BMI, body mass index (kg/m^2); MNA, Mini Nutritional Assessment.

Table 24 Adjusted Cox proportional hazards for the association of BMI according to MNA-SF score with 2-year all-cause mortality

	n	Deaths n(%)	Hazard Ratio (95 % Confidence Interval)				
			0–24 months	0–6 months	6–12 months	12–18 months	18–24 months
MNA-SF 12–14							
BMI ≥30.0	4661	1409 (30.2)	1	1	1	1	1
BMI 25.0–29.9	8177	2969 (36.3)	1.13 (1.06–1.20)	1.09 (0.95–1.25)	1.11 (0.98–1.25)	1.11 (0.98–1.27)	1.22 (1.06–1.39)
BMI 18.5–24.9	6419	2645 (41.2)	1.28 (1.20–1.37)	1.36 (1.18–1.56)	1.22 (1.08–1.38)	1.22 (1.07–1.40)	1.38 (1.20–1.58)
BMI <18.5	0	NA	NA	NA	NA	NA	NA
MNA-SF 8–11							
BMI ≥30.0	2675	1168 (43.7)	1.60 (1.48–1.73)	1.78 (1.52–2.09)	1.61 (1.39–1.86)	1.42 (1.21–1.67)	1.62 (1.37–1.92)
BMI 25.0–29.9	5728	2887 (50.4)	1.86 (1.74–1.98)	2.30 (2.01–2.62)	1.72 (1.52–1.93)	1.84 (1.62–2.10)	1.61 (1.39–1.86)
BMI 18.5–24.9	11,385	6378 (56.0)	2.12 (2.00–2.25)	2.59 (2.29–2.93)	2.00 (1.79–2.23)	2.04 (1.81–2.30)	1.92 (1.69–2.19)
BMI <18.5	1671	1011 (60.5)	2.42 (2.23–2.63)	2.92 (2.48–3.42)	2.22 (1.90–2.59)	2.56 (2.17–3.03)	2.06 (1.69–2.51)
MNA-SF 0–7							
BMI ≥30.0	291	180 (61.9)	2.86 (2.44–3.36)	4.81 (3.74–6.17)	1.85 (1.31–2.61)	2.66 (1.89–3.74)	2.20 (1.44–3.37)
BMI 25.0–29.9	750	498 (66.4)	3.17 (2.86–3.52)	5.48 (4.62–6.51)	2.29 (1.86–2.84)	2.36 (1.86–3.01)	2.40 (1.83–3.14)
BMI 18.5–24.9	3641	2496 (68.6)	3.25 (3.03–3.47)	5.14 (4.52–5.85)	2.71 (2.38–3.07)	2.54 (2.20–2.93)	2.38 (2.02–2.79)
BMI <18.5	2288	1694 (74.0)	4.01 (3.73–4.32)	6.47 (5.65–7.40)	3.36 (2.92–3.86)	2.92 (2.47–3.44)	2.69 (2.22–3.26)

The reference group was MNA-SF score = 12–14 and BMI ≥ 30.0 kg/m^2. Analyses were adjusted for age, sex, education level, disposable income, dementia, hip fracture, chronic obstructive pulmonary disease, renal failure, rheumatoid arthritis, myocardial infarction, stroke and diabetes. BMI, body mass index; MNA-SF, Mini Nutritional Assessment-Short Form; NA, not available.

Risk factors for urinary tract infection (Paper IV)

As shown in Table 12, 101 (27.1%) participants (30.8% of women and 16.5% of men) contracted at least one UTI during the follow-up period. The UTI incidence rate was 460/1000 person-years. Participants who contracted at least one UTI during the follow-up period had lower MMSE and Barthel ADL Index scores, and some diagnoses were more common in this group, compared to those who did not contract a UTI.

In the study reported on in paper IV, univariate Cox regression analyses revealed that female sex, urinary incontinence according to the Barthel ADL Index item, more drug prescriptions, heart failure, hypertension, pneumonia, and UTI in the previous year were risk factors for UTI contraction during the 9-month follow-up period, while higher MMSE and Barthel ADL Index scores were associated with lower risk of contracting UTI (Table 25). In the multivariable Cox regression analysis, a history of UTI in the previous year, heart failure, and hypertension were associated independently with a greater risk of incident UTI, and higher MMSE scores was independently associated with less risk of incident UTI (Table 26).

Univariate analysis revealed that urinary incontinence according to the Barthel ADL Index item, arthritis, heart failure, pneumonia, and UTI in the previous year were associated with incident UTI and higher MMSE and Barthel ADL Index scores were associated with lower risk of incident UTI among women; more drug prescriptions, heart failure, hypertension, urinary catheter use, pneumonia, UTI in the previous year, and urinary retention showed an association with incident UTI among men. In addition, higher MNA score was associated with lower risk of UTI contraction during the 9-month follow-up period among men (Table 25).

