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Evolving geriatric anthropometrics- an interplay with lifestyle changes, birth cohort effects, and survival implications.

Results from the general population study, "Good Aging in Skåne," Sweden.

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Evolving geriatric anthropometrics- an interplay with lifestyle changes, birth cohort effects, and survival implications

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in Skåne," Sweden

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Nivetha Natarajan Gavriilidou



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DOCTORAL DISSERTATION

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Abstract There is a rising proportion of aging population worldwide. The high vulnerability of older adults to morbidity and mortality introduces an enormous health and economic burden to themselves and the society. The established leading cause of death among older adults is due to chronic and vascular diseases. These conditions are related to the nutritional status and are preventable with the help of accurate assessment for timely identification and adopting relevant lifestyle changes. Anthropometrics is an efficient and widely accepted method of body composition assessment. Body mass index (BMI), a commonly used measure of body fat has several well-known advantages and limitations. Despite the widespread awareness, very little attention is paid to the consequences of inaccurate BMI classification due to errors in height estimation, particularly among older adults due to aging-related degenerative changes. Consequent under- or false diagnosis of risk groups could seriously affect the designing of optimal health interventions. We need a holistic assessment including valid and accurate body composition estimation and accounting for extrinsic factors related to weight aberrations. The overall aim of this dissertation is to identify and address the methodological issues in anthropometric measurements in Swedish elderly population aged ≥60years and address the role of comorbidities, socio-demographics, lifestyle factors and cohort changes. The four studies in this thesis are based on data from the longitudinal nationally representative population study Good Aging in Skåne. Cross-sectional and follow-up study designs were applied. Descriptive statistics, analysis of variance tests and proportional hazard regression methods were adopted. Study I presented the sex- and age-specific normative anthropometric data for Swedish older adults. Comparison of the anthropometric profile in correlation with underlying comorbidities confirmed the association between cardiovascular diseases and adiposity and revealed a potential relationship between diminished functional capacity and inadequate physical activity. Study II investigated the errors in BMI classification due to inaccurate height estimation among elderly. Age-adjusted and sex-specific BMI prediction equations based on knee-height and demispans estimates were formulated. Comparison between predicted and classic BMI classifications demonstrated a striking underestimation of underweight and overestimation of obesity, particularly alarming at the most vulnerable age of ≥80 years. Knee height predicted BMI on further investigation (study III) on the association with mortality risk identified a paradoxical survival benefit only among overweight older adults aged ≥80 years. Study IV examined the role of the birth cohort effects in waist circumference and its association with education and lifestyle factors of obesity. Older adults aged 60 years and 81 years having birth year 1952/54 and 1932/33 respectively had higher waist circumference and abdominal obesity that those born in 1941/43 and 1920/22 respectively. Waist gain was clearly influenced by higher educational attainment in the 60 year-olds, and by alcohol consumption and inadequate physical activity in 80-year-olds. Smoking prevalence and frequency of complete meal intake declined across the three birth cohorts from 2001–2013. Conclusions: Our study contributes to a holistic approach in the anthropometric assessment of body composition in elderly. It comprises: 1) A thorough description of the anthropometric profile of the population in relation to underlying medical conditions. 2) Application of proxy BMI to address the problems of misclassification from measurement errors, in relation to the paradoxical survival benefits of overweight only among the 'older' elderly and importantly 4) Account on the extrinsic factors that demonstrated encouraging patterns of educational attainment and diminishing sedentary living and warning signs from inadequate exercises in the 'young' elderly and increasing alcohol intake in the 'old' elderly. This calls for a broader action.		
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To my beloved family!

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List of papers

- I. High degree of BMI misclassification of malnutrition among Swedish elderly population: Age-adjusted height estimation using knee height and demispan. Gavriilidou NN, Pihlsgård M, Elmståhl S. *Eur J Clin Nutr.* 2015; 69(5): 565-71.
- II. Anthropometric reference data for elderly Swedes and its disease-related pattern. Gavriilidou NN, Pihlsgård M, Elmståhl S. *Eur J Clin Nutr.* 2015; 69(9): 1066-75.
- III. Knee height based BMI and mortality risk in Swedish elderly population -An overweight paradox. Results from the population study, Good Aging in Skåne (GÅS). Gavriilidou NN, Pihlsgård M, Elmståhl S. Submitted to *Journal of Nutrition in Gerontology and Geriatrics*.
- IV. Secular changes in abdominal anthropometrics and its association with education and lifestyle factors from 2001 to 2013. Birth cohorts from Swedish general elderly population study Good Aging in Skåne. Gavriilidou NN, Pihlsgård M, Elmståhl S. Submitted to *BMC Geriatrics*.

Abbreviations

ADL	Activities of Daily Life
BIA	Biometric Impedance Analysis
BMI	Body mass index
CGA	Comprehensive Geriatric Assessment
CHF	Congestive heart failure
DEXA	Dual-Energy X-ray Absorptiometry
ESPEN	European society of Clinical Nutrition and Metabolism
GÅS	Good Aging in Skåne (Gott Åldrande i Skåne)
HC	Hip circumference
H70	H70 Gerontological and Geriatric Population Studies, Gothenburg, Sweden
ICD	International Classification of Diseases
KH	Knee height
KH-BMI	BMI predicted based on knee height
MI	Myocardial infarction
MNA	Mini Nutritional Assessment
NHANES	National Health and Nutrition Examination Survey
PEM	Protein energy malnutrition
SALAR	Swedish Association of Local Authorities and Regions
SD	Standard deviation
T2DM	Type 2 Diabetes Mellitus
WC	Waist circumference
WHO	World Health Organization
WHR	Waist-hip ratio

Introduction

Demographic shift

Aging is a biological process that is inevitable and universal. The projected doubling of the ‘greying population’ by the year 2050 has major health and economic implications [1]. Today, there are approximately 900 million individuals aged over 60 years worldwide. 125 million of them constitute population over 80 years. In 2012, adults above 60 years of age constituted 11.5% of the global population, and they are estimated to double, reaching 22% or a total of 2 billion in 2050. Between 2011 and 2050, the number of centenarians (aged 100 years and above) is predicted to increase globally from around 315 thousand to 3.2 million [2]. There is a steady and dramatic global increase in the average life expectancy to about 69.3 years and 73.6 years for men and women respectively.

In Sweden, there is a clear expansion of the aging population. The national elderly population at the age of 65 years and above constitutes 20% of the total population, i.e., 1.95 million and of which 502,000 are octogenarians (aged 80 years and above) [3]. According to Swedish national department of statistics “Statistics Sweden” the >80 year old population is estimated to reach 826 thousand by 2030 and exceed 1 million by 2045. Sweden ranks first among European Union member states in the proportion of octogenarians and their number is predicted to double, reaching 1.2 million by 2060 [3, 4]. The life expectancy at age 65 increased from about 10 years in 1850 to almost 19 years in 2000 and according to 2014 estimates it is 80.2 and 83.8 years among men and women respectively [2, 5-7].

Elderly care in Sweden

According to the Swedish association of Local Authorities and Regions, SALAR, geriatric health and wellbeing occupies a significant position in the Swedish welfare policy, making the country a role model to the rest of world. The different types of living options available for Swedish elderly include receiving help and/or care at home, old-age homes, secure living, nursing homes and specialized care [8]. With rising needs for health care and support during old age, the welfare system offers institutional, home and hospital care. Municipal and state funds

cover most of the associated expenses. The total expenditure on elderly care, as per 2006, was 168 billion Swedish crowns (or around 17 billion Euros). This translates to 3.6% of the gross domestic product being allocated to the care for older adults, which is almost five times the EU average [4, 7]. SALAR has estimated that these costs will increase by 50% by the year 2035 [8]. The geriatric health policy of Sweden strives to provide access to high quality health care for the aging population, enabling them to live independently and with dignity throughout their lifespan, and to promote engagement and participation at home and in the community [9]. This is intended to cultivate social trust and enhance social capital among the senior citizen population and their relatives [4]. The “Commission on Future” is a state appointed project that addresses several important reform areas needed for the sustainable development of the country. One of these is addressing the demographic shift and the aging population [4, 10].

Changing population trends and the rising proportion of the adults over 80 years of age can have a wide-range of implications on the health and medical sector, economic policies, and labor markets [1, 10, 11]. Not only in Sweden, but also globally, this calls for innovative actions from researchers, healthcare professionals and policymakers to develop effective and sustainable disease prevention and health promotion. Significant reevaluation of health care policies will almost certainly be required in order to sustain high quality services, without endangering the fiscal integrity of the state [1, 5, 10, 11].

Aging and health

The process of aging has been defined and described in several ways. A hallmark of aging in living beings is an age-related increase in disease, disability and risk for mortality. In general, this process has been described as an age-related progressive deterioration in physiological structures and functions, associated with gradual regression of health and resulting in termination of life [12-14]. “Healthy aging” as defined in the “*World report on aging and health*”, is the process of developing and maintaining the functional ability that enables wellbeing in older age [15].

The most common causes of death among elderly are vascular diseases and associated non-communicable chronic conditions, like chronic obstructive pulmonary disease (COPD), cardiovascular diseases, type-2 diabetes mellitus (T2DM), cognitive decline, dementia, and cancer [2, 7, 10]. Strong evidence suggests that most of these are preventable and/or can be delayed in onset by simple yet effective methods like monitoring nutritional status and lifestyle modification practices [16-19]. In this way, an estimated risk reduction of 80% against cardiovascular diseases, stroke and T2DM and over 40% of cancer has

been proposed [20]. Such preventive measures are for example, physical activity, healthy diet and lack of smoking, alcohol or substance abuse. However, evidence that urbanization is accompanied by unhealthy or even risky lifestyle behaviors is less encouraging [7, 11, 21, 22]. Such risky lifestyle patterns transform the already complex ‘greying’ process into an unhealthy one.

(Mal)Nutrition in elderly

The progression toward death during old age is strongly influenced by nutritional status. Nutritional status has a major impact on disease and disability. This in turn affects the quality of the aging process, by influencing physical and mental function [23]. Accumulating research shows that imbalance in both directions of the nutrition spectrum, i.e., energy insufficiency and energy overload, are signs of poor nutritional status that have significant implications on the longevity and the quality of aging. Malnutrition is defined as a state of deficiency, excess or imbalance of energy, protein and other nutrients, causing measurable, unfavorable adverse effects on body composition, function and disease process [24, 25]. This double burden of nutritional imbalance poses tremendous challenges for the healthcare system, policy makers and the public.

Undernutrition

To date malnutrition is commonly being misworded to refer to undernutrition, probably due to undernutrition’s high global frequency and more dramatic association with morbidity and mortality compared to overnutrition’s more latent effects [26]. Undernutrition is commonly described as protein-energy (PEM) or calorie malnutrition and is characterized by a condition called “nutritional frailty,” a state of wasting characterized by loss of physiologic reserves (body weight, muscle mass, strength) increasing the vulnerability to diseases and functional disability [21, 27]. This can further compromise an individual’s ability to meet nutritional requirements at a time when the need is escalating [21, 28]. Aging is associated with biological changes like reduced appetite and energy expenditure, delayed gastric emptying, alterations in cytokine and hormonal levels, and imbalance in fluid-electrolyte homeostasis. These changes as well as adverse effects of comorbidities and medications play a synergistic role in the complex etiology of undernutrition among elderly [17, 28-31]. Protein and calorie deficiencies combined with impaired metabolism characterize PEM. This has a strong relation with the common non-communicable diseases among older adults [32-37].

Prevalence of undernutrition

The estimation of undernutrition prevalence varies widely depending on the assessment method and tools used. Due to lack of a gold standard, using a combination of different criteria of assessment has been a well-accepted practice [38]. Use of body mass index (BMI) is a very common practice in the assessment of body composition aberrations. It is defined as weight in kilograms (kg) divided by height in meters squared (m^2), and includes categories of underweight ($BMI < 18.5$), normal weight ($18.5-24.9$) overweight ($25 \leq BMI < 30$), and obesity ($BMI \geq 30$) [39-42].

Based on the statistics from The National Health and Nutrition Examination Survey (NHANES), 16% of older adults above the age of 65 in the United States are at high risk for undernutrition. The incidence ranges between 12-50% in hospitalized and 23-60% among institutionalized older adults. The risk is found to be associated with prevalence of other underlying diseases, medications, poverty, lack of health care support, social isolation and dependence in daily activities (among those in the nursing homes) [43].

The prevalence of undernutrition is high across all community and health-care settings in Europe and the risk is 40% higher in people over 65 years of age than younger ages [44, 45]. Literature evidence shows that undernutrition affects 60% of the people admitted in nursing homes, 46% of hospitalized with over 50% among older patients, and about 5% of the general population [17, 44, 46, 47]. A Swedish review of 24 studies on PEM from different care settings noted a mean prevalence of 36% during a 20-year period [47]. Undernutrition in England among seniors aged over 65 years is around 16% and among those over 85 years is 2% and only among the hospitalized older adults over 65 years of age is 29%–61% [17, 48]. In the Netherlands, the prevalence of PEM in older adults is estimated to be 33% in hospitals, 21% in nursing homes and 16% in home care, while among free-living older adults who do not receive any assistance, an estimated prevalence of 7% according to BMI cut-offs, and 5% unintentional weight loss in the last 6 months have been reported [49]. It has also been shown that the screening of undernourished patients was more frequent in nursing homes than in hospitals and home care leading to higher proportion of under-diagnosis in the latter setting [37, 49, 50].

A European multicenter study that included a total of 4010 older adults living in 11 countries showed that 11% of Swedish elderly individuals had untreated weight loss, and 1% had severe undernutrition [51]. According to a meta-analysis including 23 Swedish studies, among 4687 hospitalized elderly patients, 28% were undernourished, and among those with chronic diseases, there was 70% prevalent undernutrition [52]. The prevalence of PEM ranges from 25 to 66% depending on the clinical condition and diagnoses. This variation is partly affected by the time-

point in the course of the disease the survey was conducted, differences in the severity of the medical conditions, age at the time of examination, and how the undernutrition is defined [53].

Using the Mini Nutritional Assessment (MNA), varied results have been obtained among the different aging studies. International studies that have employed MNA among older population from different settings have shown a range of 21–50% of elderly being at risk for undernutrition [54-56]. A prospective study using MNA conducted among 318 Swedish elderly people, aged over 65 years, living in 11 nursing homes in Sweden showed 17.7% were undernourished, 40.3% were at risk of undernutrition, and 38.7% had further decline after a 2-year follow up. The latter group with worsening MNA scores had higher weight, BMI, and hospitalization rate. Among this group, 21% of individuals lived in service homes, 33% in old age homes, 38% in group-living for demented, and 71% in nursing homes [26, 57].

Obesity- An irony

Overnutrition and sedentary lifestyle result in overweight or obesity, an abnormal excessive fat accumulation that may impair health. According to the World Health Organization (WHO), between 1980 and 2008, there has been a doubling in the prevalence of obesity globally. It has also been estimated that, in 2008, more than half of adult population in the WHO Europe Region, were overweight, and obesity prevalence was roughly 20% and 23% among men and women respectively. However, not all overweight elderly are “at risk” since muscle mass in addition to fat can contribute to higher weight. This makes it very crucial to accurately identify the target population and design appropriate prevention and therapeutic strategies. Uncertainty about the effectiveness of obesity treatment among elderly still lingers due to the potential adverse effects of weight loss on the non-fat tissues (muscle and bone mass) [58].

In this context, it may be important to mention two possible phenomena related to older adults. Firstly, there is sarcopenic-obesity, where, as the term implies, the increase in weight is could be primarily due to adiposity coupled with muscle loss. This condition has been shown to be strongly associated with increased mortality risk [21, 59, 60]. Secondly, the obesity paradox, an increase in BMI above the recommended normal range for adults has not always been associated with mortality among older adults, but has shown protective survival benefits. Evidence on the obesity paradox usually estimated by BMI measures has been inconsistent and varies widely among populations. This calls for further analysis to address the possible confounders in relation to these varied results [61, 62].

Prevalence of obesity

The global prevalence of obesity is increasing progressively among all ages not only in developed countries but also in middle- and some low-income countries [63]. Increasing longevity and proportion of the aging population also leads to an expected expansion of the obese elders. Obesity has long been associated with risk of chronic diseases and mortality [64, 65].

It was estimated in 2010, the prevalence of obesity (BMI $\geq 30\text{kg/m}^2$) among American seniors aged 65 years and above was 37.4% (22 million). In Europe it was estimated between 20% and 30% (roughly 32 million) as of year 2015 (based on method of assessment, see below) [66]. The American obesity prevalence was even stratified based the different age groups of older adults and was found to be roughly 28% among those aged 65-74years, 17% between ages 75-84 and 10% among those over 85 years of age [67].

Different estimation methods were adopted in different country-based settings accounting for a wide variation in the obesity prevalence figures in Europe [68]. According to data obtained from the 2004 Survey of Health, Ageing and Retirement in Europe (SHARE), a cross-national survey of 22 777 Europeans over the age of 50 years, the prevalence of obesity ranged from 12.8% in Sweden to 20.2% in Spain among older men and from 12.3% in Switzerland to 25.6% in Spain and 21.9% in Greece among older women [69]. The OBEPI survey (France) 2006, estimated obesity prevalence to be 17.9% with a differential decreasing trend among the younger and older age groups. Abdominal obesity (waist circumference (WC $\geq 102\text{cm}$ (men); $\geq 88\text{cm}$ (women)) was estimated to be 47.6% [66]. Dutch obesity prevalence among the older adults over 60 years was estimated to be 40% and 56% among men and women respectively based on BMI. In 2005, Eiben et al estimated that among Swedish older adults aged 70-years the prevalence of overweight was 67% and that of obesity was 20% among men and in women it was estimated to be 64.3% and 23.8% respectively [70]. Around the same time, another study estimated overweight and obesity prevalence among 65-74 year-old Swedish adults. The estimates presented in their study were 47.5 % overweight and 23.7% obesity in men and 41% overweight and 34.4% obesity in women [71].

The World Health Organization's estimation and international comparison of overweight and obesity in different European countries often included all adults over 20 years of age and older. Such an estimation from 2008 showed that 53.3% of Swedish adults was overweight and 18.6% were obese [72]. A sex difference in overweight prevalence was observed with 60.2% among men and 46.6% among women. Similarly, with regards to obesity, it was 19.9% in men 17.3% in women [73, 74]. This is however most certainly subjected to age and methodological confounding. For example, a study conducted in 2011 that employed self-reporting

method of anthropometric assessment among adults aged 16–84 years, presented a prevalence rate of 49% and 13% for overweight and obesity respectively [74]. Based on the abundant available data, it is evident that there are large variations based on nationality, race/ethnic groups and genders are observed. Despite the robustness of the studies conducted there still remains a clearly alarming gap of knowledge and awareness in terms of sub-classifying the older adult population based on age. And within the elderly age bracket, slim attention is given the differences between the ‘younger’ elderly and the ‘older’ elderly groups.

Problem framework

Effective management of malnutrition offers great promise for minimizing its impacts on morbidity and mortality in the elderly. What we need is a comprehensive strategy to identify, quantify, analyze, and evaluate factors at play and thus facilitate a holistic and accurate understanding and appropriate management of nutritional diseases. Assessment of body composition is an important tool to measure the excess or deficiency in tissue components, for example, fat, protein etc. that could result in a state of disease [59]. This assists in identification of those at risk for such disease and facilitate relevant target- and problem-specific interventions. Other methods of nutritional assessment include clinical assessments, biochemical investigations and dietary examinations [17].

Factors affecting body composition assessment

With relevance to nutritional assessment there are intrinsic and extrinsic factors that are significant in the determination of changes in body composition. Among older adults such changes can be inherent to physiological aging process or pathological consequences of related comorbidities. Those factors that characterize the changes in the biological system such as inherent in tissues changes in the different body compartments, and the underlying medical conditions or disabilities can be referred to as intrinsic factors [18, 61, 75-77]. On the other hand, extrinsic factors refer to those external parameters that influence this central biological process either directly or indirectly. For example, lifestyle factors including diet, physical activity, smoking and alcohol consumption, socio-demographic determinants like marital status, education and residence, and time factors, commonly studied by birth cohort effects [61, 78-83].

Intrinsic factors

Body composition

One way of body compartmentalization is to be divided into two: the lean or fat-free tissues and adipose tissues [75]. Lean tissue comprises muscles, bones, visceral organs, cells and tissues other than adipocytes, and extracellular fluid. It is highly metabolically active and nutritional requirements are related to the size of this compartment [84]. Adipose tissue has been traditionally regarded as inactive in metabolic processes despite its more recently recognized important role in hormone metabolism and synthesis of estrogen in postmenopausal women [85].

In general, the aging process is associated with distinct changes in body composition. The rationale behind the investigation of body composition is to assess those measurable alterations that characterize and are associated with malnutrition. The most significant changes include increase in the fat stores that are re-distributed more specifically in the abdominal region and decrease in lean body mass, bone mineral density and intracellular fluid [75]. Structural changes in the body including flattening and fracture of the vertebrae, compression and attrition of intervertebral discs, dorsal kyphosis, scoliosis, bowing of legs and flattening of the plantar arch are very common [32, 86]. The consequent physical features are an excess curvature of the upper back (greater than 50 degrees), leading to a stooped forward posture usually most pronounced in the profile view (Figure 1). There is a characteristic hump on the upper back just below the neck commonly in combination with difficulty in standing upright, back pain and loss of height often worsening over the years [32, 86, 87].

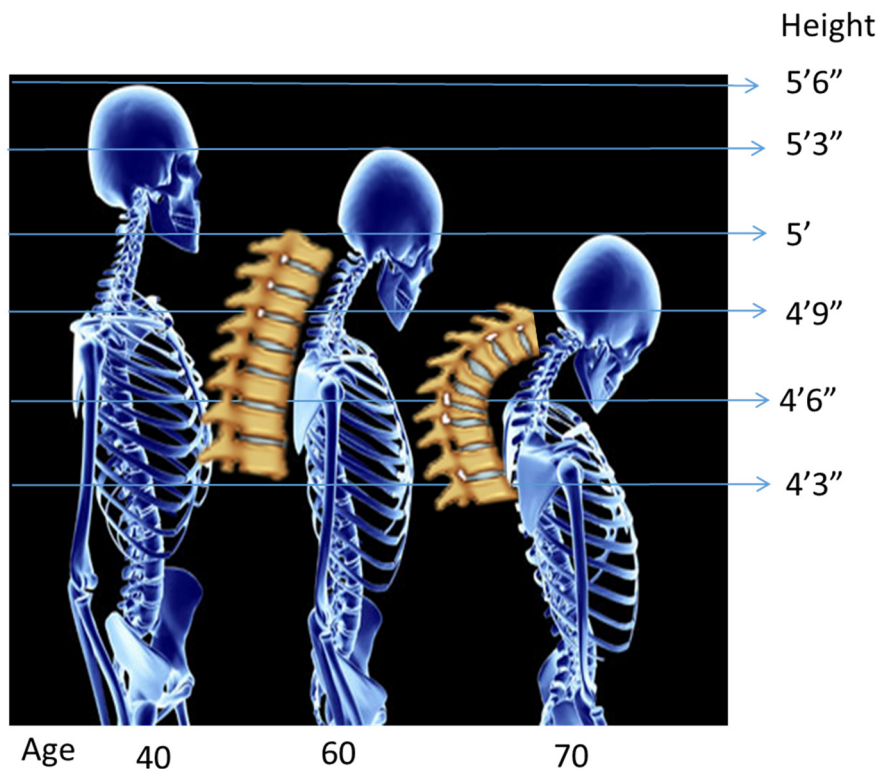


Figure 1: Height changes with aging. Osteoporosis. (n.d.) Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh Edition. (2003). Retrieved March 14 2017 from <http://medical-dictionary.thefreedictionary.com/osteoporosis>.

These aging related body changes are reported to be associated with altered physiological responses like reduced cellular water retention capacity, dehydration, loss of muscle mass, reduced resting metabolic rate and macronutrient oxidation and increased truncal adiposity [88-90]. This indicates the correlation of body composition with alterations in energy balance, where, a positive energy balance with reduced macronutrient oxidation rate could be related to changes associated with weight gain and a negative balance resulting in weight loss [18, 90-92]. There is indirect evidence suggesting the reduction in metabolic rate that occurs with aging promotes changes in body composition that promotes increased adiposity and loss of muscle mass [75].

Comorbidities/ Underlying medical conditions

There are certain aging-related common systemic and metabolic disease conditions and that can be independent and interactive risk factors for mortality [93, 94]. This is crucial to investigate because the validity of body composition assessment is strongly associated with disease states the incidence of most of the common diseases is age-dependent. In general, the common medical conditions correlated to specific body composition changes in relation to nutritional status include myocardial infarction (MI), T2DM, congestive heart failure (CHF), stroke, asthma, COPD, tuberculosis, osteoporosis, hip fracture, arthritis, cognitive impairment, dementia, Parkinson's disease, depression and cancer [19, 20, 23, 41, 80, 95-97]. Dependence in instrumental (iADL) and personal activities of daily living (pADL) are also considered as a status of diminished functional ability that is directly (due to weakness, fatigue) [68, 98, 99] or indirectly (in relation to original medical conditions or consequent disability) associated changes in body composition [51, 55, 99]. Studying such dependence could also be a proxy to significant comorbidities.

Extrinsic factors

The measurements of changing body composition do not distinguish between the causes of change, namely physiological aging or comorbidities-related. Such lacunae in information can be filled by taking into account the role of extrinsic factors such as lifestyle factors, socio-demographic determinants and temporality.

Lifestyle factors

Assessment of diet is highly complex due to fundamental conceptual problems and practical challenges. This could bewilder researchers when selecting the essential parameters that need to be examined. In general, description of macro and micronutrient composition of food consumed and total energy intake are important [16, 21]. There are however, no age-specific reference values for these parameters and the requirements of older adults are rarely specifically investigated. Another practical challenge with diet measurement is recall bias, which principally concerns poor quality of information on the dietary habits recalled during the time of examination, leading to errors in estimation [23, 100]. Such problems could complicate the process of identifying diet-disease associations, if any, and could weaken the validity and reliability of research results [23].

