CHAPTER 1

General introduction

The aging population

Life expectancy has risen remarkably over the last century in most developed countries. An almost linear lengthening of life span with a steady pace of almost three months per year in women and a little over two months in men has been reported since 1840 (1). The trend started off by saving the young until the 1950's and continued by an increased life expectancy at age 65 and later on at age 80. Over the last decades, the increase in life expectancy at birth is, apart from the increase of the proportion of people reaching old age, mostly caused by the fact that old age is prolonged in developed countries (2). Among persons aged 65 years and older, the proportion of the oldest old is growing. In many populations, the absolute number of persons aged 65 years and over has thus increased rapidly. In the Netherlands for example, more than 2.5 million persons were aged over 65 years in 2010, of whom about 650,000 persons were aged over 80 years. These numbers have increased with approximately 400,000 and 150,000 over the last ten years (3).

Obesity in the aging population

A worldwide increase of the prevalence of overweight and obesity has taken place over the last decades (4, 5). Overweight and obesity are mostly assessed by the Body Mass Index (BMI), the body weight (kg) divided by body height (m) squared. A BMI of ≥25-30 kg/m^2 is considered overweight and a BMI of ≥30 kg/m^2 is considered obese. The prevalence of overweight and obesity has increased in all age groups, including older persons. Currently, the prevalence of overweight and obesity is highest among persons aged around 60-70 years in most countries (6). In the Netherlands for example, the prevalence of overweight and obesity in persons aged over 65 years has risen from 54.9% to 56.7% over the last ten years based on self-reported data on weight and height. In persons aged 75 years and over, the percentages are somewhat lower, but the increase is steeper, from 48.3% to 51.6%. Relatively more overweight older persons are obese as compared to ten years earlier, so also within the overweight population the severity of overweight has increased (3). In participants of the Longitudinal Aging Study Amsterdam (LASA) aged 55-65 years, the prevalence of obesity based on measured weight and height in women rose from 20.5% to 27.5% between 1992

and 2002. In men, there was an even more striking increase from 9.5% to 18.4% (7). The high and still increasing prevalence of obesity in a vastly growing older population causes an enormous raise in the absolute numbers of overweight and obese older adults.

The prevalence of overweight in younger populations is rising as well. Recent generations develop overweight at younger ages and most people tend to gain weight over their life span (8-10). Children and adolescents who are obese, have a higher risk of becoming an obese adult (11, 12). As a result, the prevalence of overweight and obesity in old age is expected to keep rising the upcoming decades. Moreover, future generations will have experienced greater cumulative exposure to excess weight when they reach old age (10).

Definition of obesity using anthropometry

Obesity is a disease in which an excess of body fat causes an increased risk for adverse health effects (4). A positive energy balance, caused by dietary intake of energy exceeding the energy expenditure, results in storage of the excess of energy in the body, mostly as fat mass. For practical reasons, obesity is usually assessed by indirect anthropometric measures. By use of anthropometric indicators individuals at risk are identified, selection of individuals for/in need of interventions takes place, and the effect of changing conditions or interventions is evaluated.

The most commonly used anthropometric measures are body mass index (BMI) and waist circumference. Adolphe Quetelet was the first to describe a ratio of weight adjusted by height squared in 1832. The term BMI was introduced by Keys et al. (13) in 1972. They concluded that the ratio best indicated adiposity because of its high correlation to weight in combination with its low correlation with height and its sensitivity to differences in weight. The cut-off values of BMI are the same for men and women and were based on the shape of the association between BMI and mortality. The cut-off values for under weight normal weight, overweight and obesity, which are displayed in Table 1, are adopted in the World Health Organization (WHO) guidelines since 1995 (14). Waist circumference is a measure of abdominal obesity as is the waist-hip ratio, which denotes the circumference of the waist relative to the circumference of the hip. Cut-off values

for high risk waist circumference were proposed by Lean et al. (15) in order to correctly classify those with a high BMI and/or waist-hip ratio in adult populations. Two different action levels were proposed for men and women separately (Table 1). Action level I was formulated to be a warning to avoid further weight gain while persons in action level II should be urged to lose weight. The WHO included both the cut-off values of BMI and waist circumference in their current guidelines and states that they are applicable in adults aged ≤70 years (16).

Table 1. Categories of BMI and waist circumference according to the WHO guidelines.