Table 25 Risk factors for UTI contraction in the 9-month follow-up period in the paper IV study population (univariate Cox regression)

	Hazard ratio (95% Confidence Interval)					
	Whole sample	***p***	**Women**	***p***	**Men**	***p***
Sex (woman)	2.036 (1.194–3.474)	0.009				
MMSE score	0.931 (0.889–0.975)	0.002	0.921 (0.873–0.972)	0.003		
Barthel ADL Index	0.948 (0.910–0.988)	0.011	0.950 (0.907–0.994)	0.027		
Urinary incontinence[a]	1.775 (1.199–2.629)	0.004	1.873 (1.218–2.881)	0.004		
Number of drugs	1.053 (1.005–1.103)	0.029			1.141 (1.015–1.282)	0.027
Bensodiazepines	0.719 (0.458–1.130)	0.153	0.656 (0.398–1.084)	0.100		
Arthritis	1.458 (0.971–2.192)	0.069	1.616 (1.039–2.514)	0.033		
Heart failure	2.010 (1.351–2.992)	0.001	1.880 (1.208–2.926)	0.005	3.769 (1.368–10.383)	0.010
Hypertension	1.853 (1.244–2.762)	0.002	1.493 (0.969–2.301)	0.069	4.028 (1.398–11.608)	0.010
Urinary catheter	1.591 (0.828–3.056)	0.164			5.151 (1.933–13.729)	0.001
Pneumonia, prev. year	2.365 (1.403–3.986)	0.001	2.035 (1.127–3.676)	0.019	4.398 (1.408–13.736)	0.011
UTI, prev. year	3.235 (2.146–4.876)	<0.001	2.923 (1.866–4.579)	<0.001	4.059 (1.474–11.175)	0.007
Gynaecologic disease			1.742 (0.924–3.284)	0.086		
MNA score					0.841 (0.750–0.944)	0.003
Atrial fibrillation					0.229 (0.030–1.733)	0.153
Prostate disease					2.455 (0.892–6.757)	0.082
Stroke					2.277 (0.855–6.067)	0.100
Urinary retention					3.166 (1.021–9.819)	0.046

Data were obtained by Cox regression analysis. ADL, activities of daily living; MMSE, Mini-Mental State Examination; MNA, Mini Nutritional Assessment; UTI, urinary tract infection. [a]According to item in the Barthel ADL Index.

Table 26 Risk factors for UTI contraction during the 9-month follow-up period in the paper IV study population (multivariable Cox regression)

	Hazard Ratio (95% Confidence Interval)	*p*
UTI, prev. year	2.804 (1.824–4.311)	< 0.001
Heart failure	2.101 (1.368–3.225)	0.001
Sex (woman)	1.670 (0.972–2.872)	0.063
Hypertension	1.656 (1.095–2.504)	0.017
Pneumonia, prev. year	1.459 (0.836–2.547)	0.184
Number of drugs	0.994 (0.939–1.051)	0.827
Barthel ADL Index	0.989 (0.945–1.036)	0.642
MMSE score	0.937 (0.892–0.985)	0.011

Urinary incontinence according to the Barthel ADL Index item correlated with the Barthel ADL Index variable and was excluded from this analysis. ADL, activities of daily living; MMSE, Mini-Mental State Examination; UTI, urinary tract infection.

Discussion

This thesis presents results on malnutrition and obesity, identified using MNA or MNA-SF, and the BMI, respectively, among old and very old adults residing in the community and in residential care. The work was focused on the prevalence, prevalence trends and consequences of these conditions, in terms of mortality and as risk factors for UTI.

Main findings

The studies reported on in papers I and II, conducted with data from a population-based cohort of very old adults, revealed that malnutrition was common in this population, and more common among women than men. Nutritional status improved between 2000–2002 and 2010–2012, but this trend was reversed in 2015–2017. Obesity was common, and its prevalence increased between 2000–2002 and 2015–2017. Malnutrition according to MNA scores and low BMIs were associated with greater 5-year mortality.

The paper III study, conducted with data from the SA registry for older adults living in residential care facilities in Sweden, showed that malnutrition according to MNA-SF was common in this population and associated with increased mortality. Obesity was common and was associated with reduced mortality, including obesity of all classes, and regardless of what nutritional status the MNA-SF defined. In the study reported on in paper IV, malnutrition according to MNA was not a clear risk factor for UTI among older adults living in residential care facilities.

Methodological considerations

This thesis includes four papers describing studies conducted with four different populations, which had diverse sample selection processes, designs, inclusion criteria and settings. These factors limit the comparability of the findings. These studies, however, enabled the investigation of various aspects of malnutrition and obesity among old and very old adults.

The BMI

The BMI was used to identify obesity in all studies included in this thesis. Although this well-established measure is easy to use and cost

effective [45, 163], it does not enable distinction among muscle, fat and fluid mass; the determination of fat distribution; or consideration of age-related weight and height reductions.

In the studies reported on in papers I and III, the WHO's BMI cut-offs were used. This categorisation is well established and enables comparison among studies [45] but it is not used universally, and comparison with results generated with different BMI cut-offs is difficult. In the paper II study, BMIs were divided into quartiles, with the cut-off value for the lowest quartile (< 22.2 kg/m^2) corresponding to the indication for nutritional screening in older adults [36, 81], and the third and fourth quartile corresponding approximately to the WHO categories of overweight and obesity (≥ 25.0 kg/m^2) [45].

The MNA and MNA-SF

The MNA (papers I, II and IV) and MNA-SF (paper III) were used to assess malnutrition in the included studies. The MNA was developed to identify individuals at risk of malnutrition, and it has been validated and is used widely [98, 102, 164]. The MNA and MNA-SF are designed for nutritional screening; although MNA administration provides more information than does MNA-SF administration. Identification of malnutrition risk using these tools should be followed by thorough investigation of individuals' nutritional and health status, and possible causes of any issues identified [36]. When referring to malnutrition in this thesis, this is according to MNA or MNA-SF scores, thus indicating malnutrition risk. The MNA questionnaire contains items on depression, dementia, acute illness, pressure ulcers, number of medications, mobility, disability and living situation; care facility residence results in 1 point deduction from the score. All of these factors are indeed associated with malnutrition, justifying their inclusion in the questionnaire, but has to be considered when interpreting the results, and when adjusting analysis for variables included in the questionnaire. Also, the BMI is included in the MNA, and can have a large impact on total scores, especially MNA-SF scores (up to 3 of 14 points). Thus, these variables are not independent, which must be considered when interpreting the results. There is an important difference in how the information about nutritional status was gathered in the studies in this thesis. The paper III study was performed with SA data, which are provided without information about how nutritional screening was performed and educated and trained researchers assessed the nutritional status of participants in the other three studies.