Commonly used in nutritional screening is the dietary history obtained by using different methods such as 24-hour recall, food records, food frequency questionnaires (FFQ), dietary interviews and information on unintentional weight loss in the past months. In epidemiological studies, FFQ are most commonly used

and are considered as a reliable method of estimating dietary status [100]. This could be because FFQs could be less prone to recall problems since they do not specifically intend to capture the daily or weekly pattern [100]. In other words, a long-term assessment of dietary pattern as when using FFQ is more likely to ensure validity of the measures in contrast to 24-hour recall or food records that aims to capture a short-term assessment [101, 102]. The reproducibility and the relative validity of extensive FFQ compared with a reference method consisting of 18 days of weighed food records was found to be acceptable (correlation coefficients in the order of 0.5 to 0.8) for most food groups and nutrients [103, 104]. The FFQ used in Good Aging in Skåne (GÅS) study has been validated in a different study sample with identical age categories from 60 to 91 years using a modified diet history methods with interview and booklet with pictures as a reference method [105].

Besides diet, the other important modifiable lifestyle risk factors include, physical activity, smoking and alcohol intake. These are relatively easier to measure, and is often possible to obtain a quantitative estimate with a considerably high degree of accuracy and limited subjectivity, given that the measurement tool (often, questionnaire) used is detailed and well formulated. However, there is a certain degree of social desirability bias that can be hard to control for [106, 107]. These factors have been widely studied and well established in varied geographic and ethnic contexts, among different age groups and in relation to different disease outcomes [93, 108]. Smoking habits and physical activity have a strong direct and indirect effect on body composition, irrespective of age and disease status [109] and are hence important confounders in the investigation of aging-related weight changes. It is well known that smoking strongly increases risk of mortality and many specific causes of death, and strongly associated with lower body weight [110]. It is therefore considered as one of the primary confounders that need to be accounted for when examining body composition and mortality risk associations [41, 109, 110]. Age-related weight loss often reflects a reduction in skeletal muscle mass. Maintenance of skeletal muscle through a well-balanced physical activity routine should help to attenuate muscle wasting in older age and its associated adverse outcomes [111]. However, such exercise routine can be created after taking into account other factors like age, diseases status etc. [109, 112-114]. Examining alcohol intake has shown varied results including absence of any possible effect. Evidence suggests that light-moderate drinking is not associated with weight or waist gain in contrast to heavy (binge) consumption that has a strong association with obesity that could however be strongly confounded by other lifestyle factors like physical activity and dietary habits [115-118].

Sociodemographic determinants

Age, sex, marital status, education level and residence (urban or rural) are some of the sociodemographic characteristics of the population. Studying these variables helps in understanding the demographic and socioeconomic characteristics of the population and hence accounting for their role in the disease processes. It is useful in the identification of the risk sub-group(s) and to observe trends across the groups. Such analysis and interpretation are routinely performed when presenting quantitative findings facilitating comparison with similar investigations.

It has been shown that these factors play a significant role in pattern of energy consumption, expenditure and metabolism, and the resulting risk for disease, here weight anomalies [119-121]. There exists a vicious cycle of events where the disease-causing socioeconomic conditions are in turn negatively affected by the disease itself. For example, age-related weight loss is associated with low socioeconomic status [122] and obesity prevalence globally is a problem of middle-income countries [119]. Evidence shows that the perception of obesity could be grounded by presumed stereotypical opinions and beliefs that could lead to stigmatization and discrimination that hinder socio-economic advancement [121].

The Health Survey of England study analyzed the role of age and education in the rising trend of obesity among older adults. Abdominal obesity was higher by approximately 5% in the 'younger' age-group 70-79 years than those in the ≥ 80 years and in those with lesser educational attainment, i.e. those who left school in less than 16 years (by approximately 4%) [123, 124]. In the H70 Gerontological and Geriatric Population Studies, Gothenburg, Sweden (H70), the secular change in WC were examined among 70-year-old men and women between 1971 and 2001 [70], examining extrinsic factors like education, physical activity and discussed in terms of BMI trends. Population studies on trends in obesity, cardiovascular diseases and related risk factors, have to a large extent taken into account the role of these factors [79, 82, 123, 125-127].

Birth cohort effect

Aging and related diseases are processes that occur over a period of time. Therefore it is vital to take into account the time-factor in disease development [128]. The differential influence of risk factors on disease prevalence that is specific for age and dependent on year of birth can be referred to as birth cohort effect or generation effect [129]. The time factor can be studied by analyzing the age, period or birth cohorts. As the term suggests, age cohort effects are those unique characteristics of a population that develop during a particular life stage (or age), hence are confounded by age. Period effect is the consequence of a specific,

ecological, ubiquitous disease-causing event that is specific to a particular time period or calendar year- like war, famine, economic crisis or medical inventions affecting population in masses [128, 130].

Birth cohort effects are considered to be an interaction between age and period effects hence could be more relevant to studying secular changes [128]. Birth cohort effects examine the differential expression of disease among populations from different birth years due to differential exposure to the ubiquitous risk factors affecting the age groups differently [131]. In short, birth cohort effect is the period effect due to age-specific exposure to the risk factors. It is logical to note that studying birth cohort effects would become meaningless if it included age groups that are expected to vary in their response to similar exposures. For example, examining the birth cohort changes among ‘younger elderly’ age groups, like around 60 years, may not have a similar effect as when studying older age groups simply due to the effect of progressive changes of aging [132].

Literature reports secular trend in obesity and related diseases among different age groups. However, those specific to the older adult population are relatively slim and outdated. Age-adjusted obesity prevalence among United States adults aged 20–74 years has been effectively monitored and reported by the NHANES [133]. They have reported the trends in overall and abdominal obesity among adults in the United States between the years 1999 and 2012. The birth cohort comparison was done by observing the changes between similar aged subjects with different birth year examined at the different follow-up examinations (cross-sectional studies). In this study, however, all older adults were grouped together under age category ‘65+’ [133]. This could however mask the differences in the trends within the elderly age groups. Other NHANES studies have examined secular trends in abdominal obesity by comparing data specific for three elderly age categories having different birth year and hence examined at NHANES surveys conducted at four periods: 1988–1994, 1999–2000, 2001–2002, and 2003–2004, 2005–2006, more than two-thirds of persons aged 65 years or older are either overweight or obese [66, 67]. A decade ago, several secular trend studies were published from the H70 study among 70-year olds, examining primarily the cohort effects on anthropometric measures [70]. Another Swedish study from the late 20th century, among women age 38 and 50 years, examining the trends in waist-hip ratio (WHR), is also worth mentioning [134]. The Northern Sweden MONICA study examined the secular trend in anthropometrics of obesity and prevalence among age groups 25- 65years and with limited data on age 65-74 years [71]. A Danish study on the 10-year trend in overweight and obesity was conducted among men and women aged 30-60 years [108, 135, 136]. The Baltimore Longitudinal Study of Aging (BLSA) examined secular trends in body weight in older men born between 1877 and 1941 and compared the longitudinal trajectories in body weight between subsequent birth cohorts and found a significant

increasing trend in body weight across birth cohorts [137]. These studies are very good sources of knowledge and inspiration for further research, which however needs to address the methodological challenges of measurements in relation to assessment of body composition and concurrently take into account the role of the extrinsic confounding factors.

Anthropometric assessment of body composition

Several tools of body composition assessment are available and are specific for the target setting, purpose and available resources. The method with the highest degree of accuracy could only be by tissue dissection that is possible post-mortem. Instead, the most widely used tool is anthropometrics. Anthropometric measurements are the most preferred method to assess body size, composition and fat distribution, both at individual and population level. The word “anthropometry” comes from the Greek words ‘anthropos’ meaning man and ‘metron’ meaning measure. It is the easiest, simplest, most portable, inexpensive, noninvasive and convenient method acceptable to use to both the investigator and the subject. The ability to predict functional impairment and disease, and the sensitivity to the changes related to aging process are some of its advantages [138-140]. In particular, anthropometry is vital in the calculation of basal metabolic rate, drug dosage, cardiovascular and neurological morbidity and mortality risk assessment [39, 141].

All anthropometric measures and even the other indirect methods of body composition determination including bioelectric impedance analysis (BIA), dual energy x-ray absorptiometry (DEXA) encounter a certain degree of compromise in terms of accuracy and feasibility. They aim to measure specific body properties and later translate them based on pre-formulated equations. This could introduce potential errors that may occur either in the initial measurement phase (from tool or technique), translation phase (from assumptions made or equations used), or interpretation phase. It is therefore crucial to address these drawbacks to obtain a valid and accurate anthropometric assessment [142].

Measures of body fat distribution

Skinfold thickness, arm circumference, WC, HC and WHR and BMI are the most commonly used measurements in relation to body fat distribution.

Measures of subcutaneous adiposity

Skinfold thickness measure, an indirect method to assesses subcutaneous body fatness through the use of calipers at particular body sites [40]. Skinfold thickness can be measured at specific sites such as subscapular, supra iliac, biceps, triceps, thigh, and calf. The majority of national reference data available are for skinfolds at the triceps and subscapular locations. The measurement of the triceps skinfold (TSF) and of the upper arm circumference (UAC) are commonly used to estimate the amount of arm muscle. Arm muscle area can be used as a marker for the visceral protein proportion [132,133]. There are however certain identified drawbacks with skinfold measurement. The calipers used for this purpose has an upper limit of around 55 mm and may not be useful among extensively overweight or obese population [143]. There is considerable variability in fat distributions between the intra-abdominal, intramuscular or subcutaneous regions that are not equally accessible using the calipers and due to the practical difficulties in combining optimal tissue grip and observing the reading can introduce distortions in the precision of measurements. It is technique-sensitive and the reproducibility is shown to be lower than other measures like weight, height, girth measures due to the difficulty in exact placement of the calipers and the susceptibility to intra and inter-observer variability [144].

Measures of truncal obesity

WC is the widely employed measure of abdominal adiposity. In the examination of the correlation between fat distribution and obesity-related disease risk, WC may be an equally or more useful measure of obesity than BMI [145]. Studies have shown that waist measures can serve as a better marker of risk for chronic diseases like CVD and mortality than BMI [110, 112, 146, 147]. Despite the simplicity of use and sensitivity of measurement concerning WC, the established cutoffs for abdominal obesity are ethnicity- and age-specific [148, 149] that cannot be used for comparison purposes.

HC, WC and WHR are the commonly used measures of central obesity. Evidence suggests that the protective effect of HC with several specific-cause and all-cause mortality risk has an opposing effect as compared to WC. This emphasizes on the

importance of measuring HC along with WC to be able to optimally estimate visceral obesity [150, 151]. Several studies have also presented the strong prediction of CVD and mortality risk with the help of WHR [138, 139, 145]. Besides the practical limitations involving measurement of HC (more difficult than WC), the interpretation of WHR could also be quite complex since higher values could be obtained by increased abdominal fat (measured by WC) or decrease in lean muscle mass around the hips (measured by HC). Yet the strong associations with morbidity and mortality observed encourages the continuous use of all the three measures namely, WC, HC and WHR in assessment of abdominal obesity.

The measurements of WC, HC and WHR are not free from methodological challenges either. The placement of measuring tape, the amount of pressure applied without pinching the skin and causing tension, posture, and breathing need to be well controlled to obtain optimal standardized measurements. And this may not be always easy among older adults. The cut-off values for WC were originally established based on the identification of risk population that falls under overweight and obese categories classified based on BMI values [152]. If BMI should be considered as an imperfect measure then the validity of dependent measures would also become questionable.

Measure of overall obesity: Body mass index

BMI is an integral part of anthropometric assessments and is the most commonly used measure of body fat distribution. It is defined as weight in kilograms (kg) divided by square of height in meters (m²) and is used to identify, underweight, overweight and obese population in clinical and research settings [39-42]. The standard classification of BMI according to WHO, that applies to adults over the

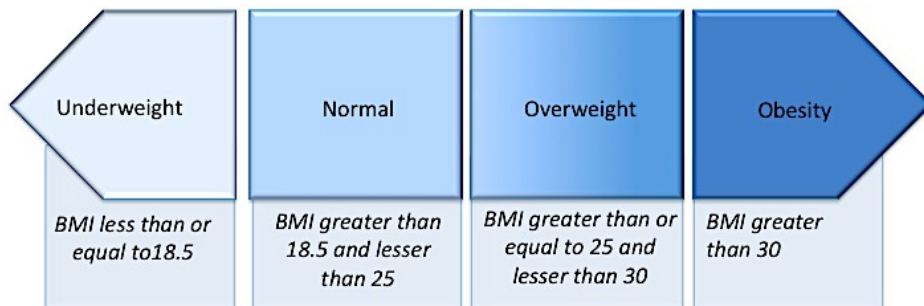


Figure 2: World Health organization classification of body fat distribution in adult population aged 20 years and above.

age of 20 years includes four categories as shown in figure 2. Sub categories

within obesity including increasing grades of severity have been developed namely, grade 1 (BMI 30–35), grade 2 (BMI 35–40) and grade 3 (BMI greater than 40) [41].

Known challenges with BMI

1. Ethnicity: BMI reference values obtained from different nationalities and ethnicities denote diversity in the body composition and changes [52, 153, 154]. For example, it has been shown that Asians have higher body fat than Caucasians irrespective of changes in body weight [155, 156]. The WHO therefore has recommended the estimation of ethnicity based reference values for BMI for adult men and women [39].
 - Fat distribution: BMI is an excellent marker of overall obesity and a strong predictor of increased risk of a wide range of chronic diseases, for example, cardiovascular diseases, T2DM, cancer, and total mortality. However, it does not distinguish between lean and fat mass [40, 84, 135]. Abdominal adiposity assessment using WC, HC and WHR has been proposed in combination with BMI to predict weight-related risk among adults [58, 110, 151, 157, 158].
2. Restrictive BMI cut-offs: Under-diagnosis of underweight elderly individuals: Gerontologists consider the both the upper and lower end of normal range of BMI cut-off is overly restrictive and recommend adjustment of the cut-offs based on the variations in BMI mortality association in older adults compared to the younger population. Several national reference cut-offs have been developed [120, 159-161] and also exists for Swedish older adults [52].
3. Problems related to aging:
 - Body composition changes are either physiological consequences of aging or result from the underlying pathological conditions common among older adults [17]. It is not easy to differentiate between the body changes resulting from physiological or pathological causes [95].
 - The comorbidities can also influence the BMI mortality association [110, 162]. Varied relationship with mortality risks observed with BMI as compared to that among young adults. Among young adults it is clear that increasing BMI is associated with risk for chronic diseases and (long-term) mortality risk. In the contrary, among older adults, there is a shift in this relationship between BMI and mortality (short-term or acute risks).

Unmet problem areas

- Height issues: Aging related changes in body structure, like kyphosis could make the process of accurate height estimation difficult. Furthermore being bedridden may further complicate the process of measurement and compromise accuracy. To our knowledge, there are no previous studies that have adequately addressed the consequences of height loss and measurement errors in height estimation among the elderly.
- BMI misclassification: The errors induced by inaccurate height estimates can result in errors in BMI classification wherein risk groups on either side of BMI spectrum namely underweight and obesity can risk being unidentified or wrongly categorized.
- BMI mortality association: The impact of BMI on mortality among older adults, however, still remains controversial. In addition, previous studies have described this relation as varying widely from a direct positive, a U-or J-shaped or an inverse association [110, 163, 164]. Hence there is a need for further examination of this association in larger, generalizable population samples. If the BMI estimated is inaccurate, the observed association with mortality may not valid.
- A cumulative problem created by misclassification and potential changes in the relationship with mortality has not been previously studied. In addition, only very few studies have examined BMI associations with mortality in the over 80-year-old population and showed no clear effect of a higher BMI on mortality particularly among the oldest-old [157].
- Differential pattern of aging-related body composition changes are observed across the different age groups of older adults. For example, weight loss with age is characterized by peripheral lipo-dystrophy during the ‘early’ aging period (60–70 years) and a generalized fat loss in the later period (>80years) [145, 165]. Hence results from investigation involving older adults from a specific age category or collective categorization of all the age sub-groups may not have similar generalizability or rather can differ strongly from each other. Consequently, a meaningful interpretation based on biological plausibility may not possible.
- Although ethnicity based BMI, as proposed by the WHO, could address the differential body changes, questions on the variability in the response to potential epigenetic factors (period effect) and generational effects remains unanswered. Furthermore, it may still not be applicable for the older adults.

Inadequate management measures

Despite the widely acknowledged limitations, it is unlikely that use of BMI will be discontinued.

Use of BMI and WC: Despite the proposed use of both the measures, it is still the case that independent use BMI is widely preferred probably because addressing overall obesity and the related risk could have an umbrella effect over abdominal obesity. This however demands good level of accuracy and may not allow any form of limitation that could functions in the opposite direction and cause risk for errors or misinterpretation.

- BMI cut-off adjustment: Most of the studies emphasize on the restrictive BMI ranges in the overweight category. Inadequate attention has been given to the problems around the underweight category [166]. It has been shown that the analyses conducted did not take into account potential confounders in the BMI-mortality risk association nor describe if the risk predicted was short term or long term [41, 157]. In general, the aim is to expand the upper limit of normal range into the ‘overweight zone’ (sometimes even beyond) and concurrently the upper limit of underweight category to the right encroaching the lower limits of normal range (Figure 3: areas shaded red in the adjusted BMI categories) [120, 159-161].

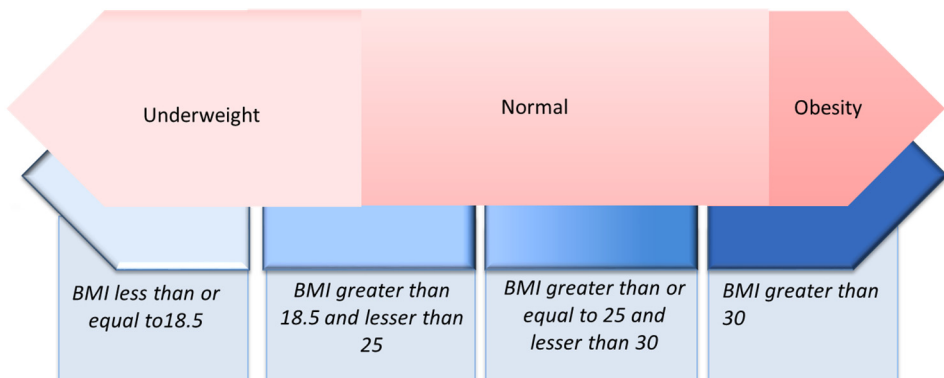


Figure 3: Approximation of proposed adjustments in BMI cutoffs (pink) to be used among older adults over 60 years of age in relation to the classic BMI

In this way, underweight under-diagnosis and inappropriate weight reduction of overweight can be minimized.

Consequence: The margins for the different weight categories are found to be very variable between the studies [166]. It is however important to remember that the lack of standardization of the category margins or cut-offs could not

only challenge the generalizability and comparison of the results [41]but also the risk for under-diagnosis could still remain. In addition, the cost of such an upward shift of the lower margin of normal category aiming to achieve better sensitivity in capturing the underweight population could be the diminishing specificity from the false positive underweight results (those who actually are normal being classified as underweight)

- Surrogate stature measurement methods using sliding calipers, self-reporting of height and predictions using regression equations have been reported [59, 86, 167, 168]. Sliding calipers, although usable among recumbent patients, are prone to errors among kyphotic patients [169]. Self-reporting is well known to be subjected to recall bias [170, 171]. Formulae exist to estimate height using proxy indicators such as arm-span, ulnar length, demispan and knee height (KH) [48, 86, 153, 172-177], as the limb skeleton is less prone to degenerative changes than spinal structures [48]. Demispan and KH are two mostly commonly used surrogates to estimate height, due to their relatively slower degeneration with age that could even be considered insignificant [32]. Population- and ethnicity-specific equations have been developed and in most cases, are applicable only to the population described [86, 154, 169, 172, 176, 178-180]. Bassey's demispan (125 adults, age 34–35, Europe) and Chumlea's KH (4750 race diverse elderly, aged over 65 years, USA) equations are most widely used [173, 174] but their international applicability is debatable. Hence, age-adjusted sex- and population-specific equations from large nationally representative samples are needed [169]. Based on our literature search, in Sweden, there are no KH or demispan based equations to estimate height and true BMI classification among the elderly.

BMI misclassification introduced by inaccurate estimation among older adults need further attention to rule out any potential misinterpretations in relation to morbidity and mortality risks that exist today. This could affect optimal weight management interventions designed to relevant target groups. To the best of our knowledge, there is no evidence on studying the effect of such misclassification in relation to mortality risk among elderly.

Knowing your population

A thorough understanding of the target population is fundamental to obtain an accurate identification of the areas of unmet needs. All the measurements made are futile if interpretations are not made in light of age, sex, ethnicity, and conditions that complicate the measurement process. Mobility impairment in bed-ridden or wheel chair users, conditions that cause limb edema, paralysis or even amputation are a few to mention. Due to a lack of standardization of measurement techniques, estimation equations and risk parameters, it is important to make population-specific interpretations, using systematic, logical, evidence-based methodology and validated protocols.

In this thesis, an in-depth examination of the anthropometric features and the status of underlying medical conditions among the general elderly population is conducted as the first step to problem management. The World Health Organization has assembled international anthropometric data for health assessment, nutrition and wellbeing, emphasizing the significance of the phenotypic impact of aging, senility and associated diseases. This urges the collection of normative anthropometric data specific for the elderly [144]. There have been several such international publications previously [28, 120, 164, 181, 182], such as the SENECA study on nutritional health in 13 Western European countries (8). In Scandinavia, similar studies have been conducted where only height, weight and BMI were measured [109, 134, 183, 184]. Hence, there is a need for additional measurements that help in the holistic understanding of anthropometric status. In this regard, it is worthy to mention the H70 study that additionally presented skinfold thicknesses and circumference measurements, although only among 70-year-olds [183, 184]. Longitudinal studies on anthropometric changes were done among 75-year-olds in three Scandinavian localities (NORA) [109] and on middle-aged Swedish women (age: 38–60 years) [134]. However, these studies have not considered the influence of underlying medical status and were targeted at specific sex- or age groups (70–75 years). In addition, the NORA study included a relatively small sample size of 450 individuals.

To the best of our knowledge, there is no recent publication on sex- and age-specific anthropometric reference data for the Swedish elderly population that takes into account common underlying diseases related to aging. This is crucial

because the incidence of the most of the common diseases is age-dependent and related to the prevalence of predisposing risk factors in the population under study. It is therefore important to estimate this based on a large nationally representative sample.

Comprehensive body composition assessment- a conceptual model

Theoretical background

To minimize the burden of body composition aberrations and promote healthy aging a broader action is needed. A logical, evidence-based and well-structured management strategy that takes into consideration the intrinsic processes and extrinsic factors that influence body composition changes. It should focus on the hallmarks of biologic aging and at the same time address the practical challenges in (height) measurement that is almost unavoidable and negligibly attended. This demands effective tools that could ensure accurate estimates and meaningful interpretation of the true state of the system and the transitions over time.

Based on the consensus arrived at within geriatric nutritional research studies, an exhaustive method of problem management taking into consideration the nuances and complexities is needed. Nutritional assessment in older people to detect malnutrition or risk of malnutrition is essential to prevent adverse outcomes [185-189]. In this context, it could be relevant to refer to comprehensive geriatric assessment (CGA), a tool used to identify physical disabilities, comorbidity, multi-medication, nutritional status, cognitive and emotional status among older adults that facilitates designing problem-based interventions. Several tools specific for the various assessments are included in the CGA. However, this has still been controversial in terms of definitions and classifications. Another popularly used nutritional assessment tool is MNA. It is widely accepted both by the caregivers and the patients and has been used in hundreds of studies in a wide range of different settings and in many countries. Many literature reviews concerning nutritional assessment tools in elderly people, and in particular the MNA, have been published [26, 54-57]. It is based on 18 self-reported questions divided four parts: divided into four parts: anthropometric measurements, global assessment, dietary questionnaire and subjective assessment. The anthropometric measurements include BMI, mid arm circumference, calf circumference and weight loss; the global assessments included six items related to lifestyle, medication and physical as well as mental health; the dietary questions include six items related to dietary intake and eating problems; and the subjective status

includes one item related to nutritional status and one to health status [26]. The maximum score is 30 points, with 24–30 defined as well-nourished, 17–23 as at risk for malnutrition and <17 as malnourished.

The proposed comprehensive model

The model proposed in this thesis is based on and inspired by the CGA-MNA theories of evaluating disease status (Figure 4). The key aim is however to address the limitations of the anthropometric domain of such evaluation process [190]. The problem framework comprises intrinsic (anthropometrics, underlying medical conditions) and extrinsic factors (lifestyle, birth cohort and socio-demographics). In a nutshell, this framework is structured by formulating a theoretical correction of measurement errors, by fine-tuning the tools currently employed, to achieve plausibly true anthropometric disease classification validated by the true link to associated mortality risks.

From a theoretical standpoint the objectives are to:

- Formulate a holistic approach in problem management
- Identify precisely the involved risk groups, the magnitude of the issue and adverse effects
- Facilitate the application in the different elderly age groups
- Deliver clear and comprehensible information to the primary stakeholders namely,
 - Target elderly population- to raise awareness and impart knowledge about disease prevalence, prevention and health promotion activities.
 - Policy makers who strive for could implement relevant disease prevention and health promotion strategies

Structural components

- *Examination* of status quo and *identification* of the problem(s)
 - Anthropometric reference data-normative values
 - Age and sex specific
 - Underlying medical conditions

- Investigation of changes across age groups
- Accurate *quantification* of the problem & *possible/hypothetical solutions*
 - Theoretical correction of (measurement) errors
 - Testing the theory using surrogate measures (prediction formula)
 - Comparing the magnitude of difference between methods
- *Evaluating* the implications of the proposed solution(s) for functional benefits
 - Age-specific relationship between BMI misclassification and mortality risk
 - All-cause mortality rules out problems of competing risks hence an acceptable validation attempt.
- *Investigating* the role of the extrinsic factors
 - Confounders and/or mediators
 - Birth cohort changes
 - Complementary anthropometrics (waist measures)
 - Lifestyle factors.