Risk categories	BMI	
	Men and women	
Underweight	≤ 18.5 kg/m^2	
Normal weight	≥ 18.5 - < 25 kg/m^2	
Overweight	≥ 25 - < 30 kg/m^2	
Obesity	≥ 30 kg/m^2	
	Waist circumference	
	Men	Women
Healthy waist	< 94 cm	< 80 cm
Action level I	≥ 94 - < 102 cm	≥ 80 - < 88 cm
Action level II	≥ 102 cm	≥ 88 cm

Limitations of current definition of overweight in older adults

With aging, the body composition changes. A (relative) loss of lean mass occurs and the distribution of fat over the body changes. At a given BMI an older adult has a higher body fat percentage as compared to younger adults (17, 18). Fat mass is increasingly stored around the organs and inside organs (visceral and

ectopic fat) and inside muscles (ectopic fat). As body fat redistributes to a more central fat distribution, subcutaneous fat on the extremities redistributes to visceral and ectopic fat (Figure 1) (17, 19, 20), causing a higher waist circumference relative to BMI in older as compared to younger adults (21). Moreover, an age-related height loss takes place which causes the BMI to increase with aging when weight remains stable (22-24). Because of these processes, anthropometric measures should be interpreted with caution in older adults. The measures might relate differently to health in older adults as compared to younger adult populations and cut-off values of anthropometric measures for the identification of overweight might shift.

Figure 1. Age-related redistribution of fat.
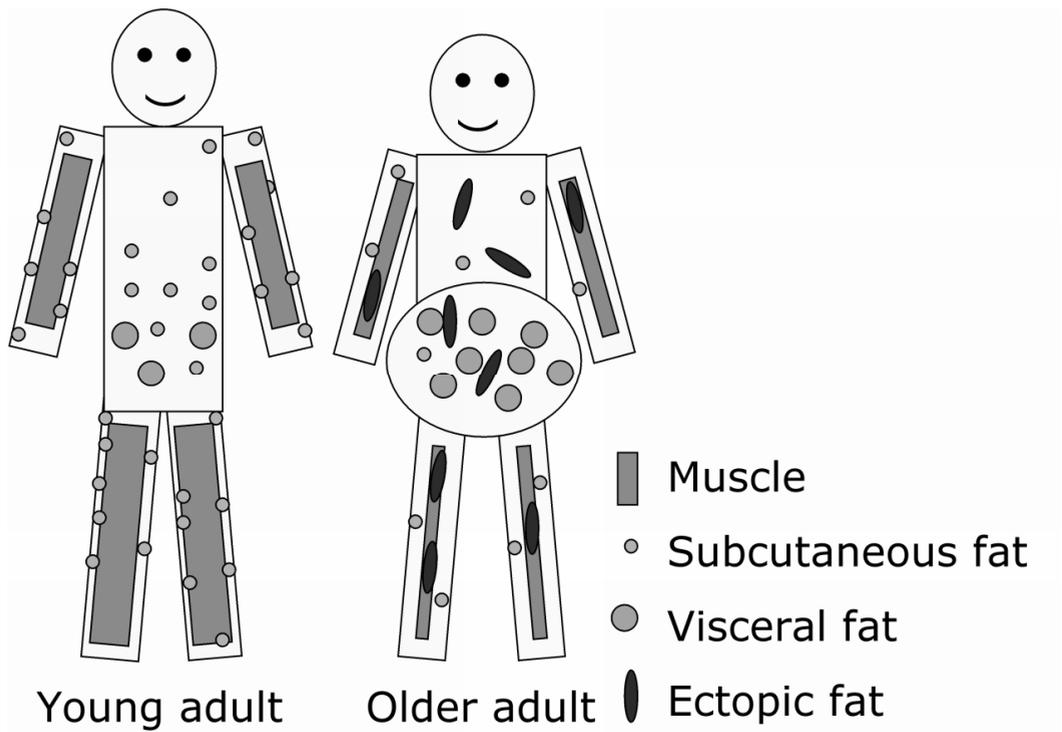
Consequences of overweight and obesity in old age

Research into the health consequences of obesity has been mostly performed in (young) adult populations. In addition, it focused mainly on mortality, cardiovascular diseases and cardiovascular risk factors like diabetes and hypertension. Overweight and obesity and its consequences do not develop over night; it takes quite some years before they emerge in clinical practice. Older persons have a lifetime of influences behind them and it might make quite a difference whether they developed overweight recently or already during childhood or adolescence.

The strength of the association of overweight and obesity with mortality declines in older adults as compared to (younger) adults and most findings suggest that mortality risks start to rise at relatively higher levels of overweight (25-30). As compared to the association with BMI, the association between waist circumference and mortality seems somewhat stronger in old age. Several reasons for the declining strength of the association between obesity and mortality with age have been suggested (26, 31). First, a survival effect could cause persons susceptible for the adverse effects of obesity to die prior to old age. Furthermore, the relative importance of a healthy BMI and waist circumference decreases because older adults have a higher (competing) risk to die from other causes. Also, obesity-related mortality risk increases over the years after the onset of obesity and the limited life span left in old age in which obesity-related health consequences can develop might play a role. Finally, a relative increasing importance of body mass (both lean and fat) as a reserve in periods of illness and confounding influences of smoking and weight loss are mentioned.