Reverse causality

Reverse causality refers to the situation in which a low BMI or malnutrition, rather than causing disease, is an effect of disease. To reduce reverse causality, the first follow-up segment can be excluded from an analysis. In the paper III study, because the proportional hazard assumption was not fulfilled, the follow-up period was divided into 6-month intervals in the mortality analysis, thus providing results for when the first follow-up was excluded. The bias created by the reversed causality can also be limited by excluding smokers, as smoking is associated with low BMIs and mortality, or individuals with chronic diseases from analyses; the latter is more applicable to samples of younger individuals with fewer comorbidities. In addition, small proportions of the studied populations were smokers and no information on smoking was available in the paper III and IV studies. Thus, the exclusion of these individuals from the analysis would likely not affect the results.

Confounding

Age and sex were considered to be potential confounders in the paper II study. However, several other factors, such as smoking, diseases, weight loss, cardiorespiratory fitness and body composition (including fat distribution), and residual confounding may have affected the associations observed. Information on some of these variables (e.g. weight loss and cardiorespiratory fitness) was not available; other such variables (e.g. dementia and depression) were excluded from the analyses because they are related to MNA items. In the paper III study, analyses were adjusted for several potential confounders, but information on variables such as smoking, body composition and cardiorespiratory fitness was not available.

Paper I study

In the paper I study, data from the Umeå85+/GERDA study were used. This population-based cohort study had no exclusion criterion, and the sample is representative of 85-, 90- and ≥ 95-year-olds. Thus, results are presented for the whole sample and for these age groups. Performing home visit probably increased the participation rate, which was overall good, in this population of very old adults. However, it seemed to differ between the cohorts, and this may have had an impact on the results. Both the selection of potential participants and the participation rate probably had a positive effect on the external validity.

The four cohorts were considered separately, and those who survived to participate more than once were subsequently included in their current age groups, as long as they fulfilled the inclusion criteria. The exclusion of these individuals would have affected the representativity of the cohorts. Analyses performed with these individuals excluded yielded results similar to those obtained for the whole sample.

The same geriatrician performed evaluations and made final diagnoses using the same methods in the Umeå85+/GERDA, FOPANU and UMDEX studies. This factor enabled the recognition of undiagnosed conditions, such as depressive disorder and dementia disorder.

Paper II study

The paper II study was also based on Umeå85+/GERDA data, with some important differences from the paper I study. The sample for the paper II study consisted of individuals from the first and second Swedish cohorts and the 2005–2006 Finnish cohort. Individuals were included only once; for those who participated twice, data from the most recent participation were included in the analyses. This approach was taken to obtain a large sample of the oldest old individuals, but increased the risk of survival bias and may have compromised the representativeness of the age groups.

Paper III study

The use of registry data, as in this study, has several advantages, including access to large datasets and the ability to perform more detailed analyses (e.g. of obesity classes in this study). However, this approach has some limitations, for example, information on data collection was not available and researchers did not perform the assessments in the paper III study, as in the other studies included in this thesis. In the study reported on in paper III, 1918 out of 49,604 individuals who were registered in SA were excluded. Most commonly because no MNA-SF score was registered, the second most common reason for exclusion was because date of death occurred before the registration (273 individuals) indicating error or delay in the registration.

The completeness of SA registration for individuals living in residential care facilities is difficult to calculate because data on the number of persons living in these facilities in Sweden are not available [18]. In 2019, as estimated 70% of this population had been registered with SA

[18]. During 2012 and 2013, the paper III study period, registration completeness was calculated as the number of assessments made per residential care facility bed [165, 166]. This method likely led to overestimation, as one bed can be occupied by several individuals over 1 year. Furthermore, reimbursement incentives were based on SA registration completeness; i.e. risk assessments were to be completed for ≥ 90% of older adults in residential care facilities in 2012, and risk assessments and preventive action plans were to be completed for ≥ 90% of these in 2013 [165, 166]. In 2013, 287 of 290 municipalities and 20 of 21 county councils were using SA [166]; 73 municipalities in 2012 and 170 municipalities in 2013 reported that risk assessments had been registered for ≥ 90% of individuals in residential care facilities [165, 166]. Thus, the reimbursement incentive may have increased SA registration, but also may have affected assessment quality. In addition, that municipalities are using SA does not guarantee that all residential care facilities in that municipality were actively registering occupants [18].

Information on diagnoses for this study was obtained from the NPR, which covers diagnoses made in specialised, but not primary, care settings, the latter of which include residential care facilities [157, 158]. Thus, the prevalence of some diagnoses was likely underestimated in the paper III study.

Paper IV study

The paper IV study was performed with data from the FOPANU and UMDEX studies, conducted by researchers at the Department of Community Medicine and Rehabilitation of Umeå University; several researchers were involved in both studies. The UMDEX study used the inclusion criteria applied in the FOPANU study with some additional inclusion criteria and included only individuals with dementia. Thus, the study population is a rather selected group, and the results of the paper IV study are not generalisable to the entire population of older adults living in residential care facilities, nor to the participants in the paper III study or to the subgroups in the paper I and paper II studies. The FOPANU and UMDEX studies involved interventions, however, adjustment for this factor, did not alter the results.