Hypothetically, this could be achieved by adopting the comprehensive model of body composition assessment. The structural components of this model includes the following:

1. Population-specific anthropometric reference data is fundamental to accurate identification of the problem areas and could facilitate comparison studies.
2. BMI prediction using proxy measures¹ that are could test for and quantify accurately the magnitude of errors in weight categorization by BMI, in other words, BMI misclassification. In this way, a refinement of the existing index is initiated.
3. Public health application and designing of new guidelines could however demand validation of the prediction equations, the ‘fine-tuned BMI’. In this process, the main challenge would be to identify the reference tool for validation. Gold standard tool with least systematic errors serve as ideal reference. The use of biomarkers or other of body composition assessments methods such as BIA or, DEXA could offer high degree of credibility. The

¹ One assumption made here is that the proxy measures employed have relatively similar merits as classic BMI.

main limitation when conducting epidemiological studies is that it could be technique sensitive that requires training or expensive. Given the resources and this should be the ultimate goal. The next possible option is to use the classic BMI as reference, which could also be the first line of control since it is the widely accepted tool with several merits. It is also important to compare the mortality risk association to validate the cut-offs used in the predicted BMI method. And hence, we have adopted this here in this thesis.

4. To obtain a holistic anthropometric assessment of body composition, incorporating waist measures, and accounting for the significant extrinsic confounders is crucial.

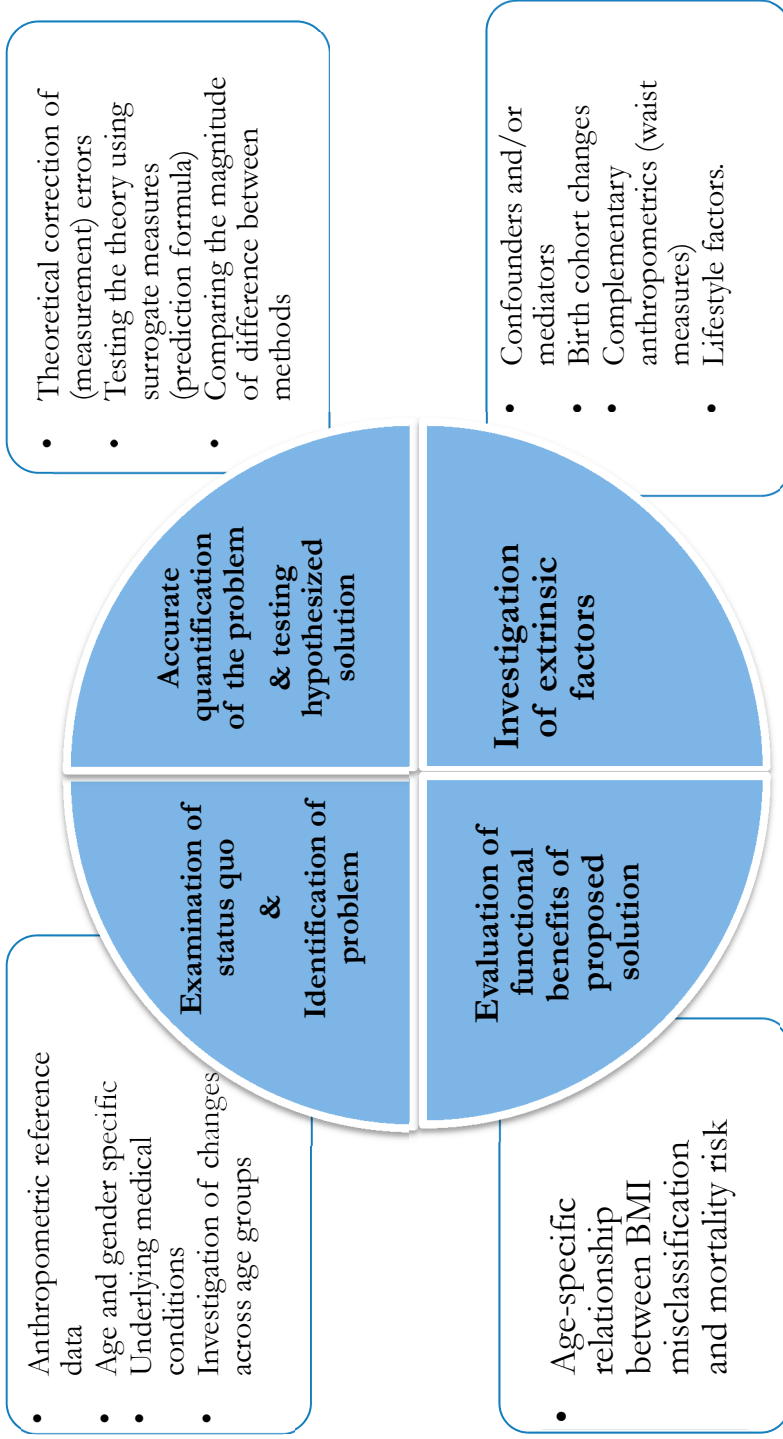


Figure 4: Structural components within comprehensive assessment of body composition.

Aims and Objectives

The overall aim of this thesis was to identify and address the methodological issues in anthropometric measurements due to biological changes of aging, among Swedish elderly population, aged ≥ 60 years, taking into account the role of comorbidities, socio-demographics, lifestyle factors and cohort changes. This was done through developing and investigating the above-mentioned multifactorial conceptual model of body composition assessment (Figure 4).

The specific objectives of this thesis were:

To describe the sex- and age-specific normative anthropometric data for a large national cohort of Swedish elderly, categorized based on incidence of conditions namely, MI, CHF, stroke, cognitive impairment, dementia, dependence in instrumental and personal activities of daily living (iADL and pADL) (Study I).

To investigate the degree of BMI misclassification among Swedish elderly by standard measured height against using age adjusted, sex specific KH and demispan predictive equations to estimate stature. We aim to compare the prevalence in underweight ($BMI \leq 20 \text{ kg/m}^2$) and obesity ($BMI \geq 30 \text{ kg/m}^2$) when classified using the classic, KH based or demispan based BMI (Study II).

To investigate the age- and sex-specific role of BMI misclassification due to methodological errors of height estimation among elderly in BMI mortality risk after adjusting for potential confounders like marital status, residence, education, smoking, physical activity, number of diagnosed underlying medical conditions (Study III).

To examine the birth cohort changes in (i) anthropometric measurements namely, height, weight, BMI, WC and HC, WHR and the prevalence of abdominal obesity; (ii) obesity-related factors such as education and lifestyle parameters (diet, smoking, alcohol intake and physical activity) in relation to WC trends among Swedish elderly population, aged 60 years and 81 years of age, at three time points (2001, 2007, 2015) (Study IV).

Materials and Methods

Source of Data

All the studies in this dissertation are based on data from the Good Aging in Skåne study (GÅS) [191]. It is a part of the longitudinal, multi-purpose population study ‘Swedish National Study on Aging and Care’ involving four research centers that collect data in four different areas of Sweden [191]. GÅS is the part of SNAC that operates in the South province of Sweden, Skåne. This is a multifaceted, public health oriented project that aims to contribute evidence-based knowledge and raise awareness about the aging process from different perspectives. The study was approved by the Ethical Committee at Lund University (LU 744–00), and all studies are carried out in compliance with the Helsinki Declaration.

The target population of GÅS includes men and women from five municipalities in Skåne. These municipalities are Malmö, Ystad, Eslöv, Osby and Hässleholm, a combination of urban and rural settings to create heterogeneity. The study subjects are from age cohorts 60, 66, 72, 78, 81, 84, 87, 90 and 93 years, with an oversampling of youngest and oldest cohorts. Based on statistical sample size calculations, the aim was to recruit 700 subjects in ages 60 and 66 years, respectively, 250 subjects in ages 78, 81, 84 and 87 years respectively, 200 subjects in the age 90 years and 100 subjects in age 93 years. The study population was formed by random invitation sent by post using the National Population Registry to individuals aged ≥ 60 years in these five participating municipalities.

Between the years 2001–2004, 2931 subjects agreed to participate in the baseline examination. Participants aged 78 years and above are followed up every three years, while those who belong to age cohort 60, 66 and 72 years are re-examined every six years.

An overview of all four studies in this thesis are described with respect to study design, sample source, selection, inclusion criteria, size and participation rate in the GÅS study (Table 1). More details on the process of population sampling and inclusion to the different studies are presented graphically in figures 5, 6, 7 and 8.

Table 1: Overview of the four studies in this dissertation: study design, population selection and sampling.

Study design	GAS examination	Year of examination	Participation rate (in GAS)	Total participants	Study Population	Age	Birth year	Inclusion criteria
I Cross-sectional	6-year follow-up	2007–2010	84%* (70%)**	3360	3142	≥60 years		Not more than one missing anthropometric variable under study
II Cross-sectional	Baseline	2001–2004	60%	2931	2839	≥60 years		Valid knee-height measurement Valid demispans measurement
III 15-year follow up to mortality	Baseline	2001–2004	60%	2931	2786	≥60 years		Valid knee-height and BMI measurement
IV Cross-sectional	Baseline	2001–2004	60%	710	710	Age cohort 60	1941-43	All men and women within age cohort
	6-year follow-up	2007–2010	70%**	740	740	Age cohort 60	1947-49	
	12-year follow-up*	2013–2015	66%**	740	740		1952-54	
	Baseline	2001–2004	60%	269	269	Age cohort 81	1920-22	All men and women within age cohort
	6-year follow-up	2007–2010	70%**	327	327		1926-28	
	12-year follow-up	2013–2015	66%**	298	298		1932-33	

*Participation rate of subjects who have previously participated in the baseline examination of GAS study.

**Participation rate of subjects recruited for the first time in GAS study. All estimations made at the time of analysis.

Sample population selection in study I

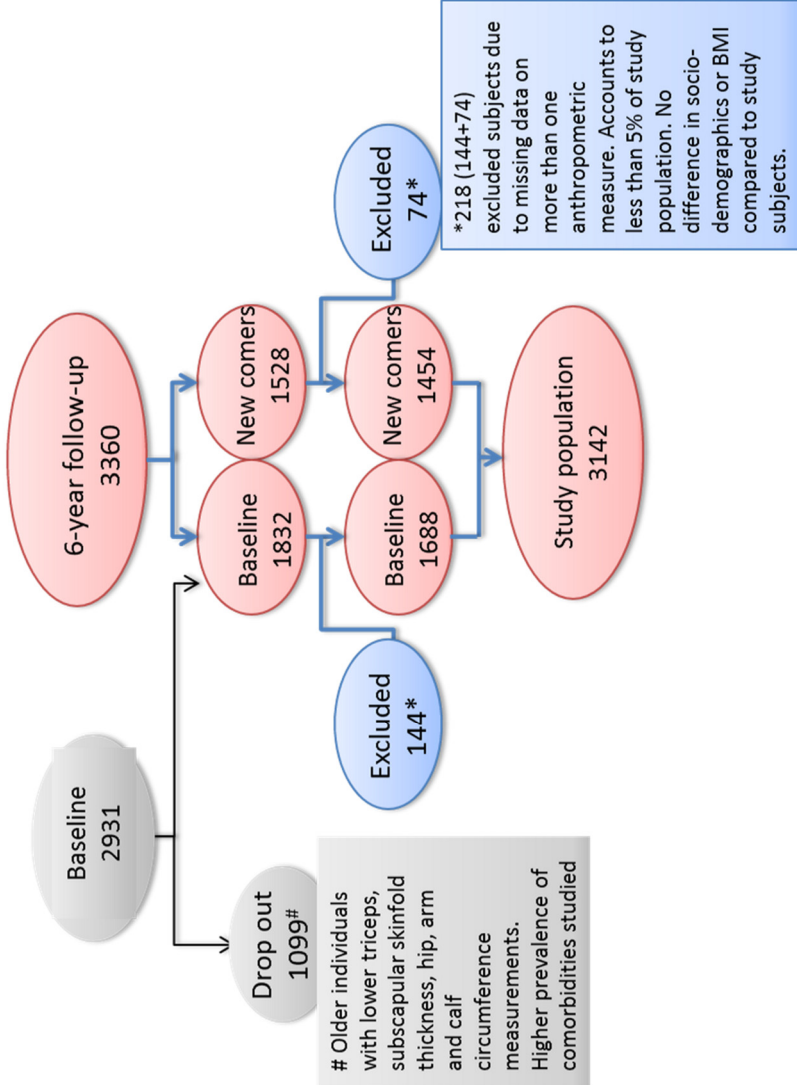


Figure 5: Overview of population sampling process in study I including participants from Good Aging in Skåne (GÅS) study

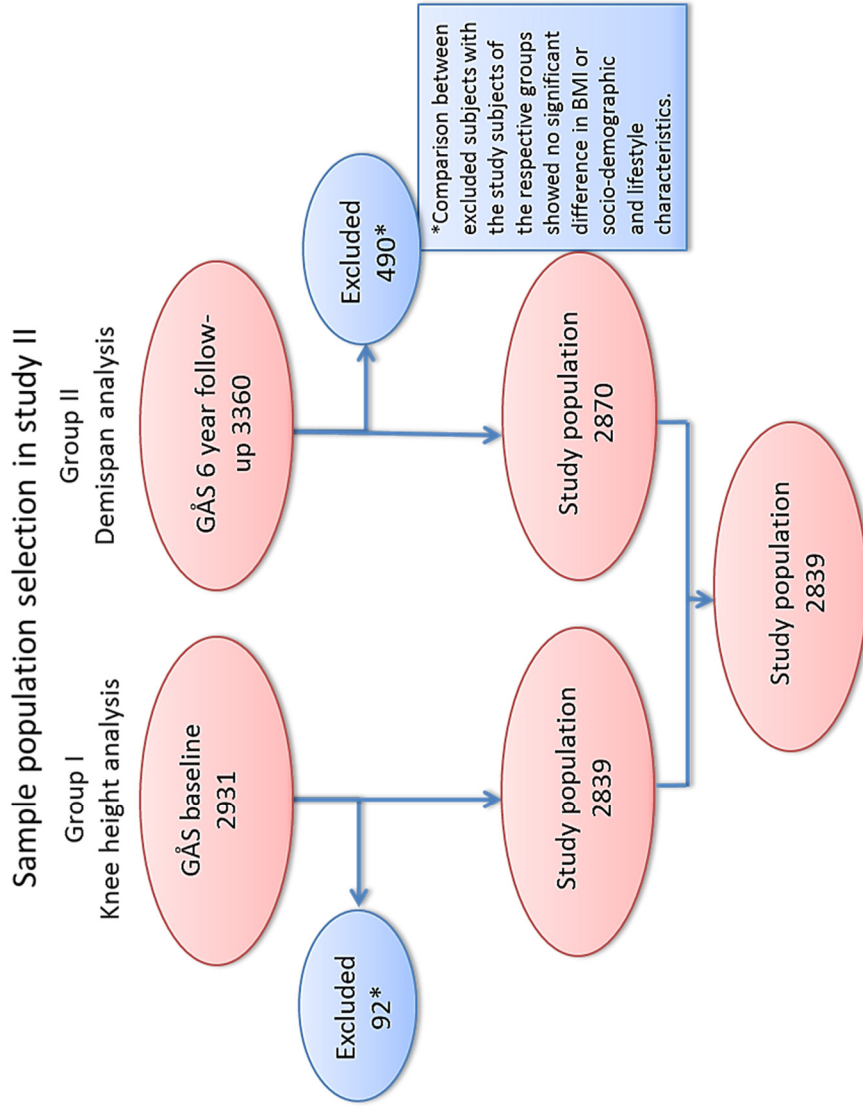


Figure 6: Overview of population sampling process in study II including participants from Good Aging in Skåne (GÅS) study

Sample population selection in study III

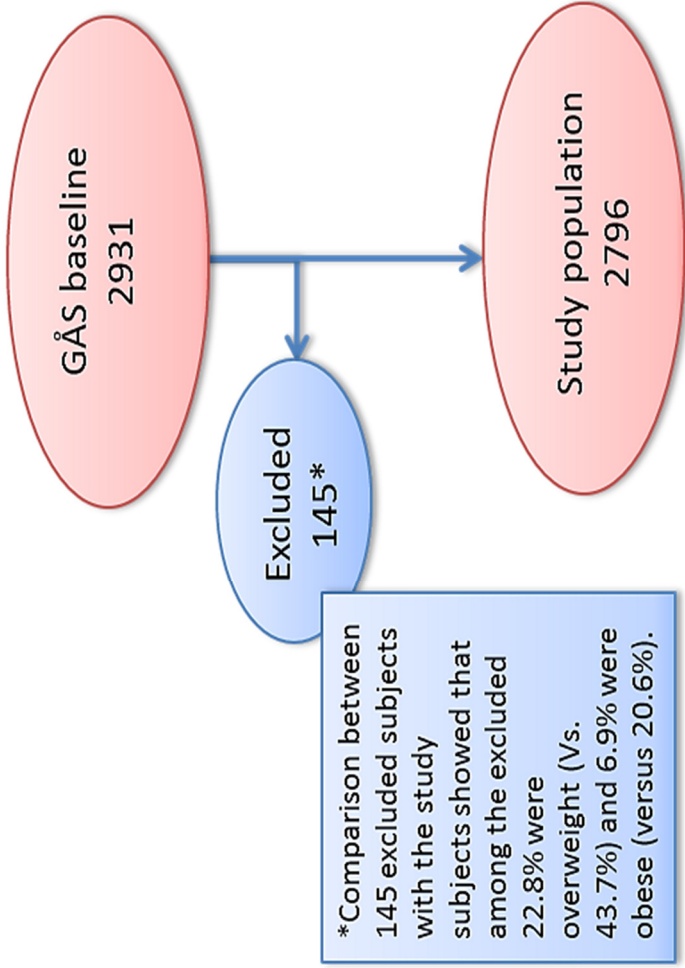


Figure 7: Overview of population sampling process in study III including participants from Good Aging in Skåne (GÅS) study

Population sampling in study IV

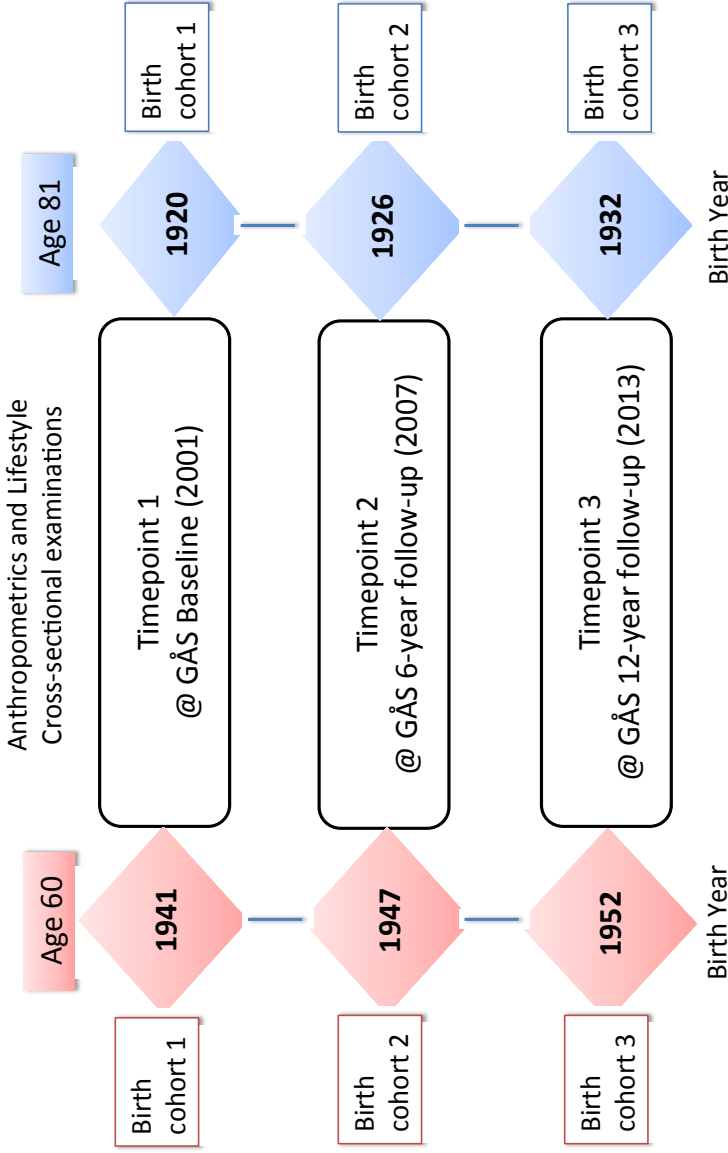


Figure 8: Description of population examined in study IV: source, age cohorts, birth year and the time-point of examination in the Good Aging in Skåne (GÅS) study. Birth year in both age cohorts was often a range over 2 years. i.e., Age cohort 60: 1941–43, 1947–49, 1952–54; Age cohort 81: 1920–22, 1926–28, 1932–33.

Variables and data collection

Examinations were done at the clinical research outpatient centers, located in the different cities, or at the participant's homes or sheltered living whenever they or their caregiver chose this option. A priori informed consent is obtained from all study subjects before the commencement of the data collection. The process is conducted by qualified physicians and nurses, and comprises medical examinations, physical and mental function tests and a survey. Data on socio-demographics, physical, mental health and social factors are collected using a close-ended questionnaire used in the survey. The questions were formulated systematically to generate study variables that are based on validated methods. Swedish language is used in the survey questions and during examinations. There were four registered nurses who were trained in and responsible for the assessments made during all examinations. Participants received simple, well-structured and identical instructions throughout the process and were welcome to obtain further clarifications if needed. Information in the questionnaire regarding functioning and life style was confirmed by medical examinations conducted by trained doctors, data from medical records and proxy information from the caregivers.

Definition of variables

Simple and easy-to-understand questions were used to collect information on the variables used in the different studies.

Socio-demographic variables

Marital status: Denoted whether the subject was single, married, divorced, widow (er) or living with a partner. This also included an option called 'särbo' in Swedish, where individuals were in a partnership but did not live together. The group 'särbo' was never combined with 'married' group but included under the 'single' category during dichotomization, together with divorced and widowed. On the other hand, option 'samboende' (referred to as living with partner in our study) denoted individuals who were unmarried but lived together, another common relationship status that is considered similar to being married. Therefore 'samboende' was grouped together with being married.

Residence: This variable was used to categorize subjects into urban or rural residents depending on the municipality they lived in. Inhabitants of Malmö were categorized as urban residents and those who lived in the municipalities Ystad, Osby, Eslöv and Hässleholm were classified as rural residents.

Education: The survey question used included the options: 1) incomplete primary education, 2) complete primary education, 3) secondary education, 4) higher secondary education or university level and 5) doctoral or licentiate studies after university.

In study III, the variable categories were

- (i) Primary or lower included options 1) and 2)
- (ii) Secondary: option 3)
- (iii) Higher than secondary: options 4) and 5)

In study IV, the variable education had categories:

- (i) Lower than primary: including option 1)
- (ii) Primary: option 2)
- (iii) Secondary and higher: option 3), 4) and 5)

Lifestyle factors

Smoking status: The related survey question “Do you smoke?” included the options: ‘1) yes, regularly’, ‘2) yes, sometimes’, ‘3) no, never’ or ‘4) no, quit smoking’. Variables in all four studies had categories:

- (i) Smokers with options 1) and 2),
- (ii) Non-smokers with option 3) and
- (iii) Ex-smokers with options 4).

Alcohol consumption: The question “When was the latest consumption of beer, wine or strong alcohol?” that was used in the studies aimed to investigate if there was active alcohol intake habit over time. The possible responses were ‘have never drunk since the last year’ referring to non-drinkers, ‘a few times in the last year but not since last month’ referring to light-drinkers and ‘have had alcohol a few times in the last month’ active-drinkers.

Physical activity: Two parameters were studied with respect to physical activity namely intensity and frequency.

The intensity of physical activity was examined using the question that had the following responses: 1) ‘Barely any physically activity’ 2) ‘very light activity, in the form of a walk very rarely, light gardening or similar, and sometimes light housework such as heating food, dusting’, 3) ‘light physical exertion about 2–4 h per week such as, walking, dancing, light home chores like cooking, cleaning, etcetera), 4) ‘moderate intensity exercise about 1–2 h per week, for example, jogging, swimming, fitness classes, heavier gardening or light exercises >4 h per week, such as home chores including vacuuming, floor/window cleaning etcetera), and 5) ‘strenuous exercise at least 3 h per week, such as tennis, swimming,

jogging’ and 6) ‘Hard exercise regularly/several times a week, such as running, skiing’.

In study I, II and III, the variable include the following categories:

- (i) Mostly sedentary including options 1) and 2)
- (ii) Mild with option 3)
- (iii) Moderate with options 4)
- (iv) Heavy with options 5) and 6)

In study IV, the variable included the following categories:

- (v) Mostly sedentary including options 1) and 2)
- (vi) Moderate with options 3) and 4)
- (vii) Heavy with options 5) and 6)

The frequency of physical activity was also investigated using the survey. The possible responses were 1) ‘Never’, 2) ‘1 time/month’, 3) ‘2 times/month’, 4) ‘Several times/week’ and 5) ‘daily’. This was examined only in study IV, where the variable included the following categories:

- (i) Never option 1)
- (ii) Rarely with options 2) and 3)
- (iii) Several times/week with option 4) and
- (iv) Daily with option 5)

Diet: The variable used for analysis was frequency of complete meals per day. This variable created based on the question: “Select food consumed at breakfast, lunch and dinner (all that apply)”. All mealtimes had similar options. The participant responded by selecting the type of food they ate for breakfast, lunch and dinner. For example, a complete breakfast included: A sandwich and a drink, cooked porridge with fermented milk and salad, fruits and drinks, or cooked food. A complete lunch/ dinner was formulated similar to breakfast, excluding the option ‘fruits and drinks’. The population was categorized into those that ate one or less, two or three complete meals per day.