A trend of decreasing obesity-related mortality has been reported, while an increase in the association between obesity and disability is seen (32). Persons with obesity live longer with disease and disability, which is likely to increase health care costs (33, 34) and decrease quality of life (35, 36). Besides mortality and cardiovascular abnormalities, research on the consequences of obesity in old age has focused on functional measures and health outcomes affecting quality of life. Obesity is associated with an acceleration of age-related declines in health and function. Because of age-related losses in muscle mass and muscle strength, older adults are particularly susceptible for the negative consequences of overweight and obesity on physical function (37-39).

Several metabolic abnormalities, like glucose intolerance and hypertension, are independently associated both with aging and with (abdominal) obesity (40, 41). Arthritis is a highly prevalent condition in old age, which is also strongly associated with overweight and obesity (42). Especially, but not exclusively, the association with knee osteoarthritis is strong, probably because of the mechanical strain on the weight-bearing joints (43). Furthermore, the prevalence of incontinence increases with age, predominantly in women. The independent association of obesity with this age-related condition has been reported repeatedly (44, 45). These obesity-related health problems have all been related to a decreased quality of life in older adults (46). Apart from the indirect detrimental effect of overweight and obesity on quality of life through the increased risk for chronic disease and functional limitations, a direct effect has been described. A strong negative association between BMI and quality of life has been described in older adults (47, 48), which was particularly strong in the physical domains. The association is partly mediated by chronic diseases and age-related losses in function, but remains existent after adjustment.

Objectives

The general aim of this thesis is to add to the limited knowledge on the assessment and consequences of obesity in old age. By carefully describing its association with important health outcomes in large samples of older adults we aim to gain the insight in the consequences of obesity in old age. Furthermore, we describe the execution of advanced analyses to establish criteria for high risk waist circumference in old age which are currently lacking.

Epidemiology

The results described in this thesis were obtained using data from large, prospective cohort studies on aging. By use of these observational data, we describe obesity measures and their health consequences. In this way, the natural course of the (development of) consequences of obesity can be described. Using population based data, the results of the study have a high potential to be generalizable to the general older population. In all chapters, data from the Longitudinal Aging Study Amsterdam (LASA) were used (49, 50, 51). LASA is an

ongoing multidisciplinary study in which a representative sample of Dutch older adults is included. In Chapter 6, data from three other prospective cohort studies on aging were used; the Invecchiare in Chianti (InCHIANTI) study, the Age Gene/Environment Susceptibility—Reykjavik Study (AGES-Reykjavik) and the Health, Aging and Body Composition Study (Health ABC). In Table 2, an outline of the data used in each chapter of this thesis can be found as well as some of the studies' characteristics.

Table 2. Data of cohort studies used in each chapter.

Chapter	Study	Years of assessment	Number of participants	Inclusion criteria	Outcomes
2	LASA	2001-2002 2005-2006	899 770	Participants aged 55-65 at baseline Complete data on overweight history and functional limitations	Functional limitations
3	LASA	1992-1993 1995-1996 1998-1999	2,000 1,478 1,271	Presence of data on pain, BMI and waist circumference	Pain
4	LASA	1995-1996	1,049	Age ≥ 70 years Complete data on self-reported mobility limitations, BMI and waist circumference	Mobility limitations
5	LASA	1992-1993 1995-1996 1998-1999 2001-2002 2005-2006	1,219 1,062 1,034 868 813	Age ≥ 70 years Complete data on waist circumference	Pain Mobility limitations Urinary incontinence Knee osteoarthritis Quality of life Cardiovascular disease Diabetes
6	Health ABC InCHIANTI AGES-Reykjavik LASA	2002-2003 1998-2000 2002-2006 1992-1993	1,310 673 5,117 1,204	Age ≥ 70 years Complete data on waist circumference Waist circumference >70 cm (women) or >80 cm (men)	Pain Mobility limitations Urinary incontinence Knee osteoarthritis Cardiovascular disease Diabetes

Outline of this thesis

In Chapter 2, we describe the possible cumulative impact of obesity over the life course on mobility limitations in late middle-age. In Chapter 3, the associations of both BMI and waist circumference with (the development of) pain are described. In Chapter 4, we use several methodological approaches in order to find the optimal method to identify an appropriate cut-off value of waist circumference for older adults aged ≥70 years. This optimal method is applied in the study described in Chapter 5, in which we develop potential cut-off values for waist circumference using a broad range of important health outcomes related to obesity. These new cut-off values are cross-validated using data of four different cohort studies from four different countries in Chapter 6. In Chapter 7, the results of the individual chapters are put into context; we discuss the over-all findings of this thesis and elaborate on their implications.

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