Information on UTIs was collected systematically in both studies, but medical records reviews were conducted by registered nurses at the

facility in the FOPANU study and by physicians in the UMDEX study. In addition, the participants' physicians made all clinical diagnoses included in the analyses. Thus, systematic criteria for UTI diagnosis were not applied. Furthermore, the two studies were conducted almost 10 years apart, during which time clinical practice regarding the diagnosis may have changed. In addition, symptoms of infection can be less evident in older adults as these individuals may have difficulty communicating symptoms, and they may have asymptomatic bacteriuria. These factors created uncertainty regarding documented diagnoses of UTI.

Separate analyses were performed for women and men because their risk factors for UTI differ [125]. The results of these subgroup analyses should be interpreted with caution, as few men contracted UTIs during the follow-up period, and there is a risk that we were unable to detect factors associated with UTI (i.e. type II error). Urinary catheter use was a strong risk factor for UTI in a previous study where the population was divided according to if urinary catheter was present or not in the analyses [129], but this factor was not examined in a subgroup analysis in the paper IV study because only 24 of the individuals included had urinary catheters.

Systemic oestrogen use does not effectively prevent UTI, but vaginal oestrogen administration may reduce the incidence of this condition [125]. There was no available information on whether the oestrogen treatment was systemic or local and this led to the exclusion of this variable from further analyses in the paper IV study.

Prevalence of malnutrition according to MNA and MNA-SF

In adults aged ≥ 85 years

The high prevalence of malnutrition risk found in the studies reported on in papers I and II, is in agreement with previous studies of very old adults, where reported prevalence of malnutrition risk have varied at high levels [111-115]. The particularly high prevalence in very old adults in residential care facilities found in the paper II study population is supported by findings in older [107] and very old adults [114].

In women and men

A larger proportion of individuals with malnutrition according to MNA in the paper II study were women, as in the paper III and as reported previously [114, 167, 168]. Possible explanations offered for the difference in malnutrition prevalence between women and men in the paper II study are speculative, as factors associated with malnutrition were not explored in this study. A larger proportion of women was living in residential care facilities, and several medical conditions (e.g. depressive disorders, dementia disorder, hypertension, heart failure and malignancy in the previous 5 years) were more common in women than in men. Women also had more medications prescribed, lower MMSE scores, and greater dependence in P-ADL. All of these factors have been suggested to be relevant to individuals' nutritional status [90]. The greater prevalence of malnutrition in women may also be an effect of survival bias, as women tend to live longer than men; although the difference in mean age was only 1.3 years, the proportion of women was greater in older age groups. The lack of a sex difference in the mean BMI may be explained by factors such as differences in body composition and the prevalence of diseases [169].

In adults aged ≥ 65 years living in residential care facilities

The high prevalence of malnutrition according to MNA and the risk thereof found among older adults living in residential care facilities in the paper III and paper IV studies confirms previous findings for populations in Sweden [168, 170] and elsewhere [107]. In the paper IV study, 72.4% of participants were at risk of malnutrition; in the paper III study, this proportion was 45.0%. This discrepancy may be explained by the greater prevalence of dementia disorder in the paper IV study population (76.4% vs. 31.9%) due to the inclusion criteria used in the UMDEX study, which reduces the MNA score by at least 1 or 2 points. However, while the prevalence of dementia is probably underestimated in the NPR data because this condition is often diagnosed in primary care; the MNA-SF administration provides information on whether dementia is present or not, regardless of the setting in which diagnoses were made.

Among those with malnutrition according to MNA-SF scores in the paper III study, dementia, previous hip fracture, COPD, rheumatoid arthritis and stroke were more common. These conditions affect nutritional status in various ways and can have direct and/or indirect impacts on MNA-SF scores [90].

Trends of MNA scores in adults aged ≥ 85 years

Few previous studies have investigated temporal trends in the prevalence of malnutrition. Saarela et al. [118] reported that this prevalence, according to the MNA score, increased among older adults in institutions in Finland during approximately the same period in which we observed decreased prevalence. The authors in the Finnish study attributed this decline in nutritional status to changes in this population, which became older and more dependent, with more comorbidities and dementia [118]. Among older adults living in residential care facilities in Sweden, the prevalence of malnutrition was lower in 2010 than in 1996 [116]. Among adults aged ≥ 70 years who received home care or lived in residential care in Belgium, the prevalence of malnutrition risk according to the MNA-SF score did not change between 2008 and 2013 [117]. The comparison of results from different samples, countries, settings and time periods is problematic, in this case especially due to marked differences in the residential care population among countries and over time. However, the paper I study provides valuable new information about the nutritional status of very old adults in northern Sweden. In the following section, possible reasons for these time trends are discussed.

Increases in the prevalence of dementia disorder, depressive disorder, malignancy, number of drugs used, and dependency in ADL in later cohorts, and in the proportion of the oldest old participants between the first and last cohorts, in the paper I study may have had negative impacts on nutritional status and MNA scores.

The national initiative regarding the preventive care in the SA registry and the resulting increased awareness may have affected nutritional status among older adults, and especially among those living in residential care facilities, where many of the SA registration is performed [15, 17]. Nutritional risk assessment has been shown to contribute to the reduction of the prevalence of malnutrition [171]. In studies evaluating SA-based nutritional screening and registration in residential care facilities (including older adults in a town in Southern Sweden, with data collection in 2014), interventions had been planned for the majority of those in whom nutritional risk was identified; the implementation and effects of these interventions, however, have rarely been evaluated [168]. Individuals with dementia and MNA-SF scores ≤ 11who underwent SA registration and the entire accompanying preventive care process did show weight gain [172]. As we did not have information on SA

registration in the paper I study, we could not determine whether or how this process affected the results.