Anthropometric variables

All measurements were made on the right side unless there was previous amputation, paralysis or contracture. Two nurses conducted the tests and also repeat them twice to calculate an average. No special attempts were made to account for potential inter-observer variation. Bedridden patients and individuals using wheelchair were not included in our studies.

Height was measured using a measuring tape with the individual standing erect with shoulder blades, buttocks and heels against a wall and straight fixed gaze. Arms were along the sides, shoulders relaxed, legs straight, knees touching each other, feet flat and heels together. Readings were made in centimeters with one decimal value. Bedridden patients and those using a wheelchair were excluded from our study.

Weight (in kg) was measured with a precision balance scales in the morning with light clothes and no shoes, after voiding bowels and bladder in non-fasting conditions. The balance was manufactured by Tanita Corporation, Japan, and calibrated annually by the Technical Medical Division at Skåne University Hospital, Malmö, Sweden. The precision of the scale was ± 50 g.

Waist circumference (in cm) was measured in standing position, with light clothing, using a steel tape measure, at a level midway between the lowest rib margin and the iliac crest, to the nearest centimeter. Based on standard cut-off values specific for men and women ($WC \geq 102$ cm (men); ≥ 88 cm (women)) [192], abdominal obesity risk categories were obtained.

Hip circumference (in cm) was measured using steel tape measure to the nearest centimeter at the level of the widest point between hip and buttock or the greater trochanters with the legs close together. Arm- and calf circumference were measured at the point of maximum convexity of biceps and calf muscles, respectively, with the limbs in completely relaxed position. All circumference measurements were made using a soft, non-elastic measuring tape, calibrated in millimeters, wound free from tension around the appropriate anatomic site.

Subscapular skinfold thickness (SST, in mm) measured the double thickness of skin, underlying connective tissue and subcutaneous fat, but not the muscle. The Harpenden caliper (Baty International, Burgess Hill, West Sussex, UK) was applied 1 cm below and at right angles to the pinch. TST was measured at the level of the midpoint between the bony upper tip of the shoulder (acromion) and elbow joint (radial) on the back of the left arm over the surface of the triceps muscle. SST was measured at the level of lower angle of scapula. TST and SST were measured in mm with one decimal and rounded to the nearest 0.2 mm [193].

KH (cm) was measured using a caliper consisting of a vertical scale with two horizontal blades at each end. The subject was in a recumbent position, with neck and back relaxed, left leg lifted and knee bent at 90° . One of the caliper blades was positioned under the heel of the left foot and the other was placed on the anterior surface of the left thigh just above the condyles of the femur and just proximal to the patella (Figure 9). The shaft of the caliper was held parallel to the shaft of the tibia, and gentle pressure was applied to the blades of the caliper. The

measurement was repeated twice and the average was noted. If seated, the leg was supported so that the knee and ankle were at a 90° angle.

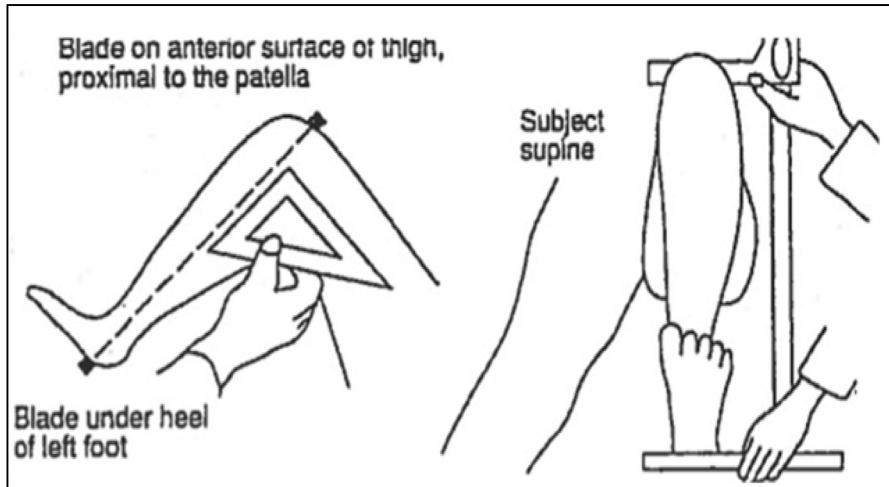


Figure 9: Schematic representation of knee height measurement and the application of the knee height calipers.

Demispan (cm) was measured with the subject standing upright with back straight, arms extended sideward at 90° to the torso, fingers stretched and the arm rested against a wall to avoid forward or backward bending. The distance between the tip of the middle finger (not nail tip) and midpoint on the sternal notch was noted using a flat, stiff tape that avoids flexion errors.

Using the estimated measurements equation-based measurements were calculated. Table 2 summarizes the calculated measurements used in this thesis.

Table 2: Overview of the anthropometric measurements calculated based on derived equations or formula.

Anthropometrics	Calculation	Equation	Unit
Body Mass Index	Weight divided by the square of height	$\frac{\text{Weight in kg}}{(\text{Height in m})^2}$	Kg/m ²
Waist-hip ratio	Ratio between the waist circumference and the hip circumference	$\frac{\text{Waist circumference in cm}}{\text{Hip circumference in cm}}$	No units
Arm muscle circumference	Using previously formulated equation	Arm circumference (cm)–(3.142 × triceps skinfold thickness (cm)).	cm
Knee-height predicted BMI *	Using equation formulated in study 2 in this thesis	Men: Height= 115.23 + 1.16 × knee height Women: Height= 104.52 + 1.23× knee height	Kg/m ²
Demispan predicted BMI*	Using equation formulated in study 2 in this thesis	Men: Height= 49.41+ 1.4× demispan Women: Height=36.34+ 1.53 × demispan	Kg/m ²

* The equations shown here were those formulated by us in study II.

Common medical conditions

Information from thorough history taking, previous medical records, medical examination and functional tests were used to investigate the presence of common medical conditions.

The categorization of somatic diseases was based on the International Classification of Diseases (ICD-10) criteria. The category ‘myocardial infarction’ (MI) also included angina and arrhythmia. Symptomatic congestive heart failure was defined from the NYHA (New York Heart Association) criteria and included

subjects with NYHA class II-IV symptoms [194]. The category ‘stroke’ included cerebral infarction, hemorrhage and transient ischemic attack. Dementia was defined based on the criteria in the Diagnostic and Statistical Manual of Mental Disorders IV according to the American Psychiatric Association Diagnostic and Statistical Manual [195]. Cognitive impairment was defined as scoring below 24 points on the MMSE (Mini-Mental State Examination) [196].

Functional ability was assessed by self-reporting on Hultér-Åsberg's activities in daily life (ADL) scale that has demonstrated high validity and reliability [98, 197]. The variable was coded into independence in daily living activities, dependence in instrumental activities (iADL) and dependence in personal activities (pADL). It is an 11-step scale (0–10) where score-0 corresponds to completely independent individuals and score-10 to those who are dependent on all 10 instrumental and personal activities. pADL includes questions relating to hygiene, dressing/undressing, toilet use, mobility and food intake and iADL includes questions on grocery shopping, cooking and cleaning. A reduced pADL implies a reduction in iADL; however, the opposite does not apply [198].

Mortality

Information about mortality/survival status and the date of death for the deceased population was obtained from the Swedish Civil Registry. The dataset used is updated to year 2016 [199]. All relevant information was extracted by matching the social security number of the individual concerned.

A summary of the variables used for the purpose of analysis specific to each study in this thesis can be found in Table 3.

Table 3: Overview of the different variables used in the four studies

Study	Descriptive variables	Anthropometrics	Medical conditions	Mortality
I	Sociodemographic determinants: Age, sex, marital status, residence, education; Lifestyle factors: smoking habits, alcohol consumption and physical activity	Height, weight, WC, HC, calf circumference, triceps- and subscapular skinfold thickness, BMI, WHR, arm muscle circumference.	MI, CHF, stroke, dementia, cognitive impairment, iADL and pADL dependence	-

II	Sociodemographic determinants: Age, sex, marital status, residence, education; Lifestyle factors: smoking habits, alcohol consumption and physical activity	Height, weight, knee height and demispan.	No units	-
III	Sociodemographic determinants: age, sex, marital status, residence, education; Lifestyle factors: smoking habits, alcohol consumption and physical activity	Height, weight, knee height predicted BMI.	MI, stroke, diabetes, tuberculosis, asthma, chronic obstructive pulmonary disease, osteoporosis, hip fracture, arthritis, dementia, Parkinson's disease, depression and cancer.	Survival status (dead/alive) and date of death
IV		Sociodemographic determinants: age, sex, marital status, residence, education, birth year. Lifestyle factors: smoking habits, alcohol consumption and physical activity and dietary frequency/ episodes of complete meals per day.	Height, weight, BMI, WC, HC, WHR.	-

MI: myocardial infarction, CHF: congestive heart failure, ADL: instrumental activities of daily life, pADL: personal activities of daily life, BMI: Body mass index; WC: Waist circumference, HC: Hip circumference, WHR: Waist: Hip ratio. Descriptive variables include both the demographic variables and the obesity related explanatory variables examined in our studies.

Data analysis

Study I

Data were categorized according to sex and age groups of 60–64, 65–69, 70–74, 75–79, 80–84 and over 85 years. Results are expressed as means, standard deviation (SD) and 10th, 25th, 50th, 75th and 90th percentiles. The assumptions of analysis of variance were tested by inspecting the standardized regression residuals. This did not raise any serious concerns regarding normality and homoscedasticity. One way analysis of variance test was used in two settings: to test the differences in the mean values of the all the anthropometric measures across the different age groups and between the groups with and without each underlying diseases studied.

The association between the underlying conditions and anthropometric measures was investigated using linear regression analysis. Age- and gender-adjusted linear regression coefficient was presented for every anthropometric variable among those with the condition compared with their respective reference groups (no myocardial infarction, stroke, dementia, independence in ADL, and absence/asymptomatic congestive heart failure).

An attrition analysis was carried out to examine and compare the nonparticipants (n=1099) with the participants. The nonparticipants recruited at baseline dropped out for various reasons like death or migration (data not shown).

Study II

Simple linear regression analysis was performed by including men and women aged 60–64 years as a reference population. KH- and demispan-based equations specific for men and women were formulated with measured height as the dependent variable (Y) and KH (X_1) or demispan (X_2) as the independent variable, respectively. The equations obtained were based on the following formula: $Y = \text{Constant} + B_i * X_i + \text{error term}$, $i=1, 2$. The constants, as well as the slopes B_1 and B_2 , were estimated. The equations were then applied to other age groups to calculate the predicted height based on KH and demispan at different ages. The analysis was conducted among the two sub population groups (Figure 6) where the groups had valid KH (group I) and demispan (group II) measurements respectively. Using the height prediction equations specific for men and women and the data on body weight, KH-BMI and demispan-BMI were calculated. The prevalence of underweight ($\text{BMI} \leq 20$) and obesity ($\text{BMI} \geq 30$) based on BMI

values obtained by using the classic method versus the predicted method, independently versus KH and demispan were presented.

Study III

Age- and sex specific proportional hazard regression models were formulated. The model was adjusted for explanatory variables namely marital status, residence, education, smoking, physical activity and number of diagnosed medical conditions. The respective reference groups for the variables included: BMI levels: normal/underweight BMI level, age 60–69 years, married status, urban residence, university or higher education level, non-smoker, heavy physical activity. Critical p value ≤ 0.01 , * $P \leq 0.05$. Based on the WHO guidelines of categorizing BMI levels, we organized our study population in four categories:

Underweight: $\text{BMI} < 18.5 \text{ kg/m}^2$,

Normal: $18.5 \leq \text{BMI} < 25 \text{ kg/m}^2$,

Overweight: $25 \leq \text{BMI} < 30 \text{ kg/m}^2$, and

Obese: $\text{BMI} \geq 30 \text{ kg/m}^2$.

With only 32 participants (1%) in the underweight group, i.e., $\text{BMI} < 18.5 \text{ kg/m}^2$, this category and the normal BMI category were merged.

All tests that were performed with the category of subjects that included both normal and underweight groups were also tested excluding the underweight group. No difference was observed in the results obtained (Results not shown).

Study IV

The population included all individual from age cohort 60 and 81² that had three different years of birth (Figure 8). In other words, there were two groups of age cohort 60 and 80 respectively. Within each age category, there were three independent groups of individuals having different year of birth forming three birth cohorts. In our study, the birth years of the different birth cohorts of the two age categories were as follows:

Age cohort 60: 1941–43, 1947–49, 1952–54;

² As mentioned earlier, the age cohort 81 also included individuals from age cohort 84 aiming to improve the sample power

Age cohort 81: 1920–22, 1926–28, 1932–33.

Within each age category, the earliest birth cohort were participants from the GÅS baseline examination conducted in year 2001. The intermediate birth cohort included individuals from GÅS 6-year follow-up examination conducted in year 2007 and the latest birth cohort comprised participants GÅS 12-year follow-up examination conducted in year 2013 (table 1). Comparisons were made mainly between earliest (examination 2001) and latest (2013) birth cohorts to achieve a maximum span of 12 years between the groups.

Comparisons were made between the earliest and latest birth cohorts independently among the two age cohorts (60 years and 81 years). $P \leq 0.05$ was considered statistically significant. Abdominal obesity categorization was done based on standard sex specific WC cut-off values (WC ≥ 102 cm (men); ≥ 88 cm (women)) [192].

One way analysis of variance test was used in two settings: 1) to test the differences in the mean values of the all the anthropometric measures across the three birth cohorts independently for 60-year-olds and 81-year-olds and 2) to test the difference in the mean WC across the three birth cohorts independently for 60-year-olds and 81-year-olds stratified based on the obesity-related factors such as education, diet smoking, alcohol, and physical activity.

All analytical tests were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp 2013, Armonk, NY, USA) was used. A p-value of < 0.05 was considered statistically significant.

Ethical considerations

All the studies included in this thesis were approved by the regional Ethics Committee of Lund University, Sweden, Registration number, LU 744-00 and were conducted in accordance with the Declaration of Helsinki. All the subjects³ gave their informed consent to participate in the study and allowing retrieval of information from the National Patient Registry, medical records. The applications for ethical review were drawn up during the primary phases of project planning. The principal investigator, Dr Sölve Elmståhl has been solely responsible for this process.

Research fraud and misconduct are interchangeably used terminologies often describing an inappropriate research process or a falsified research product. In fraud, there is a conscious act of self-servingness or intention to falsify, fabricate, plagiarize or cheat. On the other hand, in misconduct, there is intentional or unintentional lack of proper management of the research process, where participants or others involved can be exposed to unnecessary and/or unacceptable hazards.

All our study participants were properly informed about the study aims, objectives and methodology, as well as what their participation would or could entail. This information was also given to relatives if the participant wished to, for example in case of cognitive or memory difficulties. The study was conducted in a way that participants were not exposed to risk of physical, mental or integrity harm. The collected data was handed according to the established privacy rules in the Swedish health sector and academia. The anonymity of collected data was assured through the use of serial number specific for each individual and data extraction from the database was done using this serial number. No names, addresses or personal identification number was distributed for research purposes but however, the personal identification number that was noted during data collection was preserved with access provided authorized personnel in the research team. In addition, the study was intended to provide both direct and indirect benefits to its participants through nutritional and general lifestyle guidance as well as through an expected improvement in body composition analysis/anthropometric practices

³ Or informants (mostly relatives, if subjects could not themselves offer the consent, as in case of cognitive or memory difficulties)

and understanding, which can lead to improved individual and public health guidance.

None of the researchers have had conflicts of interest pertaining to our study. The project GÅS, a part of SNAC, was supported by the Swedish Ministry of Social Affairs, the county Region Skåne, the Medical faculty at Lund University and the Vårdal Institute. All the co-authors of the published studies have made significant contribution to the study conception, design, data collection, analysis, authorship and/or peer review, according to the standard publication practices.

Results

Anthropometric reference values

Results from Study I

Table 4 presents the normative anthropometric assessment of body composition. The age-related changes in height and BMI are depicted pictorially for men and women (figure 10a, 10b, 11a, 11b).

Age and sex specific investigation of anthropometrics showed that the mean BMI was $27.5 \pm 5.8 \text{ kg/m}^2$ among men and $27.2 \pm 8.1 \text{ kg/m}^2$ women. Weight differences among men aged 60–69 year olds and over 80 years was approximately 10kg and among women similar comparison showed a difference of approximately 2.5 kg between age 60–69 years and 80–84 years with a broader difference in weight by approximately 9kg with women aged above 85 years. Maximum BMI was at 65–69 years in men (28.4 kg/m^2) and 75–79 years (29.7 kg/m^2) in women. Lowest was among the oldest age group (above 85 years) in both the sexes. The mean SST, arm- and calf circumferences and AMC significantly declined with age in both sexes.

Underlying medical conditions

Age- and gender-adjusted regression model to compare anthropometric measures among elderly aged ≥ 60 years with and without the underlying medical condition (Table 5). It was found that among the other measures, there was higher BMI and waist circumference among men with MI and CHF. Men with dementia had significantly lower weight by $7.9 \pm 0.2 \text{ kg}$, subscapular and triceps skinfold thickness and calf circumference. In women with dementia, in addition to a weight difference of $11.3 \text{ kg} \pm 4.7 \text{ kg}$, there was a lower BMI by $3.6 \pm 1.9 \text{ kg/m}^2$. Subjects with ADL dependence, particularly women, showed significantly higher values of BMI (by $\sim 3.0 \pm 3.9 \text{ kg/m}^2$) and waist circumference and lower skinfold measurement. Stroke patients had higher weight and waist circumference. The age- and gender-adjusted linear regression coefficient for every anthropometric variable among those diagnosed with the medical condition compared with their respective reference groups is shown in table 6. Presence of dementia showed a

significant negative relationship with weight, BMI, hip-, arm- and calf circumferences. Stroke patients on the other hand presented with a positive association with weight and waist circumference. MI cases presented significantly higher value with respect to weight, BMI, waist-, hip-, arm circumferences and SST compared with their healthier counterparts. Similar positive association at further higher rate was observed among CHF cases.

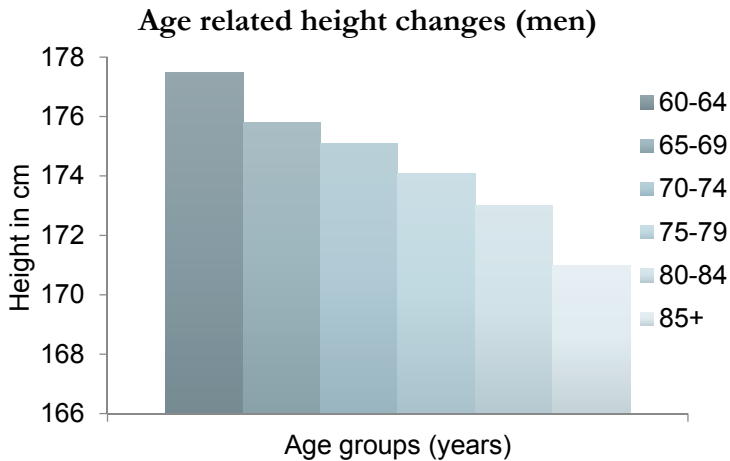


Figure 10a: Mean height estimates specific for the different age groups among men

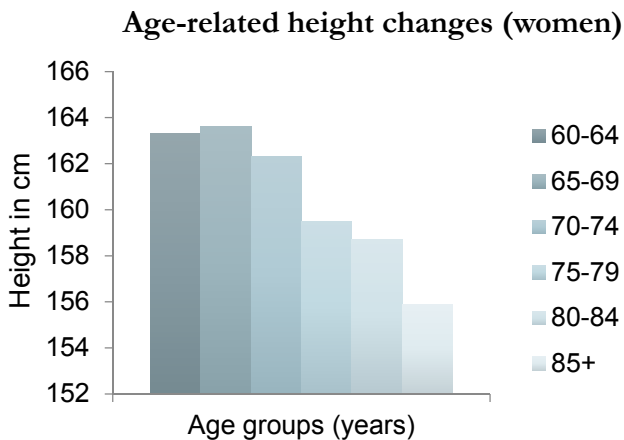


Figure 10b: Mean height estimates specific for the different age groups among women

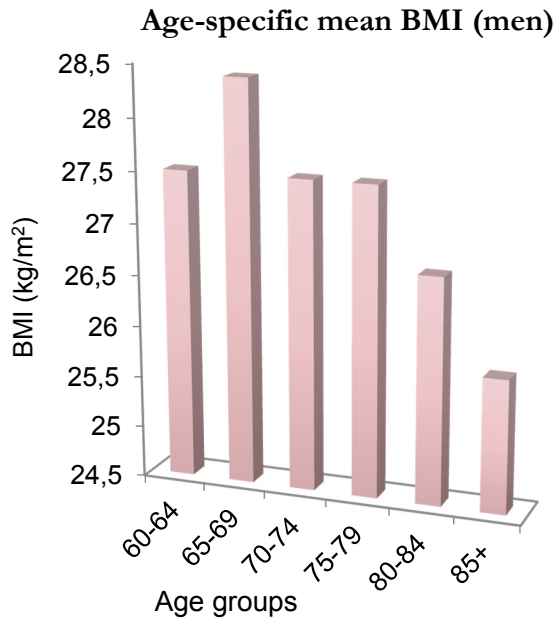


Figure 11a: Age-specific mean BMI estimates (height measured using classic method) among elderly men

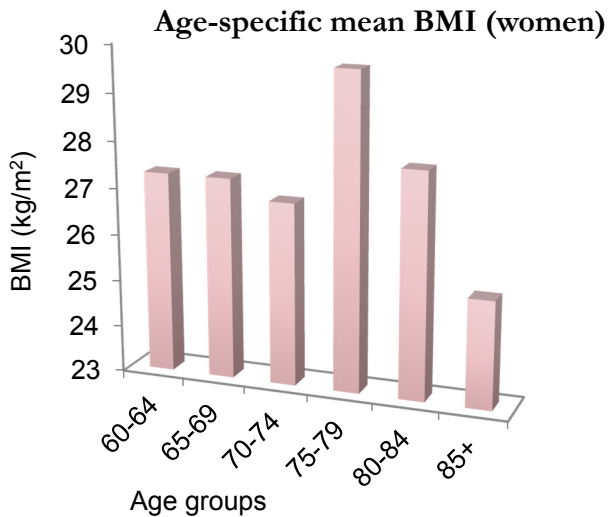


Figure 11b: Age-specific mean BMI estimates (height measured using classic method) among elderly women

Table 4: The normative anthropometric assessment of body composition for Swedish elderly men and women aged over 60 years. Mean, Standard deviation and 10th, 25th, 50th, 75th, 90th percentiles of anthropometric measurements among elderly men and women aged ≥ 60 years.