Furthermore, as a consequence of the previously described changes in the health and social care system of older adults, the prevalence of malnutrition may have been affected in individuals living in residential care facilities because of an increased frailty and malnutrition risk in this population [10, 11, 13]. Other factors that may have affected participants' nutritional status during the study period include the improvement of oral health and socio-economic development. Furthermore, despite the use of the same inclusion criteria and procedures, differences among cohorts may reflect sample variation. The observed time trends in the prevalence of malnutrition, warrants further investigation of factors potentially associated with malnutrition, along with studies investigating future development of the malnutrition prevalence.

Prevalence of underweight according to the BMI

In adults aged ≥ 85 years

The prevalence of underweight found in the paper I study is in agreement with previous reports [54, 83], and findings suggest that this prevalence is declining also among very old adults [82]. Whereas 25% of participants in the paper II study had BMIs < 22.2 kg/m^2, 3.0–7.6% of the participants in the paper I study were classified as underweight according to the WHO cut-off (BMI < 18.5 kg/m^2) [45]. These results indicate that a large proportion of individuals at malnutrition risk (BMI < 22 kg/m^2) [36, 81] are allocated to the normal-weight category, using the WHOs categories for dividing the BMI values [36].

In adults aged ≥ 65 years living in residential care facilities

The prevalence of underweight in the paper III study was slightly lower than reported previously for European populations [55, 73]. In previous studies conducted in Sweden, 41% [116] and 31.7% [168] of the populations had BMIs < 22 kg/m^2.

Prevalence of obesity according to the BMI

In adults aged ≥ 85 years

Approximately half of the paper I and II study populations of very old adults had a BMI that corresponded to overweight or obesity. These results are in agreement with those reported previously for adults aged ≥ 80 years in a European study [53], and for very old adults in Germany [83], albeit those who did not live in residential care facilities or have severe illnesses with short life expectancies (who were thus healthier than the Umeå85+/GERDA study participants) [83]. The prevalence of obesity among 90-year-olds in the paper I study was slightly higher than the reported prevalence at 6.6% among 90-year-olds in Finland [54]. That study was conducted in 2000 with inclusion criteria similar to that of the paper I study (i.e. the inclusion of all individuals for whom anthropometric measures were available). As reported by Peralta et al. the prevalence and trends of obesity may differ between countries [53], that might partly be explained by differences in lifestyle and/or dietary habits, highlighting the importance of performing studies of very old adults in different settings and populations.

In the paper I and paper II studies, the prevalence of overweight and obesity decreased with increasing age. This phenomenon has been observed in cross-sectional and longitudinal studies, and can be explained partly by age-related weight loss [39-41, 52].

In adults aged ≥ 65 years living in residential care facilities

In the paper III study, almost half of older adults in residential care facilities in Sweden were overweight or obese (primarily class I) and this prevalence is similar to that reported previously for European populations [55, 73]. In two studies conducted with older adults living in residential care facilities in Sweden, 22% had BMIs > 27 kg/m^2 [116] and 17.2% had BMIs > 29 kg/m^2 [168], respectively.

Obesity in older adults has been associated with morbidity, disability and an increased risk of admission to nursing homes [173-175]. Obese older long-term care inhabitants usually require more staff assistance and special equipment for their care, and they spend more days in the facilities than do their non-obese counterparts, which ultimately affects care costs [176]. Among older adults newly admitted to nursing homes, obese individuals require more assistance from two or more staff

members in performing ADL tasks [177]. On the other hand, obesity protects against osteoporosis and hip fracture [173]. Thus, obesity in older adults in residential care facilities is a complex issue and of concern not only for individuals but also for health care systems, and, as pointed out previously, is an issue that requires further attention [176].

In the paper III study, class I obesity was the most common form of this condition. Many published studies and reviews on this topic have focused on populations in the USA, where obesity is common and a different health care system is in place [52]. Nevertheless, obesity may be a growing concern in Sweden as well. The results of the paper III study provide valuable information about the prevalence of obesity (and its classes) in a nationwide cohort of older adults living in residential care facilities. Studies of the potential consequences of obesity in this Swedish setting would be of value.

Trends of the BMI in adults aged ≥ 85 years

Few studies have examined temporal trends in the prevalence of obesity among very old community-dwelling adults. In contrary to the study by Peralta et al. [53], obesity seemed to increase in the paper I study. Increasing mean BMIs and larger proportions of individuals with BMIs ≥ 27 kg/m^2 have been reported for residential care facility populations in Finland and Sweden, respectively [116, 118]. Increasing prevalences of overweight and obesity also have been seen in adult populations (aged 18–74 years) and among 70-year-olds in Sweden [56, 57], and the paper I study findings suggest that this trend also exists among very old adults. Further research on factors associated with obesity would be of value to understand underlying causes of this development.

The MNA and MNA-SF score and mortality

In adults aged ≥ 85 years

In Paper II, very old adults with malnutrition or the risk thereof, had higher five-year mortality, compared to individuals with a good nutritional status according to MNA. Furthermore, in Paper I, the association between MNA and two-year mortality did not differ between the four cohorts of very old adults. Identified predictors of long-term mortality include the disease burden, including the number of drugs used, I-ADL ability and cognitive function, all of which directly or indirectly

affect the MNA score [113, 138, 139]. In previous studies of non-institutionalised 85-year-olds in Spain, MNA scores were lower among non-survivors in bivariate analyses, but MNA scores did not predict 3- or 5-year mortality [138, 139]. In a study including 90-year-olds residing in the community and in institutions in Spain, MNA-SF scores were lower among non-survivors at 1 and 5 years; 1-year mortality was predicted by low MNA-SF scores, heart failure and age, while 5-year mortality was not predicted by MNA-SF scores [113, 136]. In contrary to these previous studies, poor nutritional status according to MNA was associated with greater 5-year mortality in the paper II study.