Men (n= 1491)										
Anthropometric measures		Age	n	mean	SD	10	25	50	75	90
Height* (cm)		60-64	442	177.5	6.7	169.0	173.3	177.9	182.0	185.3
		65-69	289	175.8	9.3	167.8	171.6	176.2	180.4	184.2
		70-74	231	175.1	6.3	166.7	171.6	175.0	179.0	183.0
		75-79	73	174.1	7.1	166.0	170.0	173.0	177.0	182.0
		80-84	172	173.0	6.5	165.0	169.1	173.1	177.0	181.0
		≥ 85	112	171.0	7.1	161.5	166.0	170.9	176.7	179.9
	All	1319	175.4	7.6	166.5	171.0	175.6	180.0	184.0	
Weight (kg)*		60-64	433	86.9	14.1	69.8	77.2	85.4	95.3	104.6
		65-69	280	86.9	15.3	70.3	76.7	85.5	95.4	108.3
		70-74	228	84.3	13.0	69.7	76.5	81.7	90.9	100.5
		75-79	70	83.7	11.8	70.0	74.7	82.7	90.8	97.7
		80-84	172	79.9	11.8	65.2	72.2	78.9	86.0	95.7
		≥ 85	107	75.5	11.8	58.4	68.1	75.5	82.9	90.1
	All	1290	84.4	14.1	68.5	75.1	82.6	92.2	102.7	
BMI (kg/m²)*		60-64	432	27.5	4.0	23.2	24.9	27.0	29.9	32.3
		65-69	276	28.4	9.9	23.2	25.1	27.3	30.2	34.4
		70-74	228	27.5	3.9	23.2	25.0	26.8	29.6	32.0
		75-79	66	27.5	3.2	23.6	25.5	27.4	29.3	32.0
		80-84	169	26.7	3.5	22.7	23.9	26.4	29.2	31.6
		≥ 85	106	25.8	3.7	21.3	22.8	25.4	28.7	30.9

	All	1277	27.5	5.8	22.9	24.7	26.9	29.6	32.3	
Waist circumference (cm)	60-64	449	99.2	12.2	85.2	92.0	97.5	106.0	114.6	
	65-69	304	101.5	12.9	87.0	93.0	100.0	109.0	118.5	
	70-74	237	99.4	12.8	87.0	92.3	99.0	106.0	113.1	
	75-79	84	100.3	10.5	89.0	94.2	100.3	105.9	112.8	
	80-84	173	99.4	10.3	86.4	92.2	98.5	106.8	112.9	
	≥85	107	97.3	10.4	83.9	90.2	98.0	105.0	111.6	
	All	1354	99.7	12.0	86.1	92.5	99.0	106.3	114.6	
Hip circumference (cm)	60-64	449	100.7	9.3	92.0	96.4	100.5	105.4	110.0	
	65-69	304	101.7	9.4	93.0	96.0	101.0	106.2	112.8	
	70-74	237	102.1	8.1	93.4	97.0	101.1	106.1	112.7	
	75-79	84	102.7	7.4	94.7	98.1	101.1	106.9	114.4	
	80-84	171	102.8	7.0	93.8	98.0	102.4	107.9	112.0	
	≥85	107	101.5	7.4	92.4	96.7	101.0	106.0	110.2	
	All	1352	101.6	8.6	93.0	97.0	101.0	106.0	111.7	
Waist:hip ratio	60-64	449	1.00	.47	.90	.94	.98	1.02	1.08	
	65-69	304	.999	.10	.92	.95	.99	1.03	1.08	
	70-74	237	.97	.09	.90	.94	.97	1.01	1.06	
	75-79	84	.98	.08	.90	.94	.97	1.03	1.08	
	80-84	171	.97	.07	.89	.93	.97	1.00	1.04	
	≥85	107	.96	.08	.86	.91	.96	1.02	1.07	
	All	1352	.98	.28	.90	.94	.98	1.02	1.07	
Triceps skinfold thickness* (mm)	60-64	449	17.0	10.2	6.4	9.3	14.2	21.5	34.0	
	65-69	304	13.5	7.4	6.4	8.4	11.7	16.2	23.5	
	70-74	235	13.2	6.1	7.2	9.0	11.9	16.0	21.8	
	75-79	79	12.5	5.9	6.2	8.0	11.2	15.8	19.5	
	80-84	176	11.8	5.0	6.5	8.4	11.2	14.4	19.2	
	≥85	112	11.0	5.5	5.4	7.3	10.9	13.2	17.6	
	All									

	All	1355	14.1	8.1	6.4	8.6	12.0	16.9	25.0
Subscapular skinfold thickness* (mm)	60-64	445	20.6	7.8	12.0	15.0	19.8	25.2	32.1
	65-69	305	20.4	9.3	11.6	14.4	19.0	23.95	32.5
	70-74	237	19.2	8.1	11.1	14.0	18.0	22.8	29.5
	75-79	80	17.8	6.2	10.6	13.9	17.3	21.7	24.7
	80-84	174	18.2	6.8	10.4	13.2	17.0	22.1	27.3
	≥85	110	14.97	5.7	7.8	11.2	14.6	18.7	21.8
	All	1351	19.4	8.0	11.0	14.0	18.2	23.2	30.0
Arm circumference* (cm)	60-64	450	31.1	3.1	27.4	29.2	31.0	33.0	35.3
	65-69	304	31.3	3.1	27.6	29.3	31.0	33.0	36.0
	70-74	236	30.3	2.9	27.0	28.9	30.2	32.0	34.0
	75-79	83	29.6	2.3	26.3	28.0	29.8	31.0	32.5
	80-84	178	28.7	2.6	25.5	26.8	28.7	30.6	32.0
	≥85	115	27.1	3.1	23.0	25.0	27.0	29.0	30.6
	All	1366	30.3	3.3	26.2	28.0	30.2	32.0	34.0
Calf circumference* (cm)	60-64	449	38.4	2.99	35.0	36.5	38.4	40.0	42.0
	65-69	305	38.2	4.5	33.96	35.5	37.6	40.0	42.1
	70-74	238	37.3	2.8	33.0	35.5	37.0	39.0	40.9
	75-79	84	36.7	2.5	33.5	35.1	36.5	38.4	40.1
	80-84	178	36.7	8.3	31.97	34.4	36.2	38.4	40.1
	≥85	115	34.5	3.8	30.4	32.5	34.4	36.6	39.0
	All	1369	37.5	4.5	33.3	35.3	37.3	39.5	41.5

Age	n	mean	SD	10	25	50	75	90
60-64	449	25.7	3.5	20.9	23.7	25.9	28.0	30.2
65-69	304	27.1	2.9	23.2	25.6	27.3	28.8	30.8
70-74	235	26.2	2.8	22.8	24.7	26.4	27.9	29.0
75-79	79	25.6	2.5	22.7	24.5	25.9	27.4	28.4
80-84	176	24.95	2.3	22.3	23.4	24.9	26.6	27.8
≥85	112	23.6	2.8	19.7	21.8	23.6	25.4	26.7
All	1355	25.8	3.2	21.7	23.9	25.9	27.9	29.6

* P < 0.05, statistically significant difference of mean values across age groups (analysis of variance).

Women (n= 1869)									
Anthropometric measures		n	mean	SD	10	25	50	75	90
Height* (cm)		502	163.3	6.4	155.6	158.8	163.2	168.0	171.3
		323	163.6	5.95	156.0	159.1	163.5	168.2	171.7
		239	162.3	5.8	155.0	158.0	162.3	166.0	170.0
		103	159.5	5.6	152.5	154.9	159.8	163.7	166.6
		226	158.7	5.9	152.4	155.5	159.0	162.3	166.1
		210	155.9	6.6	148.0	152.0	155.0	160.2	163.6
All		1603	161.4	6.7	153.0	157.0	161.3	166.0	170.0

Weight (kg)*	60-64	495	72.6	14.1	56.5	63.0	70.8	80.0	90.0	
	65-69	308	73.0	14.1	57.5	64.3	71.0	80.6	90.1	
	70-74	236	71.1	13.3	56.2	61.4	69.3	78.9	90.1	
	75-79	100	75.1	39.7	56.5	63.4	68.6	77.8	88.6	
	80-84	222	70.0	32.3	55.7	60.2	67.8	75.5	82.1	
	≥85	210	61.7	12.0	46.5	52.7	61.0	69.8	76.5	
	All	1571	70.8	20.2	54.8	61.0	68.9	77.9	87.9	
	BMI (kg/m²)*	60-64	493	27.3	5.3	21.6	23.4	26.4	30.2	34.1
		65-69	302	27.3	5.2	21.7	23.6	26.7	29.7	33.6
		70-74	235	26.9	4.9	21.5	23.3	26.5	30.3	33.5
75-79		98	29.7	16.9	22.6	24.6	27.4	31.7	34.8	
80-84		220	27.8	13.6	21.9	23.9	26.8	29.7	33.0	
≥85		205	25.3	4.6	19.5	22.2	25.0	28.4	31.1	
All		1553	27.2	8.1	21.4	23.5	26.4	29.7	33.4	
Waist circumference (cm)		60-64	518	89.6	13.1	73.5	80.0	88.5	97.1	107.0
		65-69	355	91.0	14.3	74.5	81.0	91.0	99.0	108.5
		70-74	253	90.8	13.5	74.0	80.0	90.0	100.0	109.0
	75-79	109	91.9	12.8	76.0	82.6	91.2	99.0	109.0	
	80-84	223	90.3	11.2	76.0	82.6	89.1	98.0	105.8	
	≥85	210	87.5	11.6	73.0	79.4	87.3	94.0	102.0	
	All	1668	90.1	13.0	74.5	80.2	89.2	98.0	107.0	

Hip circumference (cm)	60-64	517	103.7	11.6	91.0	96.2	102.0	109.6	117.0	
	65-69	355	104.3	11.2	91.6	97.0	103.0	110.0	119.0	
	70-74	253	104.6	11.6	92.0	97.5	103.6	111.0	119.2	
	75-79	108	105.0	10.0	93.0	99.0	104.0	109.8	116.1	
	80-84	224	104.4	9.4	93.5	98.0	103.0	110.7	115.5	
	≥85	209	100.5	12.3	89.0	94.9	100.8	107.1	113.5	
	All	1666	103.7	11.3	91.5	97.0	102.8	110.0	117.0	
	Waist:hip ratio	60-64	517	.86	.07	.77	.81	.86	.907	.954
		65-69	355	.87	.10	.77	.82	.86	.917	.957
		70-74	253	.87	.10	.76	.82	.86	.914	.967
75-79		108	.87	.08	.79	.82	.86	.912	.975	
80-84		223	.87	.08	.78	.81	.86	.914	.972	
≥85		209	.91	.59	.77	.81	.86	.911	.980	
All		1665	.87	.23	.77	.82	.86	.911	.962	
Triceps skinfold thickness- * (mm)		60-64	516	23.8	7.9	13.9	18.0	23.0	29.2	35.6
		65-69	352	21.4	7.3	12.5	16.0	20.5	25.2	31.7
		70-74	248	20.6	6.8	12.6	15.8	19.9	24.8	30.0
	75-79	110	18.9	6.1	12.2	15.2	18.3	22.1	26.7	
	80-84	222	18.3	6.7	9.8	13.9	17.7	22.8	27.3	
	≥85	212	16.2	6.7	8.9	12.0	15.0	19.8	24.8	
	All	1660	20.8	7.7	11.7	15.2	20.0	25.2	31.5	
	Subscapular Skinfold thickness- * (mm)	60-64	510	21.4	8.4	11.4	15.4	20.2	26.4	34.0
		65-69	353	20.7	8.6	10.8	14.4	19.8	24.9	35.4
		70-74	250	20.7	8.4	11.0	14.2	19.8	26.3	32.0
75-79		109	18.2	8.2	9.8	13.2	16.7	21.6	28.0	
80-84		220	18.1	8.4	9.0	12.0	17.1	22.3	31.0	
≥85		210	14.3	6.4	6.8	10.0	13.4	17.8	21.49	
All		1652	19.6	8.5	10.0	13.2	18.2	24.2	32.0	

Arm circumference* (cm)	60-64	520	29.8	3.6	25.4	27.2	29.5	31.9	34.5	
	65-69	355	30.5	3.8	26.0	28.0	30.0	32.5	35.0	
	70-74	252	29.8	3.9	25.4	27.0	29.5	32.1	34.8	
	75-79	110	29.1	4.0	24.1	26.9	28.8	31.2	34.0	
	80-84	228	28.6	4.7	24.5	26.4	28.5	30.5	33.0	
	≥85	218	26.8	3.7	22.0	24.4	26.7	29.1	31.6	
	All	1683	29.3	4.1	25.0	27.0	29.0	31.5	34.0	
	Calf circumference* (cm)	60-64	520	37.4	4.9	33.2	35.0	37.0	39.2	41.3
		65-69	357	36.9	3.5	33.0	34.5	37.0	38.95	41.0
70-74		253	36.6	3.5	32.9	34.4	36.2	39.0	40.5	
75-79		111	36.4	3.3	32.3	34.0	36.0	38.4	41.0	
80-84		226	35.5	3.4	31.0	33.5	35.5	37.6	39.4	
≥85		217	33.4	4.5	28.4	31.0	33.5	36.0	38.5	
All		1684	36.3	4.3	32.0	34.0	36.2	38.5	40.5	
Arm muscle circumference* (cm)		60-64	516	22.3	3.3	18.4	20.1	22.1	24.2	26.6
		65-69	352	23.8	3.1	20.1	21.6	23.7	25.6	28.0
	70-74	248	23.2	2.7	20.2	21.4	23.1	24.7	26.9	
	75-79	109	23.1	3.6	19.5	21.2	23.1	24.5	26.4	
	80-84	222	22.9	4.2	19.4	20.9	22.6	23.9	25.9	
	≥85	212	21.7	2.8	18.4	20.2	21.5	23.6	25.3	
	All	1659	22.8	3.3	19.1	20.9	22.7	24.5	26.6	

* P < 0.05, statistically significant difference of mean values across age groups (analysis of variance).

Table 5: Mean anthropometric measurements for elderly aged ≥ 60 years with co-morbidities

Men											
	Height (cm)	Weight (kg)	BMI (kg/m ²)	Waist (cm)	Hip (cm)	WHR	TSF (mm)	SSF (mm)	Arm Cir (cm)	Calf Cir (cm)	AMC (cm)
Myocardial infarction	174.1*	86.7*	28.6*	103.0*	103.3*	1.00	14.4	21.0*	30.4	37.4	25.9
	175.5	84.1	27.3	99.3	101.4	0.99	14.1	19.2	30.3	37.5	25.8
Stroke	173.6	83.7	27.7	101.1	102.7	0.98	13.7	19.4	29.7	36.5*	25.4
	175.4	84.4	27.5	99.7	101.6	0.99	14.2	19.4	30.3	37.5	25.9
Dementia	173.8*	76.9*	25.5	98.2	101.1	0.96	11.4*	16.5*	27.8	34.8*	24.3*
	175.6	84.8	27.5	99.8	101.7	0.99	14.4	19.6	30.4	37.5	25.9
ADL Dependence	173.3*	80.0*	26.6	99.2	102.0	0.97	13.2*	18.1	29.1	35.9*	25.0
	174.6	83.6	27.3	100.6	102.1	0.99	12.6	18.5	29.6	37.3	25.7
	176.1	85.4	27.7	99.5	101.5	0.99	14.6	19.9	30.7	37.8	26.1
Cognitive impairment	172.0*	80.8	27.2	99.2	101.7	0.98	13.0*	17.5*	29.2*	36.5*	25.1*
	176.0	85.1*	27.6	99.8	101.6	0.99	14.4	19.8	30.5	37.7	26.0

CHF	173.3*	86.5	28.8*	106.4*	105.8*	1.0	13.8	20.1	30.2*	37.1	25.5
	175.5	84.2	27.3	99.1	101.3	0.99	14.2	19.3	29.3	37.5	25.9
Symptomatic											
Abs/.Asymptomatic											

Women

	Height (cm)	Weight (kg)	BMI (kg/m ²)	Waist (cm)	Hip (cm)	WHR	TSF (mm)	SSF (mm)	Arm Cir (cm)	Calf Cir (cm)	AMC (cm)
Myocardial infarction	158.4*	70.2	27.7	92.6	105.2	0.88	20.7	19.0	28.7	35.6	22.3
	161.5	70.8	27.1	89.9	103.7	0.87	20.8	19.6	29.4	36.4	22.8
Stroke											
Yes	159.6*	71.0	27.9	93.0	105.9	0.88	20.1	18.9	29.6	35.4	23.4
No	161.5	70.8	27.2	90.0	103.6	0.87	20.8	19.6	29.3	36.4	22.8
Dementia											
Yes	157.6*	59.5*	23.7*	86.9*	96.4*	1.1*	16.1*	15.1*	27.1*	32.9*	22.1
No	161.7	71.2	27.3	90.0	103.8	0.9	21.0	19.8	29.4	36.5	22.8
ADL											
Dependence	158.0*	72.3	29.0*	90.1*	104.0*	0.87	19.2*		28.1*	35.4*	22.1*
iADL	160.6	72.1	28.0	92.4	105.4	0.86	20.3	17.7*	29.8	36.1	23.4
pADL	162.5	70.1	26.5	88.6	102.6	0.87	21.2	20.1	29.2	36.6	22.5
Independent							19.7				

Cognitive impairment Yes No	157.8*	68.1*	27.3	91.4	103.3	0.92*	20.9	19.6	29.5*	36.7*	22.6
	162.2	71.8	27.3	89.9	103.9	0.87	21.1	19.8	28.9	35.2	22.9
CHF Symptomatic Abs/.Asymptomatic	158.2*	72.9	28.9*	95.6*	108.8*	0.88	19.8	19.5	30.2*	35.8	23.7*
	161.7	70.6	27.0	89.6	103.2	0.87	20.9	19.6	29.2	36.4	22.7

* $p < 0.05$ denotes significant difference of mean anthropometric values between the risk and reference groups in each co-morbidity (analysis of variance). CHF: Congestive heart failure Cir: circumference, ADL: activities of daily life, TSF: triceps skinfold thickness SSF: subscapular skinfold thickness, AMC: arm muscle circumference. Abs/No: Absence of the disease/condition; Yes: presence of the condition.

Table 6: Age and gender adjusted regression model to compare anthropometric measures among Swedish elderly ≥ 60 years with and without co-morbidities.

	Height (cm)	Weight (kg)	BMI (kg/m ²)	Waist (cm)	Hip (cm)	WHR	Skinfold triceps (mm)	Skinfold subscapular (mm)	Arm Circum (cm)	Calf Circum (cm)	AMC (cm)
Myocardial infarction	-0.8	2.8*	1.1*	3.6**	1.7*	0.01	1.5**	2.0**	0.5*	0.3	0.1
Stroke	-0.5	1.5	0.7	2.5*	1.6	0.003	0.8	0.7	0.5	-0.4	0.3
Dementia	-0.1	-6.3**	-2.5**	-1.4	-4.0*	0.14	-1.4	-1.3	-0.8	-1.6**	-0.4
ADL											
Dependence											
iADL	-1.3**	1.7	1.2*	1.5	1.6*	-0.01	0.3	0.3	-0.1	-0.49	-0.2
pADL	-0.4	2.8	1.2**	3.3**	2.3**	0.01	-0.3	0.8*	0.6**	0.72	0.7**
Cognitive impairment§	-2.8**	-2.0	0.1	1.15	-1.1	0.03	0.25	0.35	-0.07	-0.6**	-0.2
Congestive heart failure	-0.3	7.2**	2.6**	8.2**	6.1**	0.01	1.8**	2.9**	1.8**	0.9**	1.1**

* $p < 0.05$. ** $p < 0.01$, § Mini Mental State Examination (MMSE) score below 24; Reference group: no myocardial infarction, stroke, dementia, independence in ADL, dementia and absence/asymptomatic, congestive heart failure. Circum: circumference, ADL: activities of daily life, AMC: arm muscle circumference.

BMI misclassification

The BMI estimates in the different age groups as observed in study I were tested further to investigate the consequences of the errors from estimating height in the elderly.

Results from Study II

Prediction equations formulated using KH and demispan were as below.

KH-based equations:

Men: *Predicted height based on KH (cm) = 115.23 + 1.16 x KH (cm);*

Women: *Predicted height based on KH (cm) = 104.52 + 1.23 x KH (cm).*

Demispan-based equations:

Men: *Predicted height based on demispan (cm) = 49.41 + 1.4x demispan (cm);*

Women: *Predicted height based on demispan (cm) = 36.34 + 1.53x demispan (cm).*

Height predicted using KH was higher than measured height in both sexes and the difference tends to increase with age. Consequently, KH-BMI was lower than BMI among each age group in both sexes. The difference between classic BMI and KH-BMI was 0.45 kg/m² among men and 0.98 kg/m² among women.

Comparison of the prevalence of underweight (BMI ≤ 20) and obesity (BMI ≥ 30) was done based on BMI values obtained by using the classic method versus the predicted method, independently versus KH and demispan (Table 7). Such difference can be appreciated from figures 12 and 13. The differences between underweight prevalence with respect to comparison of KH-BMI and classic BMI classification (green and yellow bars in the figures 12 and 13) was 5.4% and 8.6% respectively, among women. There was general underestimation of underweight by the classic BMI classification. Similar comparison with demispan and classic methods (dark and light blue bars) showed that it was 10.0% (classic BMI) versus 16.5% (demispan based BMI) indicating a significant underestimation of underweight.

The KH-BMI also indicated higher prevalence of underweight than classic BMI. Underweight prevalence is twice as high in 80–84 and over 85 years of age

compared with BMI assessment. Women aged over 85 years have underweight prevalence of 21.3% by KH-BMI compared with 11.3% by BMI.

DS-BMI showed a slightly higher value (2.1%) than classic BMI (1.5%) among the 65–69 year old men. The other groups showed little or no differences. However, among women aged over 85 years, there is 16.5% underweight by DS-BMI compared with 10% by BMI.

Table 7: Distribution of the prevalence of undernutrition (BMI ≤ 20) and obesity (BMI ≥ 30) classified using classic, knee height-based and demispan-based BMI among Swedish elderly men and women aged ≥ 60 years.

Sex	Age	Group I				Group II			
		Classic BMI	KH-BMI	Classic BMI	DS-BMI	Classic BMI	KH-BMI	Classic BMI	DS-BMI
		≤ 20	≥ 30	≤ 20	≥ 30	≤ 20	≥ 30	≤ 20	≥ 30
Men	60-64	1.9	24.2	2.5	26.1	1.2	20.4	1.0	18.4
	65-69	1.8	20.6	1.8	20.6	1.5	22.0	2.1	24.7
	70-74	1.5	20.6	1.6	21.1	0.8	20.2	0.8	19.8
	75-79	1.7	15.8	2.5	12.5	0	13.6	0	13.6
	80-84	2.7	16.5	5.9	7.4	1.0	16.7	1.0	10.9
	≥ 85	5.6	8.0	11.7	4.9	3.0	12.7	3.7	9.0
	All	2.4	19.0	3.9	17.5	1.3	19.1	1.4	17.1
Women	60-64	4.9	21.1	4.9	19.7	2.9	21.7	3.0	21.2
	65-69	2.6	23.3	2.3	21.9	3.3	19.6	2.5	19.6
	70-74	3.7	26.2	3.7	17.1	3.3	22.9	4.8	20.3
	75-79	6.9	24.3	8.3	16.7	1.7	24.6	2.5	18.2
	80-84	2.9	19.9	9.0	10.3	4.6	18.5	5.4	12.7
	≥ 85	11.3	10.4	21.3	3.7	10.0	12.7	16.5	6.5
	All	5.4	20.0	8.6	14.6	4.2	19.9	5.4	17.3

BMI: Body mass index; KH: knee height, DS: Demispan. Values entered in percentage. Group I: populations subgroup for KH analysis, Group I: populations subgroup for demispan analysis.

KH-BMI based obesity prevalence was 17.3% in men and 14.6% in women, which was lower than classic BMI based prevalence estimate with corresponding values namely, 19.9% and 20.0%. Among men, it is notable at 80–84 years of age and among women it is notable as early as 70–74 years of age (26.2% by BMI and 17.1% by KH-BMI). KH-BMI estimates among men aged 80–84 years (7.4%) are almost half of that estimated by BMI (16.5%). Over 85 years, the KH-BMI obesity prevalence is further lower (4.9%); that is, when BMI classifies 1 in 10 men as obese, it is 1 in 20 according to KH-BMI. In addition, when 2 in 10 women aged 80–84 years are obese by BMI, only 1 in 10 is according to KH-BMI.

Overall obesity prevalence estimated by DS-BMI was lower than that by BMI in both sexes. For example, the values were as follows: 16.7% by BMI vs 10.9% by DS-BMI among men aged 80–84 years. Among women aged 75–79 years, it was 24.6% by BMI vs 18.2% by DS-BMI. BMI-estimated obesity prevalence was almost twice that estimated by DS-BMI among the participants aged over 85 years, with small or no difference in younger groups.

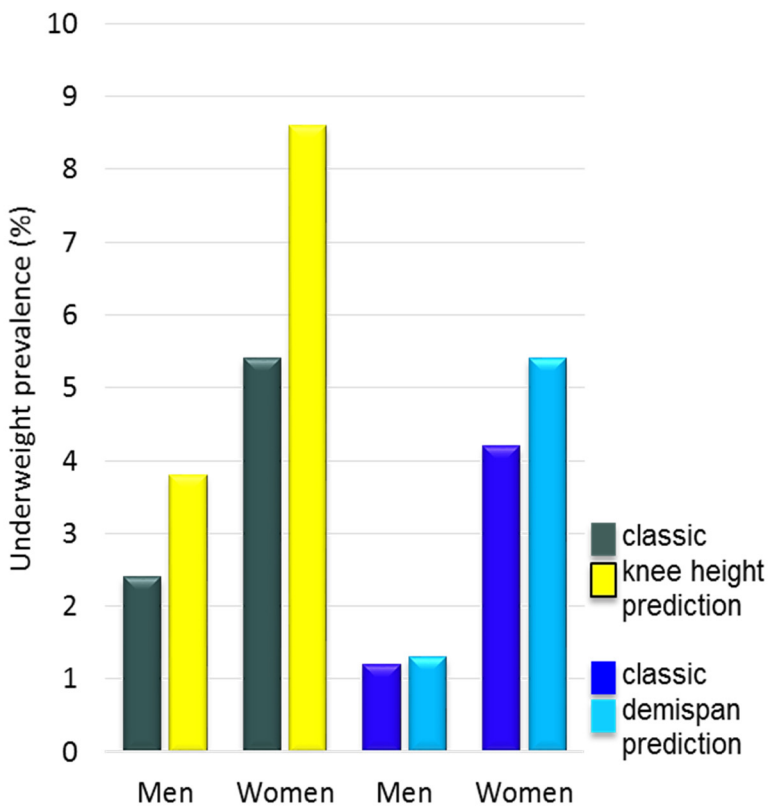


Figure 12: Comparison of underweight (BMI ≤ 20) prevalence estimated by classic method and prediction based on knee height and demispans.

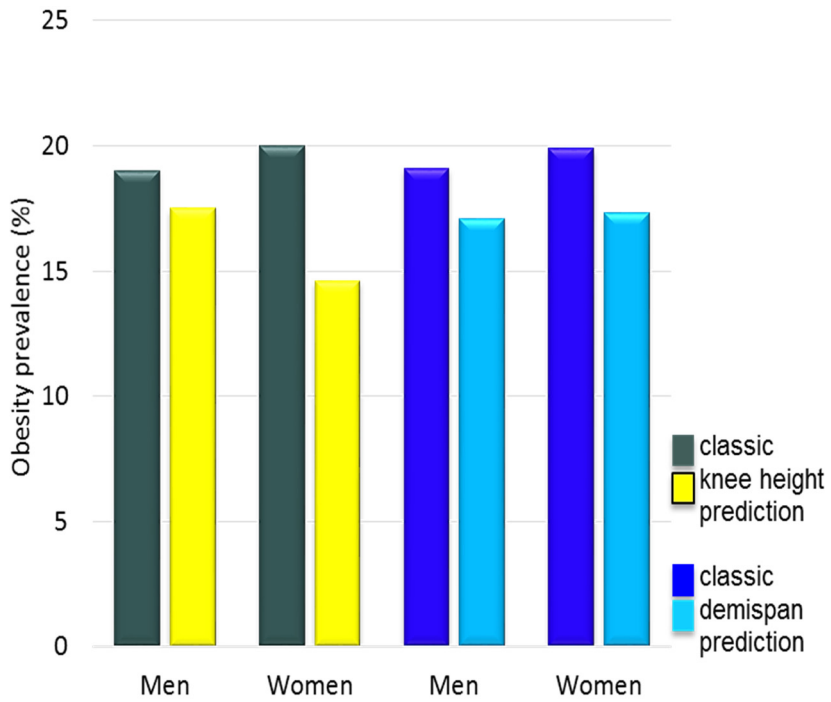


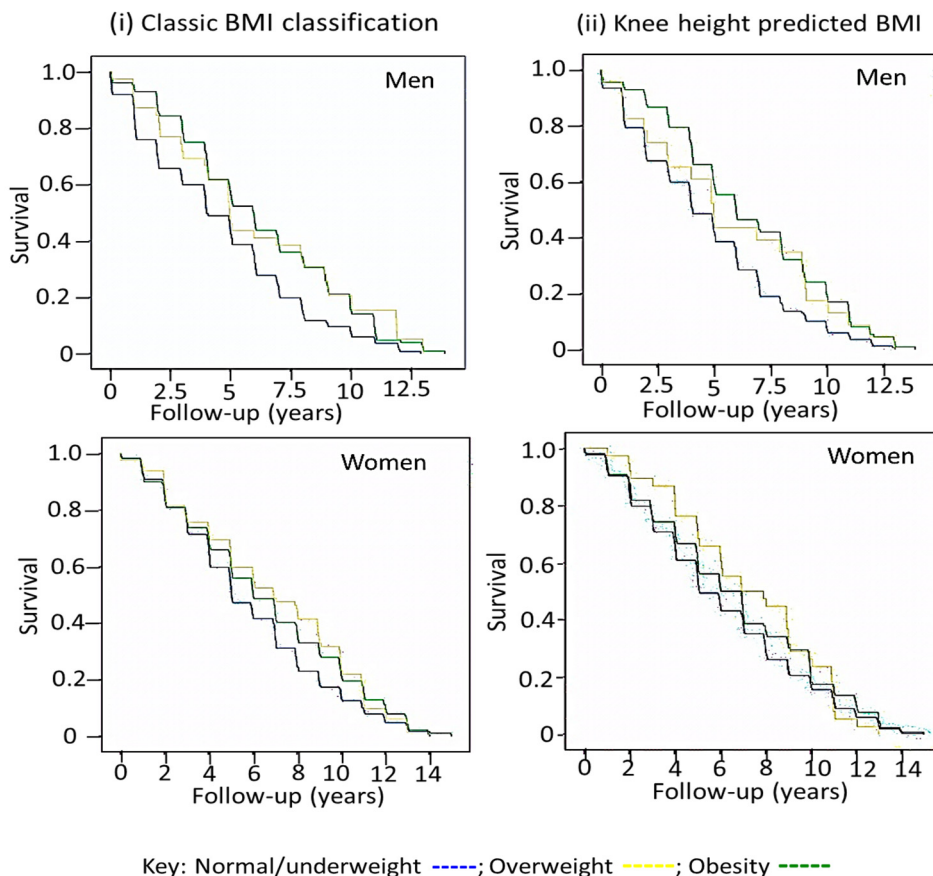
Figure 13: Comparison of obesity (BMI ≥ 30) prevalence estimated by classic method and prediction based on knee height and demispan

BMI and true survival benefits

Results from Study III

Irrespective of the method of BMI estimation, i.e., classical and KH-BMI, and after adjusting for confounders, namely, age, marital status, residence, education, smoking, physical activity, number of diagnosed medical conditions, there seems to be a lower mortality risk among overweight men (classic BMI: overweight: HR=0.72 (0.60–0.87); KH-BMI: overweight: HR=0.81 (0.67–0.97). and women (BMI: overweight: HR=0.87 (0.70–0.98); KH-BMI: overweight: HR=0.81

Figure 14: Kaplan Meier graphs demonstrating the survival function of BMI categories based on (i) classic and (ii) knee-height based prediction method among Swedish older adults aged 80 years and above.



(0.67–0.97). Among obese men, there was also a lower mortality risk according to classic BMI (HR=0.71 (0.56–0.93)) but not reaching statistical significance by KH-BMI (HR=0.81 (0.61–1.06)). The number of cases of death within the different weight categories classified by both classic and KH method are shown in Table 8.

According to the classic BMI, in comparison with the reference group (normal/underweight BMI) there is a lower mortality risk, in overweight men and women (men: HR=0.67 (0.52–0.87); women: HR=0.79 (0.64–0.97)) and obese men (HR=0.60 (0.41–0.89)) aged ≥ 80 years. According to KH-BMI, compared to the reference group a lower mortality risk was observed in overweight men and women (men: HR=0.71 (0.55–0.92); women: HR=0.77 (0.62–0.95)) aged ≥ 80 years. Obese men and women aged ≥ 80 years, irrespective of the method of BMI estimation, did not have an increased mortality risk. The survival benefit was however not statistically significant when using KH-BMI (Table 9). The difference in the survival function of the BMI categories in both the classic and KH (Figure 14).

Table 8: Total number of death events in the different BMI categories during the 15 year period of follow-up to the mortality. Cases distributed in the different BMI categories classified based on classic and knee height based BMI in men and women ≥ 60 years.

Cases of death N(%)	Classic BMI		Knee height based BMI	
	Men	Women	Men	Women
Reference group	217 (37.0)	301 (42.4)	271 (46.2)	413 (58.2)
Overweight	270 (46.1)	260 (36.6)	238 (40.6)	204 (28.7)
Obese	99 (16.9)	149 (21.0)	77 (13.1)	93 (13.1)

Reference group: Normal and underweight BMI category.

Table 9: Hazard ratios (HR) for all-cause mortality according to classic BMI and knee based BMI for the different age-groups among Swedish elderly men and women.

		Men		Women	
Age	KH-BMI categories	BMI mean (sd)	Adjusted HR (95% CI)	BMI mean (sd)	Adjusted HR (95% CI)
60-69years	Overweight	27.31 (1.41)	0.91 (0.61-1.37)	27.30 (1.43)	0.90 (0.54-1.50)
	Obese	33.43 (3.39)	0.94 (0.58-1.53)	33.46 (3.10)	0.97 (0.54-1.73)
70-79years	Overweight	27.10 (1.38)	0.84 (0.57-1.22)	27.22 (1.40)	0.88 (0.58-1.33)
	Obese	33.14 (4.18)	0.71 (0.41-1.22)	33.21 (3.41)	1.31 (0.81-2.13)
80+ years	Overweight	27.01 (1.41)	0.71 (0.55-0.92)*	27.19 (1.53)	0.77(0.62-0.95)§
	Obese	32.52 (5.06)	0.73 (0.46-1.15)	32.41 (2.51)	0.87 (0.61-1.25)
		Men		Women	
Age	Classic BMI categories	BMI mean (sd)	Adjusted HR (95% CI)	BMI mean (sd)	Adjusted HR (95% CI)
60-69years	Overweight	27.26 (1.41)	0.84 (0.56-1.26)	27.18 (1.44)	1.04 (0.61-1.77)
	Obese	33.30 (2.98)	0.71 (0.43-1.17)	33.65 (3.42)	1.14 (0.64-2.04)
70-79years	Overweight	27.16 (1.40)	0.71 (0.48-1.06)	27.28 (1.38)	0.94 (0.61-1.46)
	Obese	32.92 (4.11)	0.89 (0.53-1.48)	33.61 (3.46)	1.23 (0.78-1.95)
80+ years	Overweight	27.06 (1.34)	0.67 (0.52-0.87)§	27.17 (1.49)	0.79 (0.64-0.97)*
	Obese	32.85 (5.59)	0.60 (0.41-0.89)*	32.63 (2.90)	0.83 (0.63-1.09)

sd: standard deviation, BMI: Body mass index kg/m², HR: Hazard ratio. Adjusted for marital status, residence, education, smoking, physical activity, number of diagnosed medical conditions (myocardial infarction, stroke, diabetes, tuberculosis, asthma, chronic obstructive pulmonary disease, osteoporosis, hip fracture, arthritis, dementia, Parkinson's disease, depression and cancer). Reference groups: BMI levels: Normal/underweight, Age group: 60-69 years, marital status: married, urban residence, higher than secondary, non-smoker, heavy exercise. § p<0.01, *p<0.05.

Birth cohort effects on waist size, education and lifestyle

Analysis of extrinsic factors

Besides the primary analysis done in studies I-III, the pattern of distribution of sociodemographic and lifestyle factors provided a description of baseline characteristics of the study population. In general, an almost similar distribution of the sexes was seen, namely, 44.5% men and 55.5% women respectively. Table 10 depicts the distribution of the other extrinsic factors under study.

Table 10: Distribution of socio-demographic and lifestyle variables in the population samples in this thesis.

Extrinsic factors	Study I	Study II Group I	Study II Group II	Study III
Socio-demographic				
1. Married	58.6	53.6	58.3	54.6
2. At least primary education	40.6	51.7	41.4	51.0
3. Urban residence	68.7	63.0	68.7	64.0
Lifestyle				
4. Smoking*	15.2	16.9	15.4	17.1
5. Active alcohol drinkers**	69.6	59.2	69.4	Not estimated
6. Physical activity				
a. Mostly Sedentary	6.8	8.3	6.8	6.9
b. Moderate exertion [§]	26.5	24.9	26.4	25.5

All estimates in percentages; *Regular + irregular smoking, **alcohol intake until the last 30 days. Group I: population involved knee height analysis, group II: population involved in demispans analysis. § Moderate exertion: Moderate intensity exercises for 1-2 hours per week or >4 hours of light activities

Results from Study IV

In study IV, age- sex specific cohort changes in girth measures, lifestyle factors, and prevalence of abdominal obesity and the role of obesity-related factors such as education, smoking, alcohol consumption and physical activity in the changes in WC were examined. This was done by comparing men and women earliest birth cohort (examination year 2001) and the latest birth cohort (examination year 2013) respectively within each age group. The intermediate age cohort includes participants examined in the year 2007.

Birth cohort changes in anthropometrics

The birth cohort trends in BMI, waist circumference and abdominal obesity prevalence in two different age cohorts namely 60 and 81 are depicted in the figures below.

BMI

Figure 15 shows the pattern of distribution of mean BMI among the participants from both age cohorts across the three different birth cohorts. The mean BMI in

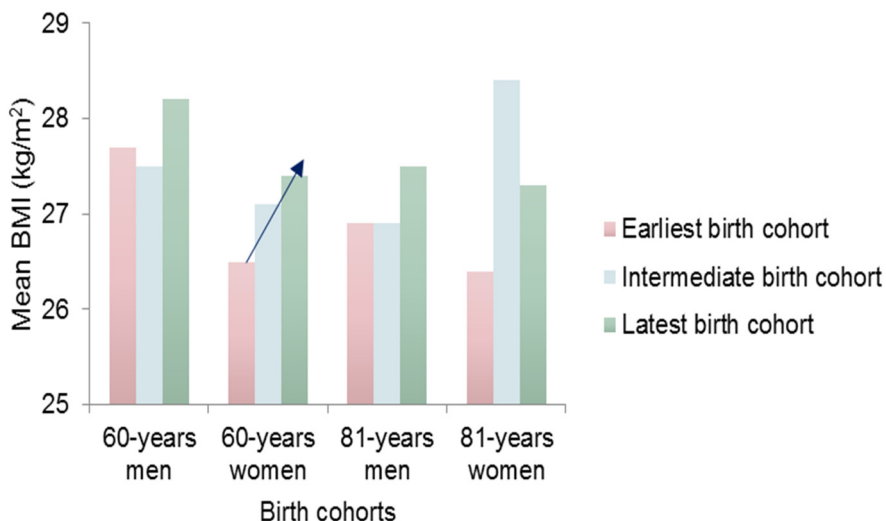


Figure 15: Birth cohort effect on the secular trend in mean BMI (kg/m²) among 60- and 81-year-old men and women from three different birth cohorts. Birth years in age cohort 60: 1941–43, 1947–49, 1952–54; Age cohort 81: 1920–22, 1926–28, 1932–3. ↑ indicates a statistically significant increase in BMI ($p < 0.01$).

the latest cohort among both ages and sexes were all above 25 kg/m².

Trends in BMI was tested by comparing the earliest (birth year 1941–43 for age cohort 60 and birth year 1920–22 for age cohort 81, examined in 2001) and the latest birth cohort (birth year 1952–54 for age cohort 60 and birth year 1932–33 for age cohort 81, examined in 2013). There was significant increasing trend observed only among 60-year-old women.

WAIST CIRCUMFERENCE

Among the 60-year-olds, there was an increase in mean WC by 2.6cm and 2.4cm

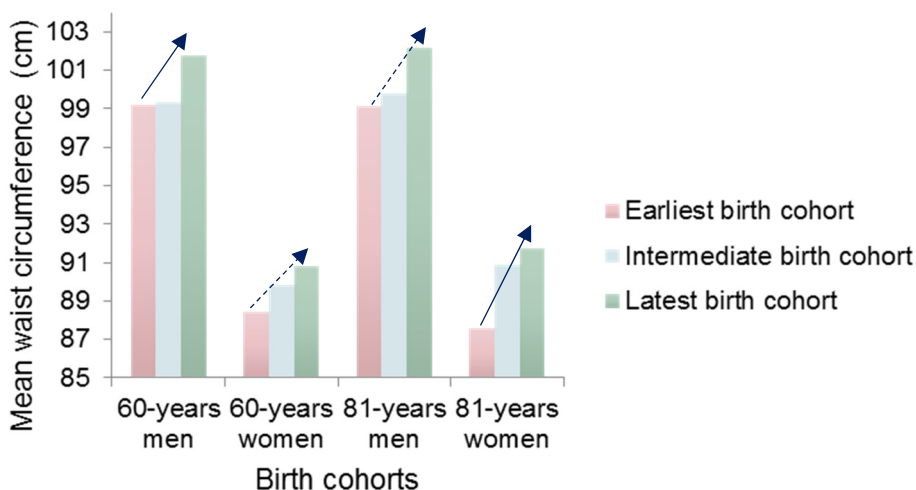


Figure 16: Birth cohort effect on the secular trend in mean waist circumference (cm) among 60- and 81-year-old men and women from three different birth cohorts. Birth years in age cohort 60: 1941–43, 1947–49, 1952–54; Age cohort 81: 1920–22, 1926–28, 1932–33. ↑ indicates a statistically significant increase in waist circumference ($p < 0.01$), dotted arrow indicates $p < 0.05$.

among men and women respectively, when comparing the earliest and the latest birth cohorts. Such increase was even larger among the 81-year-olds men ($\Delta 3.1$ cm, and women ($\Delta 4.1$ cm) (Figure 16).

There was also a significant increase in HC in men and women in both age cohorts with highest values among the latest birth cohorts (age 60: 1952–54; age 81: 1932–33). In 60-year-old men: 103.9cm, women: 104.2 cm, 80-year-old men: 104.7cm and women: 105.6 cm.

ABDOMINAL OBESITY

Prevalence of abdominal obesity was estimated based on standard WC cut-offs (WC ≥ 102 cm (men); ≥ 88 cm (women)). There was an increasing trend observed among 60y-old-men (37.5% to 47.6%) and 81-year-old women (45.3% to 66.1%) when comparing the earliest and latest birth cohorts (Figure 17).

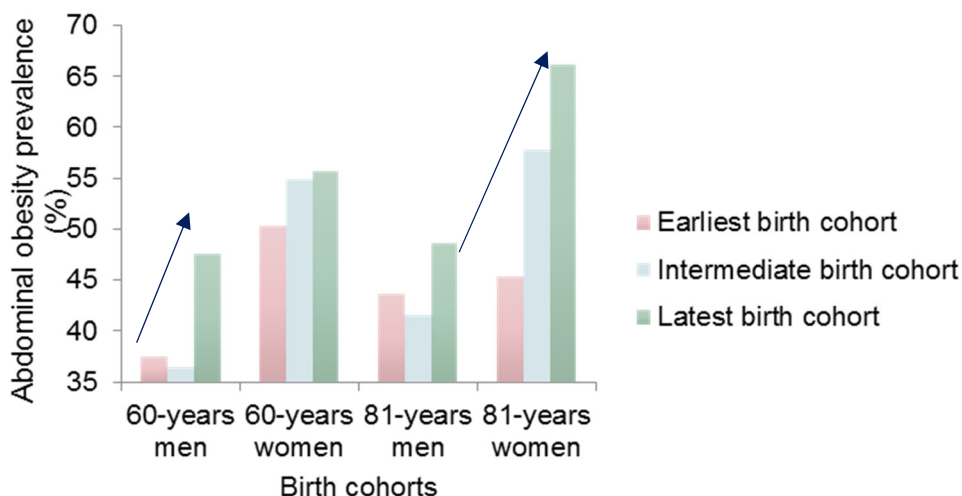


Figure 17: Birth cohort effect on the secular trend in the prevalence of abdominal obesity (Waist circumference ≥ 102 cm (men); ≥ 88 cm (women)) among 60- and 81-year-old men and women from three different birth cohorts. Birth years in age cohort 60: 1941–43, 1947–49, 1952–54; Age cohort 81: 1920–22, 1926–28, 1932–33. \uparrow indicates a statistically significant increase in the prevalence of abdominal obesity in the latest birth cohort compared to the earliest, $p < 0.01$.

Birth cohort changes in obesity-related extrinsic factors

The effect of birth cohort in education, smoking, alcohol consumption, physical activity and diet were examined independently among 60-year-olds and 81-year-olds (Table 11). Statistical significance was at p value ≤ 0.05 if otherwise indicated to be ≤ 0.01 .

60-year-old

A rising trend in educational attainment was found with higher proportion of individuals with above secondary level of education in the latest birth cohort (birth

year 1952–54) compared to the earliest birth cohort (birth year 1941–43) both in both men (rise from 60.2 to 69.6%) and women (rise from 62.5–76.9%). There was a higher proportion of individuals who consumed less than 1 complete meal per day in the latest birth cohort than the earliest in both men (from 7.4%–19.1%) and women (4.3%–17.3%). The prevalence of smoking decreased in both men and women. No significant trend was seen in alcohol consumption in both men and women across the three birth cohorts but the proportion of active alcohol consumers in the latest birth cohort (birth year 1952–54) was 82.3% in men and 76.4% in women. The prevalence of ‘mostly sedentary’ form of lifestyle decreased from the earliest to the latest birth cohorts in both men and women and moderate intensity physical activity decreased from 70.2% to 67.7% in men and increased from 83.3 to 86.1% in women. Frequency of physical activity showed no significant trend in 60-year-old men however, there was a decrease in daily exercises from 52.5% to 38.6% and an increase in several times/ week from 31.1 to 39.9% between the 60-year-old women earliest and latest birth cohorts.

81-year-old

There was significantly rising trend in the proportion of individuals who consumed one or less complete meal per day for men (4.7% to 23.7%) and women (8.6% to 30.7%) when comparing the earliest (birth year 1920–22) and the latest (birth year 1932–33). There was a decreasing trend in smoking from 12.1% to 8.3% in women and an increasing trend in active alcohol consumption from 51.5% to 69.2% in men. Although the intensity of physical activity did not show any change in prevalence across the three birth cohorts in both men and women, among women there was a decrease in daily physical activity decreased from 50.0% to 33.6% and increase in prevalence of physical activity several times/week (19.7% to 34.5%). No significant secular trend was observed with respect to education.

Table 11: Summary of the secular trends in the obesity related explanatory variables education, diet, smoking, alcohol consumption and physical activity across the three birth cohorts between 2001 and 2013 among men and women in the age cohorts 60 and 81 years respectively.

Trend across three birth cohort	Age cohorts	High education level	Poor diet	Smoking	Active alcohol intake	Physical activity frequency	Physical activity intensity	
Earliest to latest birth cohorts	60 years	Men	↑	↑	↓	↔	↔	↓ mostly sedentary
		Women	↑	↑	↓	↔	↓ Daily ↑ several times/week	↓ mostly sedentary
	81 years	Men	↔	↑		↑	↔	↔
		Women	↔	↑	↓		↓ Daily ↑ several times/week	↔

↑ indicates a significant upward trends, ↓ indicates a significant upward trends ↔ indicates lack of any significant trend (significance at p value ≤ 0.05) by comparing the earliest (birth year 1941-43 for age cohort 60 and birth year 1920-22 for age cohort 81, examined in 2001) and the latest birth cohort (birth year 1952-54 for age cohort 60 and birth year 1932-33 for age cohort 81, examined in 2013). Variable education refers to the proportion of individuals with above secondary level of education, Poor diet refers to the frequency of consumption of complete meals per day indicating there was higher proportion of individuals who consumed less than 1 complete meal per day), smoking (prevalence of smokers).

Changes in WC in relation to obesity-related factors

Table 12 highlights the specific categories or sub groups within the different explanatory variables such as education, diet, smoking, alcohol consumption and physical activity (intensity) where a significant increasing trend in WC was

observed, the maximum being among the latest birth cohort (examination year 2013) of men and women in age cohorts 60 and 81 respectively.

Table 12: Summary of the association between trend in waist circumference across the three birth cohorts between 2001 and 2013 and the explanatory variables examined (education, diet, smoking, alcohol consumption and physical activity) among men and women in the age cohorts 60 and 81 years respectively.

Trend across birth cohorts	Age cohorts	High education level	Poor diet	Smoking	Active alcohol intake	Physical activity intensity	
From 1941-43 to 1952-54	60 years	Men	↑	↔	↑ Smokers & non smokers	↔	↑ moderate physical activity
		Women	↑	↔	↑ Smokers & ex-smoker	↔	↑ moderate physical activity
From 1920-22 to 1932-33	81 years	Men	↔	↔	↑ Smokers	↑	↔
		Women	↔	↔	↑ Non-smokers	↑	↑ physical inactivity

↑ indicates a significant upward trends, ↓ indicates a significant downward trends ↔ indicates lack of any statistically significant trend (significance at p-value <0.05) by comparing the earliest (birth year 1941-43 for age cohort 60 and birth year 1920-22 for age cohort 81, examined in 2001) and the latest birth cohort (birth year 1952-54 for age cohort 60 and birth year 1932-33 for age cohort 81, examined in 2013). Variable education refers to the proportion of individuals with above secondary level of education, Poor diet refers to the frequency of consumption of complete meals per day indicating there was higher proportion of individuals who consumed less than 1 complete meal per day), smoking (prevalence of smokers).

Regression analysis was done to test the effect of birth cohort on mean WC and abdominal obesity prevalence, adjusted for sex and the obesity-related factors such as education and lifestyle parameters (diet, smoking, alcohol intake and physical activity). A significant birth cohort effect on mean WC and abdominal obesity was observed in both the ages after adjusting for these factors (Table 13).

Table 13: Regression models for birth cohort difference in mean waist circumference and prevalence of abdominal obesity estimated by waist circumference ≥ 102 cm in men, and ≥ 88 cm in women within age cohorts 60 years and 81 years in the Swedish population study Good Aging in Skåne.

	Birth cohort difference	Beta coefficient	Standard error	p	95 % C.I.
60-year-old	Mean waist circumference	1.68	0.35	0.00	0.96-2.37
	Abdominal obesity prevalence	0.20	0.06	0.00	1.09-1.38
81-year-old	Mean waist circumference	1.87	0.56	0.00	0.78-2.96
	Abdominal obesity prevalence	0.26	0.10	0.01	1.07-1.58

Models after adjusted for gender and obesity related explanatory factors such as education, physical activity, diet, smoking and alcohol consumption. The variable birth cohort had categories as earliest, intermediate or latest birth cohort corresponding to the respective birth years in both age cohorts;

Birth year for age 60: earliest birth cohort: 1941-43, intermediate: 1947-49, latest 1952-54; Birth year for age 81: 1920-22, intermediate: 1926-28, latest: 1932-33; p: p-trend for cohorts; * p trend for all the three cohorts (critical value: ≤ 0.05); C.I: Confidence Interval; Abdominal obesity prevalence based waist circumference ≥ 102 cm (Men) and waist circumference ≥ 88 cm (Women). Reference groups: Earliest birth cohort, secondary and higher education, non-smoker, heavy exercises, and non-drinker (no intake since the last year).

Discussion

The findings in this thesis suggest that there was a serious BMI misclassification introduced by the inaccurate height estimation due to aging. Previously missing and urgently needed age- and sex-specific reference values for anthropometric measurement were presented for Swedish older adults. These also demonstrate the body composition profile at different ages among elderly.

The misclassification of weight categories results in a general underestimation of underweight and overestimation of obesity, particularly striking at age ≥ 80 years. To address this problem, we have formulated age- and sex-specific BMI prediction equations using KH and demispan as proxies to estimate height and hence BMI. KH-BMI was more effective than classic BMI in identifying the misclassification of underweight and obesity, showing alarming differences in men aged ≥ 70 years and in women aged ≥ 80 years. Furthermore, KH-BMI also showed a significant paradoxical relationship with mortality risk among the overweight population aged ≥ 80 years. Waist circumference, an important measure of abdominal obesity, showed an increasing trend in 60-year and 81 year-old elderly in three birth cohorts between 2001 and 2013. This trend was related to high educational attainment and inadequate physical activity in the younger elderly (60 years) and to high alcohol consumption in men and sedentary living in women in the older elderly age (80 years).