Comparison of these findings with those of the paper II study is problematic, as the models used in the previous studies included more potential predictors of mortality than did those used in the analyses performed in the paper II study. We adjusted for sex and age because the MNA includes several items related to dementia, depression, functional decline and other conditions affected by these factors. More extensive adjustment likely would have altered the results of the paper II study.

Investigation of the complex association between malnutrition and mortality among very old adults is difficult. Many factors associated with malnutrition are also associated with mortality, and malnutrition can exacerbate factors associated with mortality, creating a vicious cycle and generating reverse causality. This phenomenon is described in greater detail in the section of Methodological considerations.

In adults aged ≥ 65 years living in residential care facilities

As found in the paper III study, poor nutritional status has been associated with mortality in previous studies of older adults living in nursing homes [109, 116, 135], although a recent study of older adults living in such facilities in Spain revealed no association between malnutrition according to the MNA score and mortality [127]. However, individuals with short life expectancies and those who had lived in the facilities for <1 year were excluded from that study [127]. Such exclusion of individuals who may have malnutrition because of illness (which reduces the possibility of reversed causality) may alter the relationship between malnutrition and mortality. In contrast, associations persisted during all time periods, but were strongest during the first 6 months of follow-up, in the paper III study, likely due to the probability that some SA-related assessments were performed for individuals with

short life expectancies [13]. This statement is speculative, however, as information about the circumstances of SA registration were not available.

The BMI and mortality

In adults aged ≥ 85 years

In the paper II study, mortality was lower among individuals with BMIs ≥ 24.7 kg/m^2 than among those with BMIs < 22.2 kg/m^2. These results are similar to findings from populations of very old adults in Denmark and China [78, 79], whereas Lisko et al. [54] found increased mortality among normal-weight than among overweight men and no difference among women in a study of 90-year-olds in Finland. Low BMIs were associated with increased mortality among very old adults in the paper II study, as reported previously [77-80, 178]. In contrast, no association between underweight and mortality was found among 90-year-olds in Finland (only three women in that sample were underweight) [54] or among men aged > 76 years in Italy [179].

The paper II study, conducted with a relatively large sample of very old adults, adds valuable information about associations of BMIs with long-term mortality. Potential explanations for these findings are discussed in greater detail in the Obesity paradox section.

In women and men

The paper II study also revealed differences in the association of the BMI with mortality between men and women; mortality rates were lower among women with BMIs of 24.7–27.9 kg/m^2 and men with BMIs of 22.2–24.6 kg/m^2. Such sex differences have been reported previously [54, 76, 77]. The use of the BMI as a measure may contribute to these differences, as women have larger proportions of body fat than do men with the same BMIs [47]. Age-related decreases in height may also have a larger effect on the BMI in women than in men [38]. All of these factors may have contributed to the sex difference in the paper II study, although further investigation is needed.

In adults aged ≥ 65 years living in residential care facilities

In the paper III study, the 2-year mortality rate was lower among obese (BMI ≥ 30.0 kg/m^2) older adults living in residential care facilities in

Sweden than among their normal-weight and overweight counterparts. These findings are in accordance with previous reports [55, 73, 74]. This association was maintained for all obesity classes relative to normal-weight individuals. Few studies have involved examination of associations between obesity classes and mortality in residential care populations, and to my knowledge no such study has been conducted in Europe. The association of more severe obesity with mortality may differ between those newly admitted to and already residing in nursing homes in the USA [75]. No such analysis could be performed in the paper III study because the SA registry does not contain data on the timing of residential care facility occupancy. Comparison of the results of studies conducted in different regions is problematic due to variation in populations, health care systems and residential care.

Studies of older adults in general have revealed the least mortality among those with obesity class I; associations with obesity classes II and III are more diverse. In a large study conducted among older adults in Taiwan, class II–III obesity was associated with increased mortality [63]. However, those researchers did not have information about diseases or medications used, and they employed the international BMI cut-offs. As Asian populations have larger percentages of body fat and different fat distributions than do white populations [180], the WHO recommends the use of different BMI cut-offs [181]. In a large systematic review and meta-analysis of data from older adults throughout the world, no association between obesity overall (BMI $\geq$ 30.0 kg/m^2), obesity class I or obesity classes II and III and mortality was found [71]. In a meta-analysis, Winter et al. [62] found that mortality increased with BMIs $\geq$ 33.0 kg/m^2 among older adults. With BMIs classified using the WHO system, lesser mortality was found for overweight individuals, no association was found for obesity class I and borderline significantly greater mortality was found for obesity classes II and III in comparison with BMIs of 21.0–24.9 kg/m^2 [62]. Among older adults in Norway, compared to BMI 25.0–27.4 kg/m^2, mortality was greater among men with class I obesity (divided into BMIs of 30.0–32.4 and 32.5–34.9 kg/m^2) and class II–III obesity, and among women with BMIs of 32.5–34.9 kg/m^2 and class II–III obesity [182]. Thus, heterogeneous associations between more severe obesity and mortality in older adults have been reported, with indications that class II–III obesity may be associated with greater mortality. Overall, however, information on this association, especially among older adults living in residential care

facilities, is lacking. Thus, the results of the paper III study add valuable information on this topic, as they indicate that even more severe obesity classes are associated with lesser mortality among older adults living in residential care facilities.