Examination of status quo and problem identification

Anthropometric assessment of body composition

Anthropometric reference data for Swedish older adults are presented in this thesis. This could facilitate the interpretation of differences and patterns in phenotypic changes with aging. A brief description of the observed anthropometric profile is discussed in relation to relevant literature. Men were taller, heavier and had higher BMI than women (as expected) with a gradual age-related height loss

in both sexes. This can most likely be attributed to bone degenerative diseases associated with aging [87]. The loss of weight with age, mostly in the 80-year olds, could be due to sarcopenia from disuse atrophy and senility [32, 200]. These were similar to the results from the SENECA study (men: 75 ± 10.4 kg, 71.1 ± 12 kg; women: 64.5 ± 12.4 kg, 62.8 ± 1 kg, in Denmark and Norway, respectively) [201]. However, the mean values of weight loss were relatively higher in our study. Weight difference between 70-year olds and ≥ 85 year-olds (men: $8.8 \text{kg} \pm 1.2$ kg; women: $9.4 \text{kg} \pm 1.3$ kg) was almost twice that reported by the H70 study (Men: 3.2kg; Women: 5.1kg) [164]. The mean BMI in men and women, which based on the WHO classification of weight categories can fall within the overweight group ($25\text{--}30 \text{ kg/m}^2$). The distribution of mean BMI among different age groups showed an inverted U-trend that is also noted in a similar Italian study [32]. Here the maximum BMI was at 75–79 years which was preceded and followed by lower values. Such lower values of BMI in later life could be related to physical inactivity and sarcopenia common in these age groups [109, 114]. There is also a possibility of selective attrition of subjects with morbidly high BMI and associated medical conditions such as MI and stroke [32, 200]. Mean BMI in our study was similar to that in SENECA (Finland: 27.3kg/m^2), whereas for 75-year-olds was higher compared to Swedish cohort of the NORA75 study (25.3kg/m^2) [201].

According to our data, there was an overall tendency towards increasing BMI in both men and women compared to the past two decades, according to SENECA and H70 studies [164, 201]. The high WHR among women (0.87) indicates the prevalence of abdominal obesity. TST was also higher among women similar to SENECA's Norwegian (women: 24.3cm; men: 18.4cm) and Danish population (women: 20.7cm; men: 11.3cm) and the NHANES study's American population (women: 22.5cm; men: 15.3cm) [161, 201]. Previous studies have shown the effects of the late post-menopausal non-estrogenic condition on fat redistribution, and the sarcopenia associated with loss of type-2 glycolytic fibers [85, 201]. Visceral adiposity is often coupled with the progressive loss of fat and muscle tissues in the extremities [85, 202]. This can be appreciated by lower arm-circumference among women similar to the Norwegians and Danes in the SENECA study [201, 203].

Role of underlying medical conditions

We found significant anthropometric differences between elderly with or without the common medical conditions. Subjects with MI had higher weight, BMI, waist, hip and arm circumference, and skinfold thickness, indicating a higher prevalence of subcutaneous and central adiposity [204]. Similarly, CHF patients had higher weight, waist circumference and skinfold measurements indicating a strong association and/or predisposition to the disease [204, 205]. Central obesity is a

well-known predisposing factor for MI and CHF [206]. It has also been reported that MI and CHF patients display weight gain due to fluid retention and use of beta-blockers [205, 207]. After MI, cardiac adaptation to excess body fat could affect cardiac function directly or through increased risk of diabetes, hypertension, and release of inflammatory cytokines, leading to cardiac failure [205, 206]. ADL-dependent patients, particularly women, had higher BMI, waist- and hip circumference and lower TST. This could be due to reduced physical training leading to the replacement of muscle mass, fat accumulation and weight gain [208].

Quantification of BMI misclassification & Examination of KH- and demispan-BMI

Based on the reference data presented, it is difficult to determine the cause of the observed height loss and it could be related to either physiological aging or inaccuracies in the estimation of height due to postural changes [169, 178]. Such postural changes can arise from conditions such as kyphoscoliosis, which worsens with age causing greater difficulty in accurate height measurement. This is confirmed by the widening difference between the measured and predicted height with older age groups concordant with other similar studies [169, 178, 209].

Based on our results, there is an alarming underestimation of underweight and overestimation of obesity among Swedish elderly. This is in agreement with studies among elderly in a Swedish hospital setting, and non-institutionalized elderly from England [167, 169]. The BMI cut-off used to define underweight in this study was ≤ 20 kg/m². Despite using a higher cut-off than the WHO recommendation, i.e., 18.5 kg/m², the underweight underestimation was remarkably high.

This was effectively identified by demispan-BMI in both the youngest and oldest age groups. KH-BMI detected marked underweight prevalence in men aged 80 years and above and in women aged 70 years and above when height changes are most pronounced [136]. This difference between men and women could be attributed to the hormonal changes in postmenopausal women that in turn are related to earlier osteoporosis, bone loss and fat redistribution [85], functional dependence and undernutrition [99]. The average prevalence of undernutrition among those hospitalized and in special accommodations in Sweden has been reported to be 32.2% and 31.7% respectively [210]. The prevalence of elderly undernutrition is rising globally due to complex somatic, psychologic and social

determinants [18, 76]. The morbidity and mortality risks of low BMI are well established among Swedish women [211] and other elderly populations [70, 136, 212].

On the other hand, obesity prevalence estimated by classic BMI was roughly double as high as KH- and demispan-based BMI among men aged over 80 years and women aged over 70 years, and doubles thereafter with the older age groups. [167, 176]. As discussed above, this could be attributed to the loss of height owing to degenerative conditions that is more prevalent with older ages. Our demispan observations were concordant with those from the study by Hirani et al [176] among non-institutionalized elderly and with those from the study by Frid et al [167] among hospitalized elderly. However, statistical testing for agreement was done in these and other similar studies that compared the use of demispan or KH instead of measured height.

Based on our results, we could say that KH-BMI performed much better than the classic BMI in the detection of unidentified underweight individuals and false classification of obesity. Demispan BMI although very effective with obesity prevalence was apparently not as sensitive as KH-BMI in regards to underweight detection. Therefore KH-BMI could be considered an effective tool in BMI classification of weight categories among older adults. The implications of BMI misclassification were further analyzed in study III to examine and evaluate the functional benefits of the KH-BMI proposed in the study II.

Evaluation of survival implications of KH-BMI

Based on our results after adjusting for confounders such as smoking, education, physical activity, residence, marital status, and comorbidities, regardless of the method of BMI estimation, overweight elderly had a lower mortality risk, compared to normal/underweight individuals. In addition, based on classic BMI classification, there was also a protective association between obesity and mortality risk found among men.

Overweight paradox

However, after age stratification, KH-BMI classification demonstrated a paradoxical protective association between overweight and mortality only in older adults aged ≥ 80 years. It confirms the J-shaped association of BMI and mortality with a clear survival benefit in the overweight elderly population [87, 213]. The

protective effect of overweight might be attributed to resilience among individuals who survived the adverse effects of elevated BMI in the middle age. This resilience could be accentuated by good healthcare, protective metabolic effects of increased lean body mass, being a genetic carrier of mortality resilience, good immune response and repair function, and availability of nutritional reserves to support aging and related states of illness [157, 165, 214]. Higher BMI among older adults, particularly those aged over 80 is likely to indicate sufficient lean mass rather than fat stores (adiposity) [97]. Sometimes, there is a status of sarcopenic-obesity, where a stable BMI reflects higher true adiposity together with aging-associated muscle loss [113, 166]. Hence, elevated BMI among the over 80-year-old individuals might indicate residual muscle mass stores. Lean mass is independently associated with lower mortality and considered an indicator of a healthy lifestyle during the younger adult ages that include muscle-building levels of physical activity [157, 215]. Conversely, lack of lean mass (sarcopenia) is a salient feature of frailty, which due to co-existing intrinsic and extrinsic risk factors increases the risk for mortality [66, 84, 216].

Misclassified obesity paradox?

In comparison with the normal/underweight group, obesity, classified by classic BMI, did not correlate with an increased mortality risk particularly in men aged ≥ 80 years. This relationship was not significant when classified using KH-BMI. This could be due to BMI misclassification of those individuals who were falsely classified as obese by the classic BMI and later were re-classified as overweight by KH-BMI. Further investigation is however recommended here, using larger samples to study the effect of the different grades of obesity and to rule out the potential problem of lower statistical power in the obese group. However, in our study, the mean classic BMI (men: 32.6 kg/m², women: 32.9 kg/m²) was within grade 1 level of obesity, most likely supporting the misclassification explanation. Lack of higher grades of obesity could be due to potential attrition of morbidly obese subjects and raise concern regarding adequate representation of obesity in the study. In addition, there is also a possible effect of height loss (from study I) with age translated into increasing BMI [87]. Lack of distinction between fat and fat-free weight could lead to misinterpretation of high BMI from muscle mass as overweight or risk for obesity [217].

These findings were consistent with some of the previous studies that also showed a protective effect of overweight and varied results with obesity. In general, evidence suggested that obesity at lower range mostly had moderate mortality risk and increasing risk at the upper range of BMI [41, 140, 158, 218-220]. A large meta-analysis of 97 cohort studies with 2.88 million participants and 270000 deaths, which used the WHO cut-off points for overweight and obesity, found

summary hazard ratios for mortality of 0.94 (95% confidence interval 0.90 to 0.97), 0.97 (0.90 to 1.04), and 1.34 (1.21 to 1.47) for a BMI of 25–<30, 30–<35, and ≥ 35 , respectively, suggesting a protective effect of overweight and modest obesity [41]. Aune et al's meta-analysis of 230 cohort studies with >3.74 million deaths among >30.3 million participants also indicates a lower mortality risk in overweight people, although, the effect is likely to be confounded by smoking and pre-diagnostic weight loss [110]. The study was however not confined to older adults and the recommendation to restrict analyses to specific groups, e.g. only a non-smoker population might cause serious risk for including an over-selective study sample that is unrepresentative of the general population. On the contrary, another meta-analysis by Janssen and Mark showed no increase in mortality risk among overweight individuals in comparison with those with normal BMI (estimated risk 1.00 with 95% confidence interval: 0.97–1.03), and a moderate risk increase for the obese individuals (1.10, 1.06–1.13) [157]. There are no studies performed previously taking into account the effect of BMI misclassification due to inaccurate height estimation and height loss in older adults, the differential body change pattern through the years of aging and other related confounders of body composition assessment.

There is also a possibility that there is no actual survival value in BMI levels above normal and being overweight during old age, rather the BMI levels represent a relative state of better health in this range than the categories on either side of the spectrum, importantly, the deficient state to the left. This, however, can be considered sufficient to motivate the continuous use of BMI despite the limitation in differentiating fat mass or fat-free mass. As far as older adults are concerned, this limitation could likely be overridden by the benefit of using BMI used as a marker for modest progression of age-related degenerative process.

Geriatric paradox

Several studies have focused on the pathophysiology and the implication of reversal of mortality association in older age exhibited by well-established risk factors of chronic diseases, BMI, blood pressure and serum cholesterol [221]. Among the geriatric population, when the exposure to these risk factors is within specific thresholds, there is a paradoxical shift of association with morbidity and/or mortality. This is referred to as 'reverse epidemiology.' The obesity paradox can be explained as one such phenomenon [19, 222]. It is therefore important to explore the biological plausibility of such a paradox to adapt health messages, plan health interventions and modify disease prevention guidelines for older adults [221].

There are protective factors related to increased adiposity above limits accepted as normal limits during young adulthood. These agents could have contributed to the resilience to diseases and adverse outcomes among older adults. This could be explained by different potential mechanisms. Below are a few:

1. **Metabolic protection:** Circulating inflammatory cytokines, their precursors like tumor necrosis factor- α , lipophilic toxins and other endotoxins are common in relation to chronic diseases. They contribute to or are the consequences of the breakdown of lipid depots in the body leading to wasting and in severe cases death [19]. These catabolic metabolites are counteracted and even sequestered by lipoproteins and adiponectins that are more abundant in cases of overweight and obesity.
2. **Genetic protection:** The segment of older adults who enjoy this favorable effect of overweight (by BMI) is those older adults aged above 80 years. In Sweden, this groups accounts for about 5% of the population. Genetic-make up may lie behind the survival of a fittest minority. However, this could be prone to epigenetic confounding and cross-ethnic variations [78, 81, 223].
3. **Relative protection of overweight** considering the acute risks from nutrition deficiencies. There is higher mortality risk from underweight than excess and the effect of overweight can be seen as a momentary protection offered by excess reserves against death from deficiency.
4. **Reversed causation:** Although there are debates around “reversed causations” [221], it is more logical to state that, in the presence paradoxical protection at higher doses of a risk factor (here, adiposity), among particular age-groups, the direction of causality of the disease cannot be established. It is still unclear if lower doses of risk factor (underweight) is a potential risk for disease or if they occur as a consequence of the existing disease condition, which progresses to unfavorable outcomes.
5. The noted increased BMI among older subjects might represent a well-sustained healthy lifestyle in the form physical activity adequate to produce cumulatively higher proportion of lean mass than among middle-aged adults, thereby contributing to the survival benefit.

The geriatric paradox deserves further attention due to its significance in older adults. This might involve systematic revisiting of causal chains, examining disease differences with advancing age and modifying methods of evaluation to develop valid health guidelines. With regards to BMI, it is important to be cautious about making premature decisions in adjusting weight management at an individual clinical level based on epidemiological study results.

Investigation of extrinsic factors

According to the model proposed in this thesis (Figure 4), in order to achieve a reasonably comprehensive anthropometric assessment, we consider it to be important to take into account extrinsic factors. The observed protective effect of higher BMI estimated after addressing BMI misclassification from height estimation errors could most likely be influenced by extrinsic factors that affect body composition. Such extrinsic elements examined in our studies are discussed below.

Birth cohort effect on waist size related lifestyle

Waist girth, a good complement to BMI in measuring obesity was the principal anthropometric measure investigated in relation to birth cohort effect on body composition. We found that WC and the prevalence of abdominal obesity were higher in the latest birth cohort in both the younger (60 years) and the older (81 years) age cohorts. An increasing pattern in waist size indicating a tendency toward abdominal obesity was related to a general generational effect evident among both ages 60 and 81 years, high educational attainment and inadequate physical activity in the younger elderly (age 60 years) and to higher alcohol consumption in men and sedentary living in women in the older elderly age (80 years).

Furthermore, our study results on secular trends across the three birth cohorts and its relationship with waist measures were in agreement with other similar studies. Despite the scarcity of recent Swedish studies on age-specific secular trends in WC and abdominal obesity, some useful comparisons were possible. In congruence with our study results, the NHANES study that analyzed the trends in the mean WC and the prevalence of abdominal obesity among American adults between 1988 and 2008 also showed an increase in mean WC among 60 and 80-year-old men and women [224]. Men over the age of 60 alone showed a significant upward trend in abdominal obesity in the latest birth cohorts [225]. Similar results could also be seen among 70-year-old men and women from the H70 study (1971–2000) [70]. Contrastingly, a decreasing trend was reported in WC and abdominal obesity prevalence among 60–69 years-old Spanish women with no significant change among men [79]. These studies highlight the significance of the differential pattern of body composition changes between the different ages of older adults and between sexes.

We examined in our study, the secular trends in the obesity-related factors were examined in relation to three birth cohorts namely 1941–43 (earliest), 1947–49

(intermediate), 1952–54 (latest) in the ‘younger’ age cohort 60 and 1920–22 (earliest), 1926–28 (intermediate), 1932–33 (latest) in the ‘older’ age cohort 81.

Education was the only socio-demographic determinant examined in relation to the secular trend in WC. In general, it was encouraging to note that there was an increasing trend in educational attainment in both men and women in age cohort 60. On average, in the latest examination conducted in 2013–15, 69.6% men and 79.6% women in aged 60 years were estimated to have secondary and higher education. On one hand, such numbers are promising in terms of better cooperation and positive responses to health promotion interventions and messages. On the other hand, in line with previous research, we also observed a clear association between higher education levels and increasing WC and abdominal obesity. Higher socioeconomic status has been shown to be associated with obesity, and higher educational accomplishment could indicate advancement in socioeconomic status [70, 224].

With respect to dietary habits, we found that the frequency of consumption of complete meals per day has been significantly lower in latest birth cohorts compared to the earlier in both ages. However, this was not related to abdominal obesity trend. This could be mostly like due to the properties of the variable used in the study that could have been a restrictive diet parameter unable to capture the different functional dimensions of diet in its entirety. This is acknowledged as a potential study limitation. On the other hand, the inherent complexity of diet assessment is almost an unavoidable challenge common to all survey examinations. A well-structured FFQ as used in our study is a very useful tool to obtain valid assessments of dietary habits and to reduce bias associated with unclear definitions and other controllable issues like recall problems [23, 100]. It is important to ensure that it comprises clearly defined and easily understood questions comprising choices that are mutually exclusive, and are updated to the recent trends in food habits.

The other lifestyle factors examined were physical activity, smoking and alcohol consumption. Overall it was encouraging to note that the ‘mostly sedentary’ form of lifestyle was reducing in age cohort 60 years similar to the results found in another Swedish population study among 70-year-olds, H70 study. They showed that physical inactivity decreased among 70-year-old men and women but there was an increasing BMI unrelated to physical activity [70].

Although we observed decreasing trend in ‘daily’ exercising in women of both age cohorts most likely due to lowered functional capacities associated with aging [226], it was positive to note that exercising several times per week increased among the same groups. In addition to the decreasing trend in inactivity, there was an increase in moderate intensity exercising particularly among 60-year-old women.

However, there was a remarkable waist-gain by 14.3cm among 81-year-old women in the latest cohort who reported physical inactivity and a marginal increase among those moderately physically active younger elderly (age 60). This could indicate that the amount of exercise performed by older adults is probably inadequate to avoid waist gain and abdominal adiposity [111]. Among the 81-year-olds such suboptimal exercise intensity could however be expected due to the lowered strength and functional capacity associated with frailty and/or other comorbidities such as dependence in ADL [93, 99, 111, 208, 227]. The explanation for the observed waist gain in the moderately physically active 60-year-old individuals however remains unclear. According to the definition of the variable, moderate physical activity refers to light exertion exercises for more than 2 hours/week or moderate intensity exercises such as jogging, swimming, fitness classes, heavier gardening etcetera for about 1–2 h per week. On average this should meet the WHO recommendation of 150 minutes exercise per week to prevent overweight and obesity in adults [65]. Therefore our results could indicate either a residual confounding in the association or bias in the information reported by the participants who could have overestimated the time or the degree of exertion actually made probably for reasons of ‘social approval’ during the survey [106, 107].

To better understand the relationship between the waist-gain and physical activity status it is therefore important to perform further analyses. Such analyses could involve an in-depth examination of the independent and interactive role of physical activity in abdominal obesity by investigating the frequency, intensity, type, and duration of exercise performed and maintained [226].

Smoking: The declining prevalence of smoking in the latest birth cohort (examined in the year 2013) compared to the earliest (examined in the year 2001) was reassuring. This was found among 60-year-old men and women and 81-year-old women comparable to similar results observed among 70-year-old women in the H70 study on obesity trends [70]. The lowered smoking prevalence among the younger cohort (60 years) sends a positive and promising signal to public health promotion efforts in the ‘younger’ elderly that could lead to future health benefits in later life.

However, an increasing trend in WC observed had a differential relationship with the smoking status in men and women in both ages. In the younger age cohort (60 years), men and women smokers showed an increasing trend in WC. In addition, men non-smokers and women ex-smokers also showed a similar trend. With respect to the older cohort (age 81), WC gain was a finding among men smokers and women non-smokers. In line with our results, a Swedish study among women aged 38 and 50 years that observed secular trends in WHR [82, 125] also reported that WC and WHR were rising in both the age-cohorts but was not explained by

the smoking status [82]. It is important to note that the age of the population in the comparison study was much lower than our study population but showed a similar association or ‘lack of association’ between smoking and waist measures trends. The H70 study from Gothenburg however studied the role of smoking in BMI trends among 70-year-old adults between 1971 and 2000. An upward trend in BMI was demonstrated among smokers, ex-smokers and non-smokers in the study population except among non-smoking men where no change was found [70]. This may not be an optimal comparison with our results in terms of the anthropometric measures examined (BMI versus WC). We know that smokers with lower weight (or BMI) could present with higher waist measures [228]. It is however interesting to note the similarity in the differential association between smoking status and obesity trends seen in both the studies. In contrast, cross-sectional studies have shown that WC and not body weight is higher in smokers compared to non-smokers [228-230]. This inconsistent relationship between smoking and abdominal obesity in older adults could most likely be an indication of the presence of residual confounders (Please see end of this section).

Alcohol intake: Increasing trend in alcohol consumption was only observed in 81-year-old men and there was an associated upward trend in WC observed in both men and women age 81 years. Similar results were found in a population-based study among 807 men (age 70 years) called ‘Uppsala Longitudinal Study of Adult Men’. In their study, there was a strong association between high alcohol consumption that was estimated using a 7-day dietary record, and increased abdominal obesity measured by WC and WHR [115, 231]. Several prospective studies however do not point toward a significant role of alcohol consumption in obesity development. A prospective cohort study among 16,587 US men aged 40–75 years showed no significant association between alcohol consumption and increase in waistline [232]. This study however included a younger population group than the age cohort in our study where the association was evident. Another Nordic prospective cohort conducted in 1993–2002 including 43,543 Danish men and women showed that drinking frequency was inversely associated with changes in WC in women and was not associated with changes in WC in men [117].

In general, on one hand, there is a biological plausibility of increased adiposity, weight gain, and obesity in relation to alcohol consumption. This could be due to the high energy density and concentration of non-nutritious empty calories in alcoholic beverages that could contribute to excess energy consumption or the inhibitory role of alcohol metabolites on fat degradation [117, 233]. On the other hand, evidence suggests that these mechanisms are hugely modified by the frequency of drinking [117, 233]. Light-moderate consumption of alcohol is less likely to be a risk factor for obesity than heavy intake that has a strong association with weight as well as waist gain [116, 118]. It is therefore important to obtain data on the quantity and frequency of alcohol in such analyses. However, in our

study, we aimed to identify the individuals who were current consumers of alcohol indicating active alcohol intake habit over a time span. We did not investigate further the frequency of consumption during the time span of drinking, the quantity or type of drinking (e.g. light, heavy or binge) or test the role of confounders [115-118]. Active alcohol consumption examined in our study refers to having had the latest drinking episode within the last month. This could however act as a proxy measure of a higher frequency of intake in relation to the other available options such as ‘not having drunk in the last year’ or ‘only sometimes in the last year though not in the last month’. Based on the observed association between alcohol and WC trend there is tendency to relate to consumption of excess quantities of alcohol that has contributed to this waist gain among the 81-year-old adults.

In the investigation of the association between WC and extrinsic factors affecting body composition such as education, smoking, alcohol and physical activity, it is important to take into account possible interactions between the factors and residual confounding. Some of the potential residual confounders include psychosocial factors, stress, underlying medical conditions or comorbidities, environmental conditions, medications and healthcare [11, 17, 21, 70, 77, 82, 110, 136, 234-238].

Importance of age-categorization

Age (categorical), sex, marital status and residence described the background demographic profile of the population in all the studies conducted. Considering the potential confounding effect of these factors, the regression analyses (including hazard regression) conducted in our studies accounted for these determinants wherever relevant. Age and gender categorization was done in all studies to examine the differential effect of anthropometric changes, magnitude of BMI misclassification, mortality risk of BMI, and birth cohort effect across the different subgroups.

Based on our results, the youngest age category of 60–69 years most likely does not share the issues of BMI measurement and body composition assessment to the same extent as the adults aged over 80 years. This could simply be because of less time elapsed since the onset of aging, a progressive process that is associated with degenerative changes affecting body form and composition. 70–79 years of age can be seen as an intermediate phase of transition from mild to showing more evident signs of aging. After accounting for sex differences, being in this phase could explain the clearly identified anthropometric changes like height and weight, and BMI misclassification of underweight and obese categories. It is expected that the 70-year-olds would show a higher rate of participation, better engagement and

performance in the different examinations simply due to relatively better cognitive and physical skills than older individuals, thus contributing to the power and the validity of studies [239]. Care has to be taken when comparing results from studies where all older adults have been pooled into one category or investigated together with younger adults [110, 133, 225]. Such studies using classic BMI or WC in their analyses have also identified similar findings as in our study [35, 97, 110, 157, 211]. It is however recommended whenever possible to make age-specific comparisons either with studies targeting a particular age group [70, 200, 240] or those that adopted age categorization [97, 224].

In general, there can be potential drawbacks to using the identical analysis methodology across the different age groups in the study population. Age-specific assessment is important to precisely capture the differences in the stages of aging, incidence or severity of related body changes, anthropometric profile, association with disease or mortality risk, response to lifestyle modification and even the future continuation of the use of classic BMI to assess body composition. This could facilitate designing targeted prevention and health promotion interventions.

Methodological considerations

Generalizability of results

As mentioned earlier, ‘Good Aging in Skåne’, the data source for this thesis, is an extensive, longitudinal, randomized population study conducted among adults over the age of 60 years. It was designed with an implicit aim to conduct nationally representative research, generating results that could be applicable to the general elderly population. With that aim, all participants were randomly invited, using the national population registry, forming a large heterogeneous sample from five different municipalities of South Sweden (Skåne). These municipalities combine rural and urban settings, which is particularly significant in the context of anthropometrics [241]. In addition, Malmö, one of the study municipalities, has a high proportion of foreign-born individuals (31%) [242]. However, there could be a possible underrepresentation of ethnic diversity, resulting from language⁴ difficulties and/or cultural differences. However, the national proportion of foreign-born older people (65+ years) estimated at the end of 2011 was 11.7%, where nearly one-third was originally from other Nordic

⁴ Swedish language was the medium of instruction used in the survey and during the examinations.

countries, the majority from Finland, who migrated around age 35 and have lived for several years in Sweden [3, 243]. This indicates a relatively smaller proportion of foreign-born older adults compared to younger individuals in the country. The proportion of foreign-born individuals who participated in the GÅS study include 9.8%, 17.8% and 13.3% at the baseline, 6-year follow-up and 12-year follow-up examinations respectively. The ethnic diversity represented within our study could therefore be considered adequate. Moreover, there was also a fairly balanced sex ratio at all examination phases (approximately, 44% men and 56% women). The randomized study design discourages voluntary participation of study subjects, and the synthesizing of data from multiple sources such as survey interviews, medical examinations, physical function tests and use of medical records could serve as a methodological triangulation in data collection that could in turn contribute to the study validity. In addition, the exclusion of bedridden patients and individuals using a wheel chair would not only ensure a study population that more closely resemble the general population but could also minimize the risk of overestimation of BMI misclassification from measurement errors that could be expectedly higher in this vulnerable group.