In the paper III study, underweight was associated with increased 2-year mortality. This finding is in accordance with previous international [55, 73, 84] and Swedish [116] reports.

The MNA and MNA-SF score and BMI

In the research conducted for this thesis, malnutrition according to the MNA or MNA-SF score co-existed with overweight and obesity in older adults living in residential care facilities (paper III study) and in very old adults (paper II study). Malnutrition and obesity are linked by the concept of sarcopenic obesity, as both contribute to reduced muscle mass and function [42, 43, 183, 184]. However, we do not know whether sarcopenic obesity was present in the study populations, as sarcopenia was not measured in the studies included in this thesis. Further research on this topic would be of value to understand the potential consequences of the combination of malnutrition and obesity, especially in very old adults.

The MNA-SF score, BMI and mortality

In the paper III study, higher BMIs were associated with lesser mortality in individuals with good nutritional status and those with malnutrition risk, according to MNA-SF scores. Mortality was greater among malnourished individuals, according to MNA-SF scores, regardless of BMI but particularly among underweight individuals. Several possible explanations for these results can be offered. Higher BMIs may reflect nutritional reserve, which is depleted in underweight individuals, making the latter frailer and more susceptible to adverse events.

The obesity paradox

The obesity paradox encompasses the phenomenon of obesity as a well-established risk factor for several diseases, but also as a protective factor in patients with established disease [70]. It has been observed, for example, in people with hypertension, coronary heart disease, atrial fibrillation and heart failure [70]. The evidence for the existence of this

paradox in individuals with cardiovascular disease is epidemiological, and several contributing factors have been suggested. Lavie et al. [185] proposed the possible contributing factors of non-purposeful weight loss in leaner persons, a greater nutritional reserve and less cachexia, increased muscle mass and strength and cardiorespiratory fitness, high blood pressure that allows for treatment with more cardiac medications, lower atrial natriuretic peptide levels and decreased renin–angiotensin–aldosterone system response, lower prevalence of smoking, and different aetiologies of cardiovascular disease in obese and leaner individuals. The obesity paradox has also been reported to be more evident in women than in men [186]. Smoking may contribute to this paradox via disease-related weight loss and because of weight gain and reduced cardiovascular risk upon its termination [186]. The use of the BMI as a measure of obesity may contribute to the obesity paradox, as it does not enable the consideration of fat distribution, body composition or cardiorespiratory fitness [46]. However, it has been detected in studies in which other techniques were used to measure adiposity [70]. The obesity paradox has also been observed in patients with other diseases and medical situations [187], including malignancy [68] and COPD [69].

The obesity paradox in individuals with cardiovascular disease might be influenced by ageing [186], which is accompanied by body composition changes [39, 40, 52]. Comorbidities including malnutrition and frailty also may contribute [186]. Several other potential contributors at the genetic and cellular levels have been suggested, as have neurohormonal changes, reduced energy expenditure and physical activity, and inflammation [186]. It has been suggested that obesity may be less dangerous in those who survive to old age [187].

The reduced mortality found among individuals with higher BMIs in the paper II and paper III studies reflects the obesity paradox, although potential contributing factors were not identified specifically. Regardless, obesity was not a risk factor for increased mortality in our populations.

This thesis research on very old adults entails a clear survival bias, which may have been enhanced by the inclusion of data from survivors' most recent participation in the paper II study. In addition, the survival bias may be even more pronounced in very old men due to their shorter life expectancy [6]. Thus, the potential negative effects of obesity may be underestimated in older populations.

The follow-up periods in the paper II and paper III studies were 5 and 2 years, respectively, during which time various adverse events that may affect the BMI, MNA score and health can occur, especially among very old and frail individuals. Researchers have suggested that the obesity paradox is lost with long-term follow-up [186] and that the negative effects of obesity develop over long periods of time. However, mortality was reduced among obese individuals in both studies, as has been demonstrated previously over short- and long-term follow-up periods [74].

Risk factors for UTI

Malnutrition according to the MNA score was not a clear risk factor for UTI in the paper IV study, in agreement with previous reports [130, 131], although other researchers have reported an association between malnourishment and previous UTI [110]. Previous UTI was the strongest risk factor for UTI contraction during follow-up in the paper IV study, as reported previously [128]. The majority of participants in the paper IV study had dementia disorder and dependency, which may affect MNA scores [98] and cognitive impairment and dependency are associated with UTI [128]; thus, this factor may have affected the findings obtained for the association between the MNA score and UTI. Furthermore, MNA does not provide information on specific micronutrient deficiencies that are important for the function of the immune system [188].

In agreement with the results in the study reported on in paper IV, cognitive impairment and history of UTI were risk factors for incident UTI in a study of 85-year-olds living in the community or in long-term care facilities (22%) [128]. In contrast to our findings, Shih et al. [130] found no association of hypertension or heart failure with incident UTI among people receiving home care. This population differed from that of the paper IV study, as the majority of participants were totally dependent in ADL and/or bed bound, and about half of them had urinary catheters. UTI risk factors have been suggested to differ between women and men [125]. The results of subgroup analyses conducted for women and men in the paper IV study seem to support this difference, although these results should be interpreted with caution because of low incidence of UTI among men.