Attrition

There were individuals who declined participation in GÅS examination or discontinued from the study and were lost to follow-up. During the baseline examination of GÅS about 40% declined to participate and we have inadequate data on these subjects. Attrition could be due to frailty, non-ambulance, end-stage disease conditions or disinterest. Death and migration are the also reasons for loss to follow-up. This is important to take into consideration in order to avoid selective inclusion of only individuals who are physically and cognitively healthy, in other words to avoid selection bias. In our study, improved assistance was offered in the form of home visits, reminder letters, telephone interviews and possibility to visit us on non-working days that was considered particularly helpful for those who were still employed (age 60-65 years). Such services were aimed to improve participation rate.

The sample population investigated in the birth cohort study (study IV) were subjects from similar age cohorts (60 years, 81 years) but different birth years who participated in the three different waves of GÅS examinations: baseline, 6-year and 12-year follow-up. When comparing the participation rates it is important to distinguish the comparison between subjects who participated in 2001–04 (baseline), 2007–10 (6-year follow-up) and 2013–15 (12-year follow-up) from the comparison between new subjects who participated in the examinations conducted at the three phases. The former is useful to study the rate of attrition of the individuals over 13 years (2001–13). The participation rate decreased from the

6-year follow-up (84%) to the 12-year follow-up (68%), yet was still higher than the baseline (60%). The latter examines the overall participation rate of the general elderly population in the GÅS study. The response rates at the three examinations conducted in year 2001–04 (60%) showed considerable improvement at the examinations conducted in 2007–10 (70%) and 2013–15 (66%). Such rates can therefore be considered relatively good also in comparison with other similar studies [70, 133].

Care was taken in all four studies to address the issue of attrition. There were 1099 participants from GÅS baseline who did not participate in the 6-year follow-up. A comparison between these non-participants and those who took part in study I showed that they were generally older, had lower weight, TST, SST, hip, arm- and calf circumferences indicating central adiposity and muscle loss and greater prevalence of the underlying medical conditions that were studied. The lack of participation of this group may have affected the estimated mean anthropometric reference measures. The inverted U-trend, (initial rise and decline after around 75 years of age) observed with BMI could also be partly due to the loss of subjects with obesity-related medical conditions. However, the adequately large size of our study sample and the comparability of the results with similar studies provide reassurance that the impact of this attrition was less significant.

In Study I, individuals were excluded (n=218) due to missing data on the anthropometric variables. Due to the small proportion (< 5%) of individuals with missing data, who did not differ significantly from the study subjects in terms of socio-demographics variables, we assumed that exclusion of these subjects could not have any appreciable effect on the observed results. No further data imputation was done in this regard.

In Study II, 92 out of 2931 participants (GÅS baseline study) and 490 out of 3360 participants (6-year follow up examination) were excluded because they had missing KH or demispan values respectively. Comparison of the socio-demographic and lifestyle characteristics such as age, sex, marital status, residence, education status, smoking and physical activity of study subjects and excluded individuals showed no significant difference. In terms of BMI, although the excluded individuals had BMI slightly lower than the study participants (26.3 vs 26.8 kg/m²), the values still fell within the same BMI category and could not be considered large enough to create distortions in the classification.

In the survival analysis in study III, the subjects were participants from the GÅS baseline examination (n=2931). The individuals who were excluded due to missing/invalid KH or BMI values were further examined. Among the 145 individuals excluded in the study, 65 subjects did not have KH values (but had BMI), and vice versa among 53 subjects. Based on the available data on their classic BMI, we found that 22.8% were overweight (compared to 43.7% among

study subjects) and 6.9% were obese (compared to 20.6% among study subjects) indicating an adequate representation of overweight and obesity in our study. In addition, we also compared obesity prevalence among our study subjects with the data reported by the Swedish national public health agency estimated among adults within age 65–84 years. It showed that the obesity prevalence was on average 17.1% [74] confirming the satisfactory representation of obese subjects in our studies.

Furthermore, a comparison was done between the study subjects and those who died during this 15-year follow-up period (n=1296). As one would expect, those who died were older (mean age 80.5 years \pm 9.14) than the participants, and died on average 6.6 years (\pm 3.8) after the examination. 17.1% were aged 60–69 years, 21.5% aged 70–79 years, and 61.4% aged \geq 80 years. The sex distribution was fairly even (45.2% men and 54.8 % women). Further analysis on lifestyle factors showed, 14.7% were smokers, 33.1% had ‘mostly sedentary’ form of lifestyle and only 3.7% had lower than elementary education, 42.1% were married, and 57.2% were urban residents. This socio-demographic profile did not differ widely from that of the study participants.

Despite efforts to minimize internal attrition by re-contacting subjects with incomplete data, some of these variables had missing information. This could possibly correspond to those older and very frail individuals, who because of their health status could have had difficulty to co-operate with data collection. Other reason could be that subjects attend some parts of data collection, for example survey interviews and not the medical exams or function tests.

Internal validity and reliability

Regular and periodic internal evaluation of GÅS study is conducted to improve the design, implementation, usefulness and weaknesses of the planned services. The study attempts to involve well-trained and informed multidisciplinary personnel. All anthropometric measurements made in the different studies were done by using established and/or standardized methods, using periodically calibrated measurement tools and adopting validated research protocols that are identical among all the subjects examined. This was to ensure precision and avoid systematic errors as much as possible.

Study design

Studies I, II and IV have a cross-sectional design and the study III is prospective cohort study designed to study time to death. A well-known limitation of cross-

sectional studies is the difficulty determining the time of events, as we observe a snapshot of the disease process in the cross-sectional sample population. This may however not contribute to any etiological inferences [244]. Specific to our studies, the results obtained indicate a possible association between anthropometric changes and weight aberration in older adults, and the extrinsic factors such as birth cohort, socioeconomic and lifestyle factors. To obtain a better understanding of the mechanism behind aging-related body composition changes it is important to conduct prospective cohort study in a large population to observe and measure the changes over time, adjusted for extrinsic factors.

In studies I and II we observed differences in height, weight, and BMI measures between the ‘younger’ (60-69 years) and ‘older’ (over 80 years) age groups. There was also a widening difference between measured height and predicted height with maximum stature underestimation in the oldest group (over 85 years). After examining the birth cohort effect on these measures (in study IV) we could say that the age-related changes pertaining height, weight, and BMI could be more closely attributed to aging related body changes, (e.g. vertebral degeneration) and less affected by birth cohort effects. On the other hand, we found that waist and hip circumferences showed differences between the birth cohort groups.

Data collection

All the readings were made in S.I units with one decimal value. All measurements other than height and body weight were repeated twice and average was noted in each case. In most cases, the same trained personnel performed these repeated measures, but when different persons were involved, care was taken to follow identical estimation method and protocols. No further attempt was made to adjust for inter-observer variability. Bedridden individuals and patients using a wheel chair were excluded from our study due to the difficulties in taking the measurement. Among all other subjects, measurements were made on the left side unless there was previous amputation, paralysis or contracture. Contractures diminish the movement of the joints through its normal range affecting optimal measurement process [245]. The choice of the same side was done to ensure repeatability and reproducibility of results.

Information bias

The central problem in question is the misclassification introduced by errors in height estimates when calculating BMI. In study II, prediction equations formulated were based on height estimates in 60–64-year olds, the youngest among the participants in the study sample. This was done based on the assumption that height estimations could be relatively reliable due to the expected lower prevalence of the height altering conditions and aging-related height loss in comparison with the older age groups.

In study III, the validity of the observed protective effect of higher than normal BMI relies hugely upon the reference group. The relative risk reduction observed could be biased by the elevated mortality risk among underweight included in the reference group [246]. However, in our study, there were only 32 subjects altogether within the underweight category out of which 9 had died during follow-up (total deaths in the reference group were 518). This implies a minimal risk reduction effect. We were conscious of this potential bias and as mentioned earlier, tested it by restricting the reference category only to subjects with normal BMI. We found no significant change in the results confirming that effect observed is not affected by biases in the reference category. The lack of significant results among 60 and 70-year olds might be likely due to lack of a substantial number of deaths and therefore poor statistical power.

The data on mortality used for analyses in study IV was obtained from the National Death registry. We aimed at investigating the BMI and KH-BMI association with all-cause mortality, which could address the problem of competing risks. However, future research could examine potential associations with specific-causes of mortality using existing data in the registry.

Technical issues of measurement

Use of surrogate height estimates and BMI prediction equations need to be validated to facilitate general application [247]. Our only attempt to validate KH based prediction equation was to compare the prevalence and mortality risk of the different BMI categories classified by KH-BMI and classic BMI. This is because based on its other advantages, the latter is established as the ‘standard method’ in anthropometric assessment. Such practice is not rare. Several validation studies involving more advanced assessment methods like BIA have often considered investigating the degree of agreement in relation to BMI and other anthropometrics [77, 240, 248]. Nevertheless, further validation is definitely indispensable.

The survival study IV is still the first to explore the effect of BMI misclassification in relation to mortality risk and the usefulness of KH in the prediction of height cannot be overlooked, particularly with regards to the ease of measurement and minimal need for cooperation from subjects [48, 174]. Other noteworthy strengths of this study that contribute to the validity of the observed results include the follow-up length ≥ 10 years, age and sex stratification, systematic method of measurement of height and weight instead of self-reported measures that are more prone to social desirability bias [107], and accounting for the underlying medical conditions that could have competing risk factors for longevity [141, 249].

Conceptual issues of Diet

The complexity of measuring dietary habits could also have its influence on the results obtained in our study. The diet variable used in this study primarily estimates the frequency of daily complete meal consumption and is a rather uni-dimensional estimation of dietary habits. In other words, the variable may not have captured diet structure in its entirety, taking into account, for example, calorie intake, nutrient content, food quality, portion size etcetera, which are important in relation to malnutrition [105, 250, 251]. The modern food culture has introduced changes in dietary patterns and habits [252]. It is possible that the observed result (decreasing complete meal intake) could be due to a possible misclassification of individuals who selected the option ‘other’ in the questionnaire. It could be practically challenging to including the wide range of non-standard yet complete meals that are currently not included as options in the survey question. Therefore we attempted to address the issue in two ways. Firstly, same questionnaire and identical syntax were used to estimating complete meals among all our study participants to ensure repeatability and reproducibility of results. Secondly, the option ‘other’ was included in the syntax used to estimate complete meals. This means, within every meal (breakfast, lunch or dinner) the choice of option ‘other’ was considered as ‘complete’ in relation to the other options such as ‘only fruit’ or ‘only a drink’ that clearly indicated an incomplete meal. This was to ensure that individuals who consumed one or less complete meal per day were specifically identified. However, this also means that there could be inadequate sensitivity leading to non-representation of those who actually consumed less than one complete meal but were falsely classified into ‘more number of complete meal’ consuming categories.

Confounding

We addressed the role of several potential confounders in relation to anthropometric assessment in older adults taking into account the obesity related factors that could affect body composition. BMI and WC have been investigated in relation to intrinsic changes. However, there could be other possible parameters that need further attention such as (unintentional) weight loss and BMI change over a period of time [97, 113]. A 2009 meta-analysis of the effect of lifestyle-based weight loss on all-cause mortality risk from prospective studies showed the excess risk by 22–39% [113]. Such adverse health effects were also found in relation to any form of weight change within a specified time period, i.e., fluctuations in body weight in the form either gain or loss [211]. A Swedish 15-year follow-up study among the 70-year-old population estimated body weight at baseline examination (age 70), at 5-year (age 75), 10-year (age 80) and 15-year (age 85) follow up. They examined the association between weight changes and risk for mortality during the 5 years and 10 years following age 75 of the

population. Results indicated that during both the time periods, i.e., from age 75 to 80 and from age 75 to 85, there was a higher mortality risk among individuals who lost $\geq 10\%$ of their body weight between age 70 and 75 years compared to individuals who lost 0–4.9% of their initial weight. The relative risk for mortality during the 5 years following risk age 75 was 1.36 for men and 3.53 for women and during the 10 years following risk age 75 was 1.62 for men and 2.15 for women [211].

Furthermore, another Swedish geriatric study on the association between BMI change and mortality hazard found that the mortality risk for the BMI loss group was 65% higher than for the BMI stable group (RR = 1.65, $p < 0.001$) and 53% higher for the BMI gain group than for the BMI stable group (RR = 1.53, $p = 0.001$) [97]. This study however did not take into consideration other underlying medical conditions that could play a role in BMI changes and identify if the weight loss was unintentional or not. The assessment of unintentional weight loss and changes in BMI is therefore considered an important parameter in nutritional assessment and screening tools and we consider to investigate further in association with KH-BMI [113]. The other intrinsic and extrinsic confounders that need further attention include oral health, psychological and social parameters that could play a role in body composition changes and nutritional status [17, 21, 77, 110, 234, 236].

Clinical significance

The process of determining height based on KH or demispan could make it easier to estimate a relatively valid body composition in frail and mobility impaired older adults, thereby reducing potential misclassification, underreporting of underweight and over-reporting of obesity. This is in turn important to ensure appropriate interventions among the different risk groups.

New normative data on sex- and age-specific anthropometrics in an elderly general population are presented. Access to such reference values is important in clinical risk assessment at the group level. It could be used as a monitoring tool among the general elderly population, in other words as a potential health risk indicator in health promotion. Information on the changes in lifestyle habits observed among the latest birth cohort (born 1952–54 or 1932–33) is important to be highlighted and discussed in the clinical setting to impart knowledge and raises awareness of possible future risk groups.

Implications for future research

The implication of the estimation errors that result in distorted disease detection has not been adequately brought to light. Despite the awareness of the issue, the lack of urgent measures to address the problem and revisit the established guidelines is not encouraging. Although epidemiological studies have made progress in a favorable direction a substantial amount of future work still remains.

Validation of KH method

The findings of this thesis suggest that BMI measurement errors have serious consequences in the elderly. KH equations compared with the standard method have shown substantial differences in the estimation of obesity and underweight prevalence and differential association with mortality risk at different ages. This attempt at validation needs to be extended further to determine the sensitivity of the proposed method of using surrogate height measure to estimate BMI. This is important to enhance the reliability and the applicability of the method. Lack of a gold standard anthropometric assessment of body composition could make such validation process difficult. However, it could be acceptable to estimate the correlation and degree of agreement with other widely employed anthropometric and non-anthropometric methods of assessment such as using DEXA, BIA or biomarkers [253].

Robust epidemiological studies

Longitudinal studies with greater sample power are recommended to confirm our results. The role of temporality, vital in the process of body composition change, can be studied best using follow-up studies. This can also be used to investigate the role of residual confounders like weight or BMI change and mortality risk over time. Besides study IV in this thesis, a latest study in Sweden investigating secular trends in weight aberrations was conducted approximately a decade ago and trend updates could facilitate an effective prediction of diseases. Further research on larger samples is recommended to conduct an in-depth investigation of dietary habits in older adults. In this thesis, the effect of diseases like cognitive

impairment, dementia and depression and social factors were addressed. It could be meaningful to examine further the effect of other factors that could potentially influence body composition and nutritional status among older adults, for example, alcohol/substance abuse, social isolation and poverty [11, 17, 21, 77]. Other overlapping domains that interconnect the intrinsic and the extrinsic spheres of risk factors also demand attention. Oral health, masticatory efficiency are some important elements and use of dentures are few that fall in this interlink that have also shown to associated in this nutritional status assessment. Chewing problems are with great likelihood associated with poor health and decreased quality of life [236, 237].

Comprehensive approach in need assessment

The provision of valid, reliable measurement tools can contribute to establishing holistic need-assessment methods. The MNA tool, which is widely accepted today, can be a starting point for applying the corrected anthropometric measures and further research can help in designing appropriate preventive interventions and problem-based health promotion strategies. Until the discontinuing use of classic BMI in older adults, the use of the ‘corrected BMI’ together with the ‘standard’ BMI could be a tool for accuracy check and avoid misclassifications.

Public health implications

There is a global rising trend in the proportion of senior population. The double burden of geriatric under- and overnutrition disorders needs closer attention. This not only affects the both the disability-adjusted (DALY) and quality-adjusted (QALY) life years of the elderly but it also challenges the cost-effectiveness of the public health measures addressing this issue. We are interested in developing a tool that could efficiently evaluate the population nutritional status and justify the design of health promotion strategies and measures. This can be done both at a community level to reduce prevalence of malnutrition and promote healthy lifestyle practices, but also at the policy-making level to formulate evidence-based policies, and establish health guidelines and national framework for the prevention of nutritional diseases and towards healthy aging. An effective multidisciplinary platform that engages political and operative stakeholders aligned to function on these objectives could fulfill the national contribution to the ‘Global strategy and action plan on aging and health (2016-2020)’ [15].

Conclusions

Our study contributes to a holistic approach in anthropometric assessment of body composition in elderly. This is crucial to ensure precise identification of risk groups and designing of optimal and target-specific health interventions. It comprises: 1) A thorough description of age- and gender specific anthropometric profiles of the population in relation to underlying medical conditions. 2) Application of proxy BMI (KH-BMI) to address the problems of misclassification from measurement errors and account for the paradoxical survival benefits of overweight only among the ‘very-old’ elderly and importantly 4) Account on the external confounders of body composition that demonstrated encouraging patterns of general decrease in smoking, higher educational attainment and declining sedentary lifestyle in the ‘younger’ elderly, together with warning signs from men with higher alcohol consumption and women with inadequate exercises among the ‘older’ elderly that calls for more action.

In a nutshell, aging population-specific anthropometric profile created using valid accurate and reliable measures and adjusted for extrinsic influence is the key to effective health assessment. ‘Pan metron ariston’ is an ancient Greek saying, praising symmetry and balance, which can also be literally translated to suggest that totality in measurement has a great value. That said, in the words of Albert Einstein ‘Not everything that can be counted counts and not everything that counts can be counted.’

Summary in Swedish

Bakgrund:

I hela världen växer den åldrande befolkningen. Det finns en större benägenhet att drabbas av sjukdomar och en högre dödlighet bland äldre jämfört med yngre och detta medför en enorm ekonomisk och social börda. Det är etablerat att de ledande dödsorsakerna beror på vaskulära och kroniska sjukdomar. Dessa är i sin tur starkt associerade med nutritionsstatus, och kan i vissa fall förebyggas genom diagnostisering i god tid samt med hjälp av lämpliga livsstilsförändringar. Kroppsmått, eller den medicinska termen antropometri, anses vara en effektiv och accepterad metod som används vid identifiering av riskindivider. Den syftar till att indirekt uppskatta andelen fett och muskelmassa hos en individ. Body mass index (BMI), ett kvotmått mellan kroppslängd och vikt, är den mest använda metoden i uppskattning av kroppssammansättning. Det pågår en diskussion kring styrkor och svagheter av BMI men fortsatt bred användning av BMI tyder på att fördelarna överväger bristerna. BMI används vanligtvis att mäta kroppsfetma kan BMI kan dela in befolkningen i underviktig, normalviktig, övervikt, fetma utifrån deras BMI värde. Det verkar dock saknas medvetenhet kring konsekvenserna när BMI tillämpas på äldre.

Hos äldre är kan längdmåttet underskattas framförallt på grund av ökad framåtböjning av överkroppen. Felaktig uppskattning av kroppslängd kan i sin tur ge upphov till fel i BMI och klassificering av de avvikande kategorierna, dvs., undervikt, övervikt och fetma. Detta kan leda till att sjukdomsförebyggande och hälso-främjande insatser riktas fel.

BMI anses som en utmärkt markör för kroppens totala fetma (overall obesity). Måttet har dock en begränsning i att uppskatta bukfetma på ett korrekt sätt. Omfördelning av fetma är ett vanligt fynd hos äldre. Därför bör undersökning av bukfetma ske genom att mäta midjemått, som kan vara ett viktigt komplement med information gällande status av kroppssammansättning. Dessutom skulle bestämning av kroppssammansättning påverkas av med endogena (inre) och exogena (yttre) faktorer. Till exempel, underliggande medicinska tillstånd, livsstil och sociodemografiska förhållanden. Därför rekommenderas ett holistiskt tillvägagångssätt som omfattar en giltig och noggrann metod för bedömning som tar hänsyn till den potentiella sammanblandningen av orsaksfaktorer (confounding)

Målsättning och metod

Det övergripande syftet med denna avhandling är att identifiera och ta itu med de metodfrågor som finns i kroppsmätningar hos äldre. All data som används i denna avhandling har tagits från den longitudinella nationellt representativa populationsstudien ”Gott åldrande i Skåne” med individer mellan 60 och 99 år.

Resultat

Studie I presenterade kön- och åldersspecifika normativa kroppsmått data för svenska äldre. Påverkan av bakomliggande medicinska tillstånd på kroppssammansättningen undersöktes genom jämförelse av kroppsmåttprofilen hos deltagarna. Referensdata visade en åldersrelaterad längd- och viktörlust hos båda könen. I genomsnitt var BMI 27,5 kg/m² och 27.2 kg/m² hos män respektive kvinnor. Resultaten bekräftar förhållandet mellan fetma och kardiovaskulära sjukdomar där det visade sig att patienter med kardiovaskulära sjukdomar har högre värden på BMI, vikt, midjemått jämfört med deltagare utan dessa sjukdomar. Högre BMI, midje- och höft omkrets samt hudtjocklek på överarmens baksida observerades hos äldre personer beroende av hjälp i aktiviteter i dagliga livet (ADL), och detta indikerar att otillräcklig fysisk träning leder till förlust av muskelmassa, ansamling av fett och viktökning.

Studie II undersökte tillförlitligheten hos klassiska BMI för äldre vuxna och demonstrerade åldersrelaterad felklassificering av undervikt och fetma som berodde på felaktig mätning av kroppslängd. Åldersjusterade, könsspecifika BMI-prediktionsekvationer formulerades baserade på knähöjd och halvarmspannvidd. En betydande underskattning av undervikt och överskattning av fetma observerades, särskilt bland vuxna över 80 år. Vi jämförde beräkning av undervikt- och fetma prevalens med hjälp av BMI baserat på knähöjd och halvarmsvidden. Det visade att underviktsprevalensen, beräknad med knähöjdbaserat BMI hos kvinnor i åldern 85+ år var 21 % jämfört med 11,3% beräknad med det klassiska måttet på BMI. Likaså fetmaprevalensen var betydligt överskattad med den klassiska BMI-metoden (10,4%) jämfört med knähöjdsbaserad mätning av BMI (3,7 %). Halvarmspannvidd -baserat BMI visade liknande skillnader som BMI baserat på knähöjd främst för individer över 85 år. För de yngre åldersgrupperna fanns en liten eller ingen skillnad. Denna oroväckande grad av felklassificering tillskrivs felaktig längduppskattning och kan påverka optimal hantering av patienter som faktiskt har en ökad risk.

Studie III är en uppföljande studie som ytterligare undersökte överlevnadskonsekvenser av BMI baserat på knähöjd jämfört med klassisk BMI-mätning. Knähöjdsbaserat BMI visade att det finns en skyddande effekt för de

överviktiga mot risk för död speciellt bland 80 åriga och äldre män och kvinnor. Detta är viktig information innan man planerar viktförändringsåtgärder hos äldre.

Studie IV beskriver samband mellan midjemått och livsstilsfaktorer som fysisk aktivitet, kost, rök- och alkoholvanor bland 60 och 81 åringar som föddes under tre olika födelseår (60år: 1941–42, 1947–47, 1952–54 samt 81 åringar: 1920–21, 1926–28 och 1932–33) och de respektive åren när undersökningarna gjordes var 2001, 2007 och 2013. Våra resultat visade att midjemåttet var större i den senaste kohorten i båda undersökta åldersgrupper (60-åringar och 81-åringar). Ökning av bukfetma mellan år 2001 och 2013 verkade vara relaterad till högre utbildningsnivå och fysisk inaktivitet. Frekvensen av dagliga, kompletta måltider minskade bland deltagarna under samma period. Komplettmåltidsfrekvensen hade dock inget säkerställt samband med förändringen av bukfetma- prevalensen.

Slutsatser

Noggrann bedömning av kroppssammansättningen är avgörande för att säkerställa korrekt identifiering av individer med ökad risk och insättande av hälsofrämjande insatser hos äldre vuxna. Detta skulle kunna göras med hjälp av en omfattande bedömningsmetod som kan inkludera följande:

En grundlig genomgång av åldersrelaterade kroppsmått specifikt till den befolkningen som den riktar sig mot. Detta ska ta hänsyn till bakomliggande sjukdomar och funktionsnedsättningar

Användning av ett tillförlitligt BMI mått som baseras exempelvis på knähöjd som förändras betydligt mindre med åldrande. På så visset kan man i högre utsträckning kunna klassificera individer mer korrekt än det klassiska BMI-måttet. Därmed minskar man risken för att missa hitta de undernärda och undvika fånga upp de överviktiga som obesa.

Det är också viktigt att vidare mäta midjemåttet och att alltid tänka på de andra riskfaktorerna som befolkningen är utsatt för dvs., livsstilsrelaterade riskfaktorer såsom rökning, alkohol, stillasittande, den sociala miljön, utbildning som indirekt kan påverka kroppssammansättning och orsaka ohälsa.

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Nivetha Natarajan Gavriilidou is a dental practitioner with master's degree in public health. This dissertation is a product of her active participation in epidemiological research on anthropometrics and body composition changes in older adults. Her involvement in the Swedish longitudinal population study, Good Aging in Skåne has resulted in scientific articles that focus on measurement issues specific to the elderly population, leading to inaccuracy in body mass index. She has investigated the use of knee height to address this issue.



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