The identification of potential risk factors for UTI may be useful for groups for which diagnosis is challenging, even if these factors are difficult to prevent. Having had a UTI in the previous year was the strongest risk factor for incident UTI in our research; prophylactic antimicrobial treatment has been found to be effective to prevent frequently recurring UTIs in community-dwelling older women, but its effectiveness in institutionalised populations has been less thoroughly studied [125]. Systemic oestrogen treatment and the use of cranberry products (e.g., cranberry juice or capsules) have not been found to be beneficial, but vaginal oestrogen administration may effectively prevent UTI development in women with frequent UTI recurrence [125].

Ethical considerations

Studies of older adults must be performed with careful consideration, as many of these individuals are frail and have reduced autonomy as a consequence of factors such as overall poor health, neurodegenerative disease and reduced cognitive and/or physical function. However, the inclusion of frail older adults in research is needed to enable the improvement of their health and care. All of the studies included in this thesis received ethical approval

According to the Swedish Ethical Review Act [189], research may be performed without the informed consent of an individual who is unable to provide such consent due to disease, mental disorder or deteriorating health if that research is expected to provide information that cannot be obtained via research performed with all participants' informed consent and is expected to benefit the participant. If the research is not beneficial for the individual it can still be conducted if it is expected to be beneficial for other persons with the same condition, and with a small risk of harm or discomfort for the participant. Participants who are not able to provide consent should be informed personally about the research, as should all participants, and their close relatives should be consulted about participation. If such a person expresses in any way that he or she does not want to participate or wishes to withdraw from the research, or if their close relative objects to participation, the research should not be performed [189].

In the Umeå85+/GERDA study, participants were given written and oral information about the study and gave oral consent to participation, and participation was discussed with a close relative in cases of suspected or

confirmed cognitive impairment. The researchers were medical professionals and students, and many of them had experience working with older adults. During the home visits performed for this study (which lasted an average of 2 hours in total), the researchers observed whether the participants wanted to continue, whether a subsequent home visit should be scheduled or whether the participant wanted to withdraw from the study. A similar procedure was used in the FOPANU and UMDEX studies. In all of these studies, the participants were informed that they had the right to withdraw at any time and a specialist in geriatric medicine was available for medical consultation.

In the paper III study, conducted with SA data, individuals were informed about their SA registration and were given the option to opt out. Personal identification numbers were removed from the data, and the National Board of Health and Welfare handled all personal data. The Regional Ethical Review Board of Umeå waived the informed consent requirement for this study.

Clinical implications

The prevalence of malnutrition and the risk thereof, and their associations with increased mortality, in this research highlight the need for systematic nutritional screening (MNA or MNA-SF administration) of older adults and clinical assessment of those determined to be at malnutrition risk. The complex nature of malnutrition supports nutritional assessments as part of a comprehensive geriatric assessment, and should include a nutritional and health assessment, as described previously [36], in order to determine the individual's energy and nutritional requirements, and what medical conditions, disabilities and medications that may interfere with dietary intake, nutrient bioavailability and energy requirements, thus causing malnutrition and/or micronutrient deficiencies. This complexity applies also to the interventions, which should be multifactorial and multidisciplinary, and may include, not only interventions related to dietary intake, but also to e.g., medical conditions, review of prescribed drugs, oral health, eyesight, disabilities.

Malnutrition risk was identified not only in underweight, but also in overweight and obese, individuals in this research. Although the mortality risk was lower among overweight and obese individuals than among malnourished and underweight individuals, the identification of

malnutrition risk in overweight or obese individuals could help to prevent weight loss and underweight.

Obesity was associated with reduced mortality in this research, supporting the applicability of the obesity paradox among very old adults and older adults living in residential care facilities. Based on the study results, normal-weight does not benefit survival in these populations. However, this factor must be weighed against other aspects, such as quality of life, morbidity and disabilities, which may be affected by high BMIs, although the directionality of such effects remains unknown. This is perhaps a growing matter of interest, as obesity is becoming more common also in these age groups.

In older residential care inhabitants, individuals with previous UTI, cognitive impairment, hypertension and heart failure, were at higher risk of contracting UTIs. Thus, these individuals may benefit from preventive treatments.

In light of the results of this research, the maintenance of good nutritional status, preferably with some excess body weight, would be ideal for older adults.

Implications for future research

Many factors potentially explain the changes in the prevalence of malnutrition among the four cohorts and the increase in obesity between 2000 and 2015, in the paper I study. Future studies investigating these trends further, including the identification of factors associated with the development of malnutrition and obesity in very old adults and potential differences between women and men, would be of value. Studies examining outcomes other than mortality, such as quality of life and physical function, would also help to determine whether the increased survival in individuals with obesity observed in this research is an indication of healthy ageing. Also, validation of the newly proposed diagnostic criteria for malnutrition [81] in very old adults is warranted.

As previous research has demonstrated that the entire SA nutritional care process must be completed to achieve weight gain [172], further research on how planned interventions and care steps taken with SA influence mortality risk would be of value. Furthermore, randomised controlled trials evaluating the effects of nutritional care interventions in very old

adults are also needed, as well as studies confirming the results found in paper IV.

Conclusions

In the research conducted for this thesis, the following conclusions were drawn.

The results highlight the importance of nutritional screening in older adults in residential care facilities and very old adults, since malnutrition risk was common and associated with greater mortality among these populations. Malnutrition according to MNA was not a clear risk factor for UTI in older adults living in residential care facilities. Time trends indicate an increasing prevalence of obesity whereas no change in nutritional status was observed among very old adults, although the details in these trends need further investigation. The results also confirm that higher BMIs were beneficial for survival in these populations, and in the residential care population this seems to apply also for BMIs reflecting severe obesity. Finally, in the residential care population, regardless of nutritional status according to MNA-SF, higher BMIs were associated with better survival